



# Upper-normal waist circumference is a risk marker for metabolic syndrome in normal-weight subjects



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## KEYWORDS

Waist circumference;  
Metabolic syndrome;  
Prediabetes;  
Dyslipidemia;  
Body mass index

**Abstract** *Background and aims:* To elucidate implication of upper-normal waist circumference (WC), we examined whether the normal range of WC still represents a risk of metabolic syndrome (MetS) or non-adipose MetS components among normal-weight subjects.

*Methods and results:* A total of 173,510 persons (100,386 men and 73,124 women) with normal WC (<90/80 cm in men/women) and body mass index (BMI) of 18.5–24.9 were included. Subjects were categorized as having low, moderate, and upper-normal WC for those with WC < 80, 80–84, and 85–89 cm in men and <70, 70–74, and 75–79 cm in women, respectively. The prevalence of all the non-adipose MetS components (e.g. prediabetes and borderline dyslipidemia) was significantly higher in subjects with upper-normal WC on comparison with those with low WC. Overall, the prevalence of MetS (having three or more of four non-adipose MetS components) gradually increased with increasing WC (12%, 21%, and 27% in men and 11%, 14%, and 19% in women for low, moderate, and upper-normal WC, respectively). Moreover, the risk of having a greater number of MetS components increased in subjects with upper-normal WC compared with those with low WC (odds ratios for the number of one, two, three, and four MetS components: 1.29, 1.81, 2.53, and 2.47 in men and 1.16, 1.55, 1.49, and 2.20 in women, respectively).

*Conclusion:* Upper-normal WC represents a risk for acquiring a greater number of MetS components and the early stage of MetS components (prediabetes and borderline dyslipidemia), after adjusting for BMI, in a large general population with normal WC and BMI.

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## Introduction

Obesity poses a major clinical and public health challenge [1] because of the elevated risks of metabolic syndrome (MetS) [2], cardiovascular diseases (CVD) [3], and mortality

[4]. MetS is a complex of interrelated risk factors for CVD [5,6] as a result of insulin resistance [7]. Waist circumference (WC) strongly correlates with abdominal obesity and is used in the definition of MetS [5]. Body mass index (BMI) as a measure of obesity, on the other hand, has important limitations because BMI does not discriminate abdominal fat from lean mass [8]. Thus, WC might be a better predictor of CVD [3,9].

The concept of the metabolically obese, normal-weight individuals was originally proposed several decades ago

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[10,11]. Increased WC has been noted to possibly be a risk marker of CVD and mortality even in persons of normal weight [4,12–14]. Moreover, MetS may occur at a lower weight in Asians [15], so it is important to evaluate the value of WC in detecting MetS risk, especially among non-obese individuals [16]. However, there are limited data on whether the normal range of WC still represents a risk of MetS among normal-weight subjects. In addition, it is important to detect MetS components from its early stages, such as prediabetes (impaired fasting glucose) [17], prehypertension [18], and borderline dyslipidemia (e.g., borderline-high triglycerides [TG]) [6].

In this context, the purpose of this study was to reveal the association between normal range of WC and MetS or non-adipose MetS components from their early stages among subjects with normal BMI.

## Methods

### Subjects

The characteristics of subjects have been described elsewhere [19]. In brief, subjects were individuals aged 40–74 years who underwent Specific Health Checkups and Health Guidance (Tokutei-Kenshin) [20] between April 2008 and March 2009 in Aichi Prefecture, Japan. The present study included subjects with complete data for BMI and the following MetS-related parameters [5,21]: systolic and diastolic blood pressure (BP), hemoglobin A1c (HbA1c), TG, high-density lipoprotein cholesterol (HDL-C), and WC. Most of the subjects had data on low-density lipoprotein cholesterol (LDL-C). Only subjects with a normal range of WC (<90 cm in men and <80 cm in women), the criteria of ethnicity specific cutoffs for central obesity for Asians [5], and normal range of BMI (18.5–24.9) [22] were included in this study.

All of the subjects completed a self-administered questionnaire to document their current medications for hypertension, diabetes, and hyperlipidemia, history of cardiovascular and cerebrovascular diseases, and smoking habits (current smoker or not). WC was measured at the umbilical level with the subjects standing after normal expiration. Measurement of height, weight, and BP, and blood (after fasting for >8 h) and urine sampling were performed at each medical institution. BMI was calculated and reported after measurement of height and weight. Either fasting plasma glucose (FPG) or HbA1c was measured as an index of glycemic control in this health checkup program; therefore, FPG was unknown for approximately half of the subjects. HbA1c values are presented in National Glycohemoglobin Standardization Program (NGSP) units, which were calculated using the following equation:  $\text{HbA1c (NGSP, \%)} = 1.02 \times \text{HbA1c (Japan Diabetes Society, \%)} + 0.25\%$ . The glomerular filtration rate (GFR) was estimated using the Japanese eGFR (estimated GFR) equation [23] as follows:  $\text{eGFR (ml/min/1.73 m}^2\text{)} = 194 \times [\text{serum creatinine}]^{-1.094} (\text{mg/dl}) \times [\text{age}]^{-0.287} (\text{years}) (\times 0.739 \text{ if female})$ .

This study was conducted by the Aichi Chronic Kidney Disease Epidemiology Conference with support from the Aichi Kidney Foundation. Written informed consent was not required as only the existing information was used. This study was approved by the Ethics Committee of Nagoya University School of Medicine (approval number 679).

### Definition of WC and BMI categories

Subjects were divided into three categories using WC. Subjects were categorized as having low, moderate, and upper-normal WC for those with WC < 80, 80–84, and 85–89 cm in men and WC < 70, 70–74, and 75–79 cm in women, respectively. Each WC category was further stratified into three BMI categories; low (BMI 18.5–20.9), moderate (BMI 21.0–22.9), and upper-normal (BMI 23.0–24.9) [22].

### Definitions of MetS components

Subjects were categorized as having normal BP (i.e., no prehypertension; BP < 130/85 mmHg), prehypertension (BP 130–139/85–89 mmHg), or hypertension (BP ≥ 140/90 mmHg or the use of antihypertensive drugs) [18]. Subjects were also categorized as having normal fasting glucose (i.e., no prediabetes; FPG < 100 mg/dl), prediabetes (FPG 100–125 mg/dl), or diabetes (FPG ≥ 126 mg/dl or the use of glucose-lowering drugs) [17]. Based on HbA1c levels, subjects were categorized as having no prediabetes (HbA1c < 5.7%), prediabetes (HbA1c 5.7–6.4%), or diabetes (HbA1c ≥ 6.5% or the use of glucose-lowering drugs) [21]. For lipid levels, subjects were categorized as having normal TG (<150 mg/dl), borderline-high TG (150–199 mg/dl), or high TG (≥200 mg/dl or the use of lipid-lowering drugs); high HDL-C (>60 mg/dl), normal HDL-C (40–60 mg/dl), or reduced HDL-C (<40 mg/dl or the use of lipid-lowering drugs); normal LDL-C (<130 mg/dl), borderline-high LDL-C (130–159 mg/dl), or high LDL-C (≥160 mg/dl or the use of lipid-lowering drugs) [6].

### Definition of MetS

The diagnostic criteria for the assessment of MetS components were defined according to the Joint Scientific Statement for harmonizing MetS [5] as follows: (1) elevated BP was defined as BP ≥ 130/85 mmHg or the use of antihypertensive drugs; (2) elevated FPG was defined as FPG ≥ 100 mg/dl or the use of glucose-lowering drugs; (3) elevated TG was defined as TG ≥ 150 mg/dl or the use of lipid-lowering drugs; and (4) reduced HDL-C was defined as HDL-C < 40 mg/dl in men and <50 mg/dl in women, or the use of lipid-lowering drugs. Subjects who met the fifth criteria, WC ≥ 90 cm in men and ≥80 cm in women, the ethnicity specific cutoffs for central obesity for Asians, were not included in this study. MetS was defined as the presence of three or more of these four components. Elevated HbA1c (defined as HbA1c ≥ 5.7%) was used as the surrogate marker for glycemic status [21].

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