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Neck Circumference has Possibility as a Predictor for Metabolic Syndrome in Postmenopausal Women

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ABSTRACT

Subcutaneous fat depots play an important role in regulating metabolic profile in Japanese postmenopausal women. We investigated the possibility of neck circumference (NC) as a surrogate marker for metabolic disease risk estimates in Japanese postmenopausal women. We examined the association of NC with several markers of insulin resistance, lipid metabolism and atherosclerosis in 64 healthy postmenopausal women aged 63.6 ± 7.1 years in community-based samples in Japan. As a result, NC was significantly associated with indices of whole body obesity and visceral fat accumulation, such as body mass index (BMI) and waist circumference (WC). In the analysis of biomarkers for insulin resistance, NC was positively correlated to HbA1c, homeostasis model assessment ratio (HOMA-R) and leptin. In addition, an increase in triglycerides (TG) and a decrease in HDL-cholesterol (HDL-C) were also associated with NC. Interestingly, NC was also associated with atherosclerosis-related indices. The measurement of NC is an easy, inexpensive and reproducible method for assessment of obesity, and a possible predictor to identify the risk for future metabolic diseases in Japanese postmenopausal women.

Key words: *Neck circumference, Obesity, Metabolic abnormality, BaPWV*

The assessment and management of obesity are important clinical practices for health promotion. Many studies suggest NC could be used to supplement the BMI[1-6, 9-16]. Recent clinical studies reported the significant role of subcutaneous and ectopic adipose tissues, such as pericardial and muscular fat depots, on the initiation and progression of metabolic disorders, beyond and above excess visceral fat depot[5, 8, 16]. NC is a screening measure for identifying USA children (aged 6 to 18 years) with high BMI[9, 10, 12]. Optimal NC cutoff indicative of high BMI in boys (aged 6 to 18 years) ranged from 28.5 to 39.0 cm. Corresponding values in girls (aged 6 to 18 years) ranged from 27.0 to 34.6 cm. NC is a potentially useful initial screening tool for overweight/obesity in Pakistan[1-5]. A NC > or = 35.5 cm in men and > or = 32 cm in women should be considered the cutoff point for overweight/obesity in Pakistan. It has been shown that NC >37 cm in men and NC >34 cm in women are probably the best cutoff points to determine Chinese subjects with central obesity[5, 8, 12-16]. NC >36 cm in diabetics and >37 cm in non-diabetics was the best cutoff value to determine Indian subjects with central obesity[1-5, 8, 16]. NC is correlated with triglycerides and inversely related with HDL cholesterol beyond BMI and WC in Greece[5, 8, 12-16]. NC is a good predictor of raised insulin and free androgen index in obese premenopausal Australian women[1-4, 9, 10, 12]. NC is a bedside clinical feature related to mortality of acute ischemic stroke in Brazil[4, 9-14]. The role of NC in obesity-related risk estimates in Japanese postmenopausal women is still not clear. Therefore, the aim of this study was to clarify the association of NC with metabolic-related factors as well as other traditional anthropometric measures in community-based Japanese postmenopausal women.

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MATERIALS AND METHODS

Study population

Participants were 64 generally healthy postmenopausal women aged 63.6 ± 7.1 years, who were recruited from the local community, Mihara city, in Japan. These participants were free of clinically chronic disease including cardiovascular disease, diabetes, and hypertriglyceridemia, and of medication use such as estrogen replacement therapy and diuretics. Written informed consent was obtained from all participants and the study protocol was approved by the local ethical committee.

Anthropometric measurements

Height, body weight, BMI, body fat percentage, WC and NC were evaluated in all participants as anthropometric measurements. Height without shoes was measured to the nearest 1 mm using a stadiometer and the head held in a Frankfurt horizontal plane, and weight without outer wear and shoes was assessed to the nearest 0.1 kg using a digital scale. BMI was calculated as weight divided by height squared (kg/m^2). Body fat percentage was determined by bioelectrical impedance analysis using a body fat meter. Both WC and NC were measured to the nearest 1 mm using a flexible tape measure. WC was measured at the level of the umbilicus in a standing position. NC was measured in a seated position at the level of the mid-neck, positioned just below the laryngeal prominence and spinous process of the 7th cervical vertebra, which could be easily palpated.

Laboratory assessments

After an overnight fast, a blood sample was collected from each participant for the measurement of biochemical parameters which relate to metabolic disorder. Serum TG, total-cholesterol, HDL-C and leptin were evaluated. LDL-C was estimated by Friedewald's formula; therefore participants with TG≥400 mg/dl were excluded from analysis. HbA1c (National Glycohemoglobin Standardization Program) and HOMA-R, calculated as fasting plasma glucose (mmol/liter) × fasting immunoreactive insulin (μU/ml)/405, were investigated for analysis of glucose metabolism. Biochemical measurement was performed by FML Inc. (Fukuyama, Japan).

Measurements of blood pressure, brachial-ankle pulse wave velocity (baPWV)

Every participant was rested in a supine position for at least 5 min in a quiet room before measuring the blood pressure and baPWV. Blood pressure was measured from both brachial arteries by a digital sphygmomanometer. The baPWV was measured using a volume-plethysmographic system (Form/ABI; Colin Co. Ltd, Japan) according to the manufacturer's protocol. The average of bilateral recordings of baPWV was used for analysis.

Statistical analysis

All values are expressed as mean ± SD. Anthropometric measurements, including NC, WC and BMI, were normally distributed. Data for total cholesterol, TG, HbA1c, HOMA-R and leptin levels were transformed using log base 10 to normalize their distributions. Student's t-test was applied to assess the reliability of the results. Associations among the anthropometric measurements and between the laboratory data and the anthropometric measurements were assessed using a Pearson's correlation coefficient. Statistical analysis was performed by SPSS 20.0 (SPSS Inc., IL), and $p<0.05$ was considered significant.

RESULTS

The characteristics of the 64 participants in this study are presented in Table 1. As all the subjects were Japanese postmenopausal women in the local community and non-smokers, they had similar lifestyles and backgrounds. Amongst these participants, 11 subjects exhibited 90 cm or higher in WC.

Table 1. Clinical characteristics of study participants

	Mean ± SD (n = 64)
Age (years)	63.6 ± 7.1
Height (cm)	153.0 ± 4.8
Weight (kg)	51.5 ± 7.1
BMI	22.0 ± 3.1
Body fat percentage (%)	33.4 ± 6.3
Waist circumference (cm)	80.9 ± 8.9
Neck circumference (cm)	33.0 ± 1.6
SBP (mmHg)	126.5 ± 18.8
Triglycerides (mg/dl)	105.7 ± 48.7
Total cholesterol (mg/dl)	217.3 ± 27.2
LDL-cholesterol (mg/dl)	123.1 ± 26.8
HDL-cholesterol (mg/dl)	76.0 ± 18.1
Leptin (ng/ml)	8.2 ± 6.9
HbA1c (%)	5.1 ± 0.4
HOMA-R	2.2 ± 2.4

BMI: body mass index, SBP: systolic blood pressure

Correlations among measures of fat depots

To clarify the participation of NC in adiposity, we first investigated the correlations among the

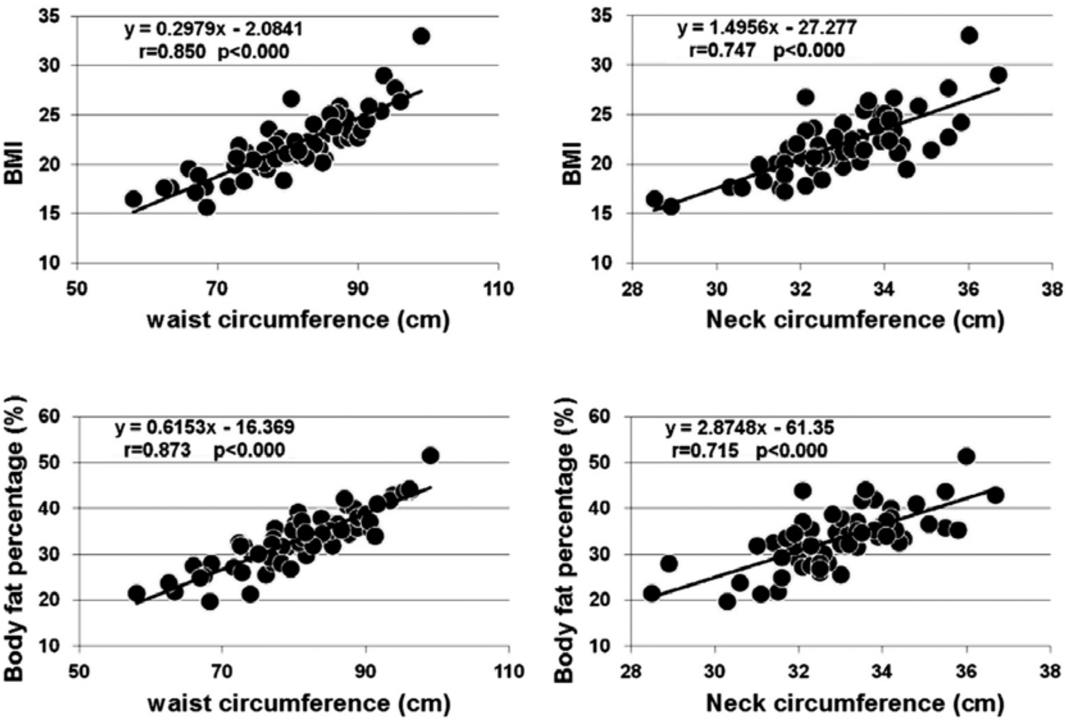

Fig. 1. Associations of neck circumference and waist circumference with BMI and body fat percentage.
NC and WC were positively correlated with BMI and body fat percentage.
BMI: body mass index

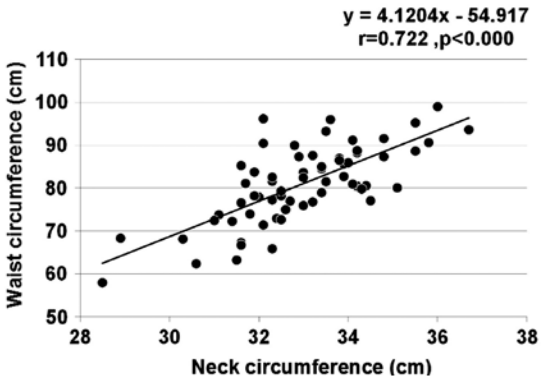

Fig. 2. Association of neck circumference with waist circumference.

Neck circumference was positively correlated with waist circumference.

Table 2. Associations of neck circumference and waist circumference with metabolic variables

	WC		NC	
	Correlation (r)	p value	Correlation (r)	p value
Log Triglycerides	0.248	ns	0.276	0.028
Log Total-cholesterol	−0.095	ns	−0.087	ns
HDL-cholesterol (mg/dl)	−0.385	0.002	−0.401	<0.001
LDL- cholesterol (mg/dl)	0.083	ns	0.114	ns
Log Leptin	0.544	<0.001	0.488	<0.001
Log HbA1c	0.355	0.005	0.298	0.019
Log HOMA-R	0.241	ns	0.263	0.039

WC: waist circumference, NC: neck circumference, ns: not significant

obesity related-anthropometric measurements. NC and WC were significantly associated with anthropometric markers of whole body adiposity; BMI (NC, r = 0.747, p<0.0001; WC, r = 0.850, p<0.0001) and body fat percentage (NC, r = 0.715, p<0.0001; WC, r = 0.873, p<0.0001) (Fig. 1). Importantly, NC was also associated with WC (r = 0.722, p<0.0001; Fig. 2) that reflects visceral fat accumulation. These observations indicated that an increase in NC was strongly correlated to elevation of central and whole body fat accumulations.

Correlations of measures of fat depots with metabolic traits

Next, we examined laboratory data related to metabolic profile, and investigated the association of these data with anthropometric markers of

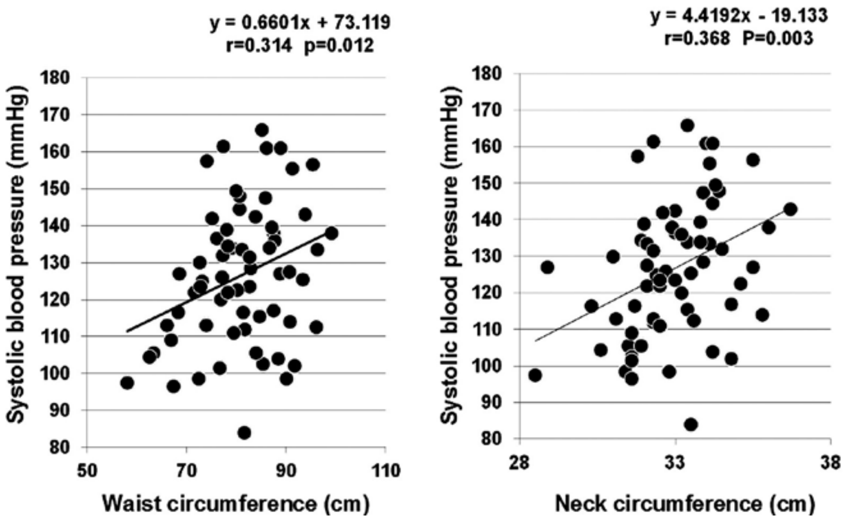

Fig. 3. Associations of waist circumference and neck circumference with systolic blood pressure.

Systolic blood pressure was associated with WC (r = 0.314, p = 0.012) and NC (r = 0.368, p = 0.003). Data were assessed using a Pearson's correlation coefficient.
p<0.05 was considered significant.

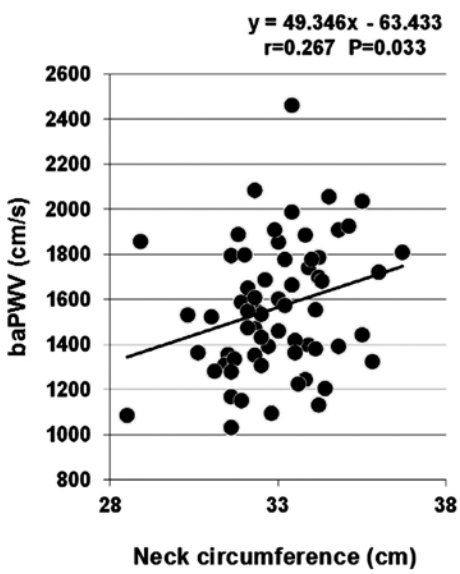

Fig. 4. Associations of neck circumference with baPWV.

NC was significantly correlated with baPWV (r = 0.267, p = 0.033). Data were assessed using a Pearson's correlation coefficient.
p<0.05 was considered significant.

obesity (Table 2). The measurement of lipid parameters demonstrated that NC contributed to both an increase in TG (r = 0.276, p = 0.028) and a decrease in HDL-C (r= –0.401, p<0.001). Total cholesterol and LDL-cholesterol were not correlated to either NC or WC. In assessment of biomarkers of glucose metabolism, HOMA-R was associated with NC (r = 0.263, p = 0.039), while both NC and WC were correlated with HbA1c (NC, r = 0.298, p = 0.019; WC, r = 0.355, p = 0.005) and leptin (NC, r = 0.488, p<0.001; WC, r = 0.544, p<0.001).

Correlations of measures of fat depots with atherosclerosis-related factors

Finally, we investigated the association of NC with atherosclerosis-related factors. Systolic blood pressure was associated with WC (r = 0.314, p = 0.012) and NC (r = 0.368, p = 0.003) (Fig. 3). Interestingly, NC was significantly correlated with baPWV (r = 0.267, p = 0.033)(Fig. 4). Therefore, NC was associated with the atherosclerosis-related factor, baPWV.

DISCUSSION

In this study, we examined correlations of NC with metabolic risk factors in community-based postmenopausal women in Japan, and demonstrated that NC was positively associated with obesity-related risk factors including atherosclerosis-related factor, baPWV. These observations suggest that NC is a possible predictor to identify the risk for future metabolic disease in Japanese postmenopausal women.

The role of subcutaneous and ectopic adipose tissue on metabolic abnormality has received considerable attention in recent clinical studies. It has been reported that lower body subcutaneous fat mediates beneficial effects on metabolic profile associated with triglyceride storage, while abdominal subcutaneous fat stimulates metabolic abnormality[1-7, 13, 14]. Based on these findings, we focused on neck fat depot as specific upper body adiposity, and measured NC for assessment of its accumulation. As a result, the present data demonstrated that an increase in NC was associated with several metabolic risk factors, including parameters of insulin resistance (leptin, HbA1c and HOMA-R) and cholesterol profile (TG and HDL-C). The association of neck fat accumulation with insulin resistance or cholesterol profile has been investigated in some clinical studies. The assessment of neck fat depot via measurement of CT scan demonstrated that larger NC correlates with these metabolic abnormalities[5, 8, 13-16]. In addition to insulin resistance and lipid metabolism, our data suggested the possibility of using NC for predicting the early stage of atherosclerotic changes. Systolic blood pressure was associated with NC, WC and BMI. NC was also associated with the atherosclerosis-related factor, baPWV. As elevated baPWV is associated with vascular dysfunction and structural deterioration, baPWV is thought to increase its values before intimal thickening of the carotid artery[10-16].

The precise biological mechanisms of neck adipose tissue on metabolic abnormality are not fully understood. A large part of the increase in NC is thought to reflect whole body obesity. Indeed, it has been reported that a positive correlation of NC with visceral fat accumulation was found using CT and MRI assessment[5-15]. In this study, the biological parameters of insulin resistance and lipid metabolism were associated with WC and BMI, as well as NC. Therefore, we thought that these parameters were affected by whole body or visceral adiposity, because neck adiposity is a small fat accumulation. However, the neck region has a unique anatomical characteristic and metabolic profile. A specificity of neck fat depot is the presence of brown adipose tissue. In adults, this adipose tissue is predominantly located in the neck and supraclavicular regions and plays an important role in energy homeostasis[5-15]. Although brown adiposities can uptake glucose and produce heat rather than store energy, the activity of brown adiposities is significantly lower in individuals with overweight or obesity[5-15]. In addition, the neck region includes two perivascular fat depots surrounding bilateral carotid vessels in a relatively small area. These fat depots are recognized as an ectopic fat, which can secrete various adipokines, such as leptin, adiponectin, and IL-6, leading to stimulation of metabolic abnormality[1-7].

For clinical screening to identify metabolic syndrome in postmenopausal women, NC has an advantage. The measurement of WC is influenced by postprandial and respiratory abdominal expansion, and clothes should be removed for accurate measurement of WC or hip circumference. In contrast, the value of NC is not affected by these physiological and environmental problems. Therefore, the measurement of NC exhibits high reproducibility with a simple procedure and short measurement time, resulting in its suitability for detecting the risk of metabolic disease in large populations.

In conclusion, the measurement of NC is an easy, inexpensive and reproducible method, and could be used to identify individuals with a higher risk of developing obesity-related atherosclerosis among Japanese postmenopausal women.

Study limitations

In this study we could not clarify the mechanism of neck fat depot in the process of atherosclerosis in Japanese postmenopausal women. These specificities of neck fat depot might lead to further facilitation to metabolic abnormality. Further investigation will be necessary to clarify the role of neck fat depot in the process of atherosclerosis and cardiovascular disease in Japanese postmenopausal women, and to confirm that our conclusions are equally applicable to men and young women.

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