

## New Criteria for ‘Obesity Disease’ in Japan

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The present study was designed to establish adequate criteria for categorizing ‘obesity disease’ in Japan in relation to obesity-related complications. The subjects were 1,193 Japanese subjects (775 men, 418 women; age: 20–84 years old, body mass index (BMI): 14.9–56.4 kg/m<sup>2</sup>) including subjects undergoing a health examination and obese subjects visiting an obesity clinic. Visceral fat area (VFA) and subcutaneous fat area (SFA) were determined by computed tomography (CT) at the umbilical level. Anthropometric parameters, including BMI, waist circumference (W), waist/hip circumference (W/H), ratio and waist circumference/body height (W/BH) ratio, were measured. Hyperglycemia, dyslipidemia, and hypertension were evaluated as obesity-related complications. The relationship between each parameter and the prevalence of the complications was investigated. The number of complications increased in accordance with BMI and the average value was greater than 1.0 at a BMI of 25. The best combination of the sensitivity and specificity for detecting subjects with multiple risk factors was a BMI of 25. BMI showed a close positive correlation with SFA ( $r=0.82$ ), even for BMI  $\geq 25$  ( $r=0.77$ ), but had a weaker correlation with VFA ( $r=0.54$ ). The obese subjects with a BMI  $\geq 25$  had no correlation between BMI and VFA because of the wide individual variation of VFA. The number of disorders was greater than 1.0 at 100 cm<sup>2</sup> of VFA and the best combination of the sensitivity and specificity for determining subjects with multiple risk factors was 100 cm<sup>2</sup> of VFA. Between the simple anthropometric values and measurement of VFA, it was proven that W had the closest relationship with VFA in both men ( $r=0.68$ ) and women ( $r=0.65$ ). The regression line obtained from simple correlation analyses indicated that the W corresponding to 100 cm<sup>2</sup> of VFA was 84.4 cm in men and 92.5 cm in women. These data suggest that obesity is adequately specified as a BMI  $\geq 25$  in Japan where the prevalence and degree of obesity remains mild. It is reasonable to establish the cut-off point of VFA at 100 cm<sup>2</sup> as indicative of the risk of obesity-related disorders and a waist circumference of 85 cm in men and 90 cm in women approximates to this visceral fat mass. (*Circ J* 2002; 66: 987–992)

**Key Words:** Body mass index; Criteria; Japan; Obesity; Visceral fat; Waist circumference

In Japan, the sedentary lifestyle and changes in diet have resulted in an increasing number of obese subjects, as in Western countries, with the attendant social problems and increased national health care costs associated with obesity-related disorders, as well as the loss in economic productivity. Because of these problems, the Ministry of Health and Welfare in Japan declared in 1996 that common adult diseases such as diabetes mellitus, hyperlipidemia, hypertension and atherosclerotic disease should be described as ‘lifestyle-related diseases’. The Ministry appealed to the nation and emphasized the importance of self-control in preventing obesity-linked disorders. However, the prevalence of obesity, defined by the World Health Organization (WHO) as body mass index (BMI)  $\geq 30$  is no more than 2–3% in the Japanese population, in contrast to the 10–20% in Europe and the USA.<sup>1,2</sup> Thus the striking feature of obesity-related problems in Japan is that they relate to degrees of overweight with a BMI  $< 30$ . Nakamura et al demonstrated that a long duration of multiple risk factors, including mild obesity, is involved in the onset of coronary artery disease in Japanese employees,<sup>3</sup> and studies of Japanese-Americans in Hawaii and Seattle also suggest that the Japanese as a race can not handle

glucose metabolism as well as Caucasians when over-nourished and are liable to develop glucose intolerance and complications even with a mild excess of adiposity.<sup>4–6</sup> It is therefore an important issue whether the classification of obesity as a BMI  $\geq 30$  is appropriate for the Japanese in view of the current prevalence of overweight and its associated complications.

In recent years, many studies have demonstrated that body fat distribution has a close relationship with the occurrence of metabolic disorders, and an excess of abdominal fat, especially intra-abdominal visceral fat, leads to obesity-related complications.<sup>7–12</sup> Accordingly, it is very important that the designation of ‘obesity disease’ includes a factor that reflects the accumulation of intra-abdominal visceral fat so that the probability of obesity-linked metabolic disorders is included. A simple indicator that reflects the mass of visceral fat is also needed to enable practical screening of patients.

### Methods

#### Subjects

The study group comprised 1,193 Japanese adult subjects (average age  $\pm$  SD 55  $\pm$  12 years, range: 20–84 years old; 775 men (55  $\pm$  11 years), 418 women (55  $\pm$  12 years)) from the general population who were either undergoing a health examination in the institutions participating in the Japanese Visceral Fat Syndrome (J-VFS) Study Committee of the Ministry of Health and Welfare of Japan (860 cases) or were visiting an obesity clinic were also included (333

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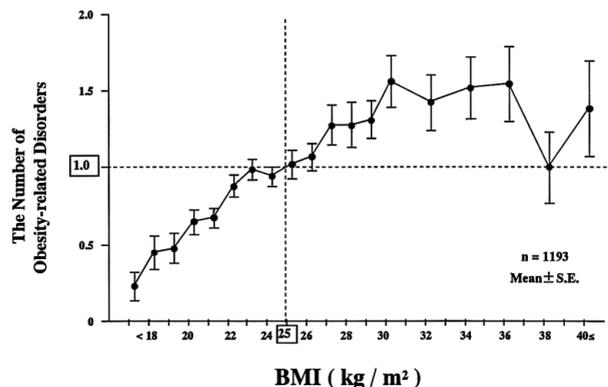


Fig 1. Number of obesity-related disorders discriminated by body mass index (BMI). Obesity-related disorders include hyperglycemia, hypertension, and dyslipidaemia. The BMI value indicates the level of BMI divided by each 1 kg/m<sup>2</sup> (BMI <30) or each 2 kg/m<sup>2</sup> (BMI ≥30). The vertical and horizontal dotted lines represent BMI and an average number of obesity-related disorders of 1.0, respectively.

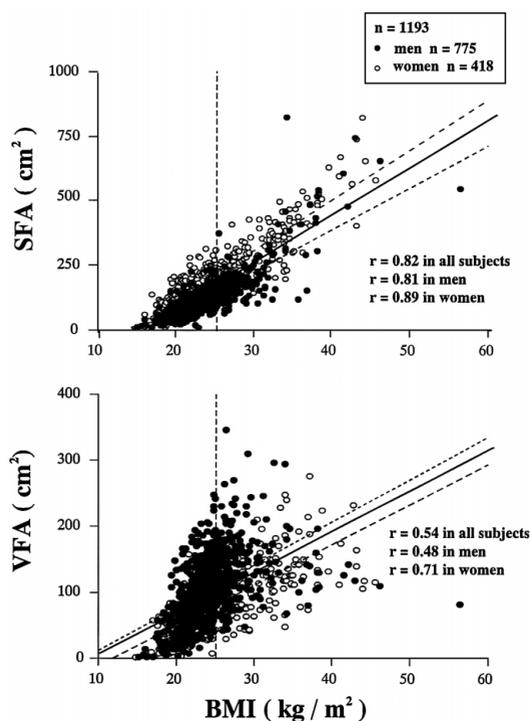


Fig 2. Correlations between subcutaneous fat area (SFA) or visceral fat area (VFA) and body mass index (BMI) in the subjects investigated. The vertical dotted line represents BMI of 25. Simple regression lines: all subjects, men and women.

cases). The subjects had a wide distribution of BMI from 14.9 to 56.4 (average  $\pm$  SD, 24.6 $\pm$ 4.6). The estimation of fat distribution by computed tomography (CT) scan was performed in all subjects and the waist (W) and hip (H) circumferences were measured in 748 of the 1,193 subjects (554 men, 194 women). A signed informed consent was obtained from all subjects and the J-VFS Study Committee of the Ministry of Health and Welfare of Japan or the Medical Ethics Committee of Osaka University approved the study protocols

#### Assessment of Obesity-Related Disorders

Venous blood samples were collected in the early morn-

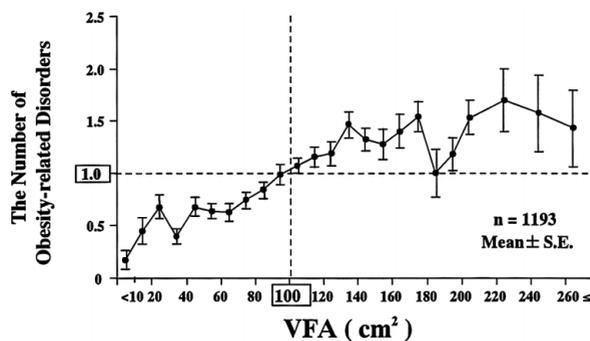


Fig 3. Number of obesity-related disorders discriminated by visceral fat area (VFA) and waist circumference. Obesity-related disorders are defined as in Fig 1. The vertical and horizontal dotted lines represent VFA of 100 cm<sup>2</sup> and an average number of obesity-related disorders of 1.0, respectively. The VFA value represents the level of VFA divided by each 10 cm<sup>2</sup> (VFA <200) or each 20 cm<sup>2</sup> (VFA ≥200).

ing after a 12-h fast. Fasting plasma glucose (FPG) and serum high-density lipoprotein cholesterol (HDL-C) were measured by the glucose oxidase method and the direct enzymatic method using a selective HDL-C measurement kit, DA-4101 (Daiichi Chemical Co Ltd, Tokyo Japan), respectively. Serum total cholesterol (TC) and triglyceride (TG) were measured by enzymatic methods. Blood pressure was measured by auscultation in the right arm after 10 min of rest in the sitting position.

Three obesity-related disorders were defined: (1) hyperglycemia: FPG  $\geq$ 6.11 mmol/L (110 mg/dl); (2) dyslipidemia: TC  $\geq$ 5.69 mmol/L (220 mg/dl) and/or TG  $\geq$ 1.69 mmol/L (150 mg/dl) and/or HDL-C <1.03 mmol/L (40 mg/dl); (3) hypertension: systolic blood pressure  $\geq$ 140 mmHg and/or diastolic blood pressure  $\geq$ 90 mmHg.

#### Identifying Abdominal Fat Distribution and Anthropometry

The intra-abdominal visceral fat area (VFA) and the subcutaneous fat area (SFA) were obtained from CT cross-sectional scans at the level of the umbilicus, as previously reported<sup>13</sup>

BMI was calculated from the height and body weight. The maximum hip circumference (H) and the waist circumference (W) at the umbilical level were measured in the late exhalation phase while standing. The waist/hip circumference (W/H) ratio was calculated. To avoid the influence of height, the waist circumference/body height (W/BH) ratio was also calculated.

#### Statistical Analysis

Age and BMI were described as mean  $\pm$  standard deviation (SD). The number of obesity-related disorders was expressed as mean  $\pm$  standard error (SE). The correlation between indicators of fat distribution and anthropometric parameters was performed by simple correlation analysis. To determine the cut-off points of BMI and VFA, we examined the number of complications (ie, hyperglycemia, dyslipidemia, and hypertension) in each BMI or VFA level. The sensitivity (probability of correctly detecting true positive) and specificity (probability of correctly detecting true negative) of each cut-off were estimated by detecting the subjects with 2 or more of these disorders. The cut-off value producing the best combination of sensitivity and specificity was selected as the optimal threshold for each parameter. The W value corresponding to each VFA was

**Table 1** Frequency of Obesity-Related Disorders in Non-Obese and Obese Subjects With Normal and High Visceral Fat Area (VFA)

	Non-obese subjects		Obese subjects	
	Normal VFA	High VFA	Normal VFA	High VFA
<i>n</i>	429	160	66	205
<i>M</i> (%) / <i>F</i> (%)	251 (42) / 178 (66)	139 (23) / 21 (8)	41 (7) / 25 (9)	161 (27) / 44 (16)
No disorders (%)	210 (49)	44 (28)	27 (41)	34 (17)
Single disorder (%)	184 (43)	84 (53)	23 (35)	94 (46)
Two or more disorders (%)	35 (8)	32 (20) <sup>†</sup>	16 (24) <sup>*</sup>	77 (38) <sup>†,‡</sup>

Disorders: hyperglycemia, dyslipidemia and hypertension are defined in Methods.

Non-obese: BMI < 25; obese: BMI ≥ 25; high VFA: visceral fat area ≥ 100 cm<sup>2</sup>; normal VFA: visceral fat area < 100 cm<sup>2</sup>.

\**p* < 0.001 and †*p* < 0.0001 vs non-obese subjects with normal VFA by chi-square test.

‡*p* < 0.001 vs obese subjects with normal VFA by chi-square test.

calculated from the regression line by simple correlation analysis. The significance of the difference in the proportion of the subjects with obesity-related disorders among the obese and the non-obese with normal or high VFA was determined by chi-square test.

## Results

### Relationship Between BMI and the Prevalence of Obesity-Related Disorders

The average number of complications in each BMI level is shown in Fig 1. The number increased in relation to the BMI and the average value was more than 1.0 at a BMI of 25 (average value ± SE, 1.02 ± 0.09) with a progressive increase for BMI ≥ 25. The sensitivity and specificity for detecting subjects with 2 or more disorders (ie, multiple risk factors) were, respectively, 0.67 and 0.57 at BMI of 24, 0.54 and 0.71 at BMI of 25, and 0.47 and 0.78 at BMI of 26. The best trade-off between sensitivity and specificity was for a BMI of 25, which supports our judgment that obesity should be specified at BMI ≥ 25 in Japanese subjects.

### Assessing Visceral Fat Accumulation by CT Scanning

The VFA and SFA were plotted in relation to BMI (Fig 2). BMI closely correlated with SFA, even at BMI ≥ 25 (*r* = 0.77), but had a weaker correlation with VFA. At a BMI ≥ 25, women showed a weaker correlation between BMI and VFA (*r* = 0.48) and there was no correlation in men (*r* = 0.05) or in all subjects (*r* = 0.06) because of the wide individual variations in VFA.

**Effect of VFA on the Number of Obesity-Related Disorders** The mean number of the disorders increased in proportion to the increase in VFA and the average value was more than 1.0 at 100 cm<sup>2</sup> of VFA (average value ± SE, 1.07 ± 0.08), further increasing beyond 100 cm<sup>2</sup> of VFA (Fig 3). The sensitivity and specificity for detecting subjects with multiple risk factors were, respectively, 0.75 and 0.57 at 90 cm<sup>2</sup>, 0.69 and 0.62 at 100 cm<sup>2</sup>, and 0.62 and 0.70 at 110 cm<sup>2</sup> of VFA. The best trade-off between the sensitivity and specificity was at 100 cm<sup>2</sup> of VFA. These results suggest that the standard value of VFA ≥ 100 cm<sup>2</sup> is appropriate in Japanese for assessing the prevalence of obesity-related disorders.

The percentage of subjects and the frequency of the 3 obesity-related disorders in 4 subgroups determined by BMI (obese: BMI ≥ 25 and non-obese: BMI < 25) and VFA (high VFA: VFA ≥ 100 cm<sup>2</sup> and normal VFA < 100 cm<sup>2</sup>) in 860 consecutive subjects (592 men, 268 women) undergoing a health examination are shown in Table 1. For men, obese and non-obese subjects with a high VFA were 27%

**Table 2** Correlation Between Visceral Fat Area and Anthropometric Parameters in Men and Women

	Visceral fat area	
	Men (n=554)	Women (n=194)
BMI	0.61*	0.63*
W	0.68*	0.65*
W/H ratio	0.54*	0.52*
W/BH ratio	0.66*	0.63*

\*Simple correlation coefficients, *p* < 0.0001.

W, waist circumference; W/H ratio, waist/hip circumference ratio; W/BH ratio, waist/body height ratio.

(161 cases) and 23% (139 cases), respectively, and for women, the percentages were 16% (44 cases) and 8% (21 cases), respectively. Of the obese subjects, 46% with a high VFA had a single disorder and 38% had 2 or more disorders. Of the non-obese subjects, 53% with a high VFA had a single disorder and 20% had multiple risk factors. In contrast, 49% of the non-obese subjects with normal VFA had no disorders and only 8% had multiple risk factors; 41% of obese subjects with normal VFA had no disorders and 24% had multiple risk factors. Consequently, the proportion of subjects with multiple risk factors was significantly higher in both obese and non-obese subjects with a high VFA than in non-obese subjects with normal VFA and, furthermore, the proportion was significantly higher in the high VFA subgroup than in the normal VFA subgroup of the obese subjects.

**Convenient and Simple Estimation of VFA** The results of the simple correlation coefficient between the convenient anthropometric parameters and the VFA determined by CT are shown in Table 2. W had the closest relationship with VFA in men (*r* = 0.68) and in women (*r* = 0.65). The sex-specific regression line analyzed by simple correlation indicated that the W corresponding to 100 cm<sup>2</sup> of VFA was 84.4 cm in men and 92.5 cm in women (Fig 4).

### New Criteria for the Diagnosis of 'Obesity Disease' in Japanese

From the results of our investigations, we have developed new guidelines for diagnosing 'obesity disease'.

(1) Obesity: this is judged by BMI at initial screening and defined as a BMI ≥ 25.

(2) Definition of 'obesity disease': 'obesity disease' is a clinical designation based on the presence of associated complications or their likely occurrence. A person in this situation needs to reduce their weight for medical reasons.

(3) Criteria for 'obesity disease':

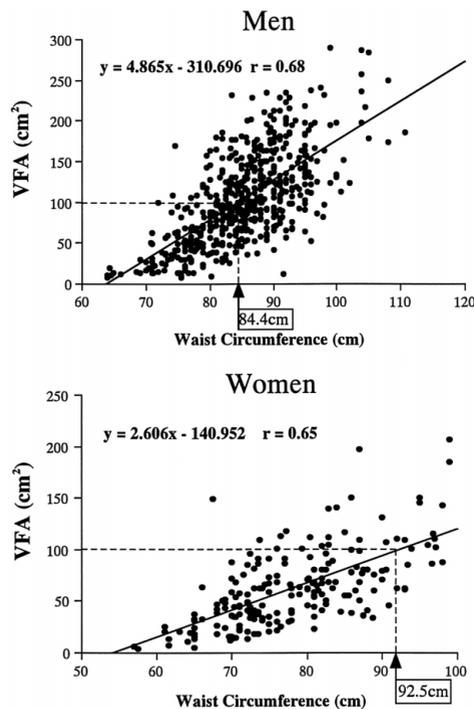


Fig4. Correlations between visceral fat area (VFA) and waist circumference in men and women. The vertical and horizontal dotted lines represent VFA of 100cm<sup>2</sup> and the waist circumference corresponding to a VFA of 100cm<sup>2</sup> by simple regression line.

- (I) high-risk obesity as specified by an excess of visceral fat confirmed by CT scan (visceral fat obesity).
- (II) obesity with complications that require weight reduction for their improvement or elimination:
  - (i) noninsulin-dependent diabetes mellitus (NIDDM) and impaired glucose tolerance
  - (ii) dyslipidemia
  - (ii) hypertension
  - (iv) hyperuricemia and gout
  - (v) coronary artery disease: myocardial infarction and angina pectoris
  - (vi) sleep apnoea syndrome and Pickwickian syndrome
  - (vii) fatty liver
  - (vii) cerebral infarction: cerebral thrombosis and transient ischemic attacks of brain
  - (ix) orthopedic diseases: osteoarthritis and lumbago
  - (x) amenorrhoea and infertility.

An obese subject with at least 1 of these 10 obesity-related disorders has 'obesity disease' regardless of fat distribution.

Although many other diseases, such as gallstones, carcinoma of the gallbladder, pancreatitis, breast cancer, uterine fibroid, endometrial carcinoma, proteinuria, renal dysfunction, pseudoacanthosis nigricans, dermatites, such as intertrigo and miliaris, tonsillar hypertrophy and carcinoma of the parotid gland, are also considered to be related to obesity, they were not included because the correlation is weaker and/or weight reduction has little effect.

(4) Criteria for visceral fat obesity:

(I) waist circumference (W) at the umbilical level measured in the exhalation phase of respiration while standing. A BMI  $\geq 25$  and a W  $\geq 85$  cm in men or  $\geq 90$  cm in women is suspected as having visceral fat obesity.

(II) abdominal CT scan at the umbilical level in the

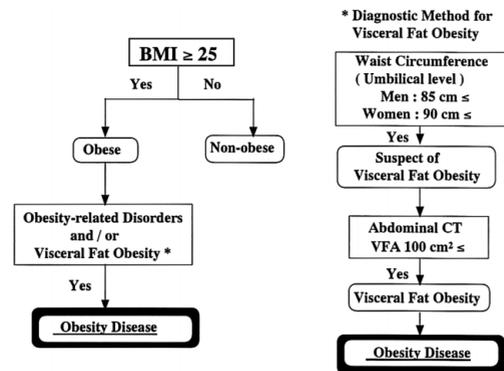


Fig5. Flow chart for the diagnosis of 'obesity disease'. VFA, visceral fat area.

exhalation phase in those suspected of having visceral obesity for determination of VFA. A VFA  $\geq 100$ cm<sup>2</sup> in both men and women is diagnostic of visceral fat obesity.

(5) Flow chart for diagnostic processing of 'obesity disease' (Fig 5). A person with a BMI  $\geq 25$  is diagnosed as obese. An obese person with obesity-associated complications and/or visceral fat obesity is diagnosed as having 'obesity disease'. Even an obese person without complications has the W measured as a screening tool for visceral fat obesity: W  $\geq 85$  cm in men or W  $\geq 90$  cm in women is suspicious for visceral fat obesity. Such subjects are examined by CT scan at umbilical level and a VFA  $\geq 100$ cm<sup>2</sup> is diagnostic for visceral fat obesity and consequently for 'obesity disease'.

## Discussion

Although obesity is often defined simply as excessive accumulation of fat in adipose tissue, many obese individuals do not have obesity-linked metabolic disorders and from the medical point of view do not necessarily need to reduce their weight. However, others, regardless of their BMI, have obesity-associated metabolic diseases and need to lose weight immediately to improve their health!<sup>4,15</sup> It is now generally accepted in Europe and the USA that 'obesity' should not be classified as a 'disease', but rather as a 'risk factor' in the clustering of diseases such as atherosclerotic diseases or diabetes mellitus!<sup>16-21</sup> Recent studies have revealed that adipose tissue produces biologically active leptin, tumor necrosis factor- $\alpha$ , plasminogen activator inhibitor-1, and adiponectin, which are closely related to the development of complications!<sup>22-26</sup> so it is important in medical terms to specify the obesity not merely as one of the risk factors, but as 'obesity disease'.

In particular, many obese Japanese subjects have a mild degree of adiposity compared with the problem in Europe and the USA. However, because Japanese with even mild obesity tend to have obesity-related complications, establishing criteria that are appropriate for diagnosing 'obesity disease' in Japanese subjects is an urgent priority. We provide the data for establishing these criteria. The WHO and the National Institute of Health in the USA (NIH) have defined obesity as BMI  $\geq 30$ !<sup>27</sup> but in Japan, the percentage of the population with such a BMI is no more than 2.0% in men and 3.0% in women!<sup>1,2</sup> so it is not practical to apply these Western criteria without any modification to the Japanese. The prevalence of a BMI between 25.0 and 29.9 is approximately 20% of the total population in Japan and

we have selected a BMI of 25 as the cut-off point of obesity for the following reasons: (1) obesity-related complications increase for a BMI  $\geq 25$ , (2) the best combination of sensitivity and specificity for detecting subjects with multiple risk factors is a BMI of 25, and (3) using this standard preserves the international coordination of the WHO criteria<sup>1,27</sup> and the recommendation of the Steering Committee of the Western Pacific Region of WHO<sup>28</sup>. On this basis, we conclude that a Japanese person with a BMI  $\geq 25$  should be classified as obese. We have conventionally adopted a BMI cut-off point of 26.4 in Japan, this being 20% in excess of the ideal BMI of 22.<sup>29</sup> The Japanese Committee also reported that the relative risk of negative health consequences of obesity in the groups with a BMI 25.0–26.4 and 26.4–29.9 were calculated as 2.5- and 3.9-fold those with a BMI  $< 25$  (data not shown). Recently McNeely et al also demonstrated that BMI  $\geq 25$  is a useful standard for identifying diabetes risk in Japanese-Americans,<sup>30</sup> which supports the setting of BMI 25 as the cut-off.

During the past 10 years or so, many researchers, including ourselves, have shown that excess visceral fat is more closely related to the risk of health problems than the BMI itself.<sup>7–12</sup> The contribution of VFA is greater in Japan where the degree of whole fat accumulation is not as severe as in Western countries; therefore, the amount of intra-abdominal fat must be taken account in the diagnosis of 'obesity disease'. We investigated the relationship of obesity-related disorders with VFA by means of CT scan and found an increased number of complications in those with a VFA  $\geq 100\text{cm}^2$ . Moreover, the best combination of sensitivity and specificity for detecting subjects with multiple risk factors was also VFA  $\geq 100\text{cm}^2$ . It is therefore reasonable to set the criteria for VFA as  $100\text{cm}^2$ . Previously, we reported that approximately 70% of patients with coronary artery disease had a VFA  $\geq 100\text{cm}^2$ , together with a cluster of other risk factors.<sup>14</sup> Després et al<sup>31</sup> also demonstrated that the subjects with a VFA  $< 100\text{cm}^2$  had fewer risks than those with a VFA  $\geq 100\text{cm}^2$ . It is also interesting that the prevalence of complications was high in the non-obese subgroup with a high VFA, suggesting that an assessment of VFA is important regardless of the degree of obesity.

Although CT scanning and magnetic resonance imaging are used to precisely measure the amount of intra-abdominal fat,<sup>2,33</sup> simple anthropometric measurements for estimating the amount of visceral fat is essential for practical screening of the general population. In the 1980s several prospective studies designed by Kissebah and Björntorp et al confirmed that the ratio of the W/H ratio was more closely associated with obesity-related metabolic disorders than a simple excess of total body fat.<sup>34–36</sup> Since then, the W/H ratio has become accepted as the clinical method of evaluating abdominal fat accumulation, but from the mid 1990s it has been suggested that W itself may be a better indicator of an increased risk of negative health consequences of obesity than the W/H ratio.<sup>37–40</sup> In 1997 WHO recommended the waist circumference as an initial screening tool and presented sex-specific cut-off points based on data from the Netherlands with increased risk at  $\geq 94\text{cm}$  in men and  $\geq 80\text{cm}$  in women.<sup>1</sup> Furthermore, the Steering Committee of the Western Pacific Region of WHO recommended that the high-risk waist circumference for Asians was  $\geq 90\text{cm}$  in men and  $\geq 80\text{cm}$  in women.<sup>28</sup> We propose that a waist circumference of 85 cm in men and 90 cm in women should be designated. These cut-off points are higher in women than in men, contrary to the WHO criteria for either Westerners or

Asians. One reason may be the different levels at which the waist circumference in women is measured: we measured at the level of the umbilicus whereas Western measures are of the minimal waist level. Another reason may be racial differences in body shape; Japanese women characteristically have more subcutaneous fat than BMI-matched Westerners. Another explanation for the difference between the WHO criteria for Asians and our criteria is that our cut-offs for waist circumference corresponded to the VFA determined by CT scan. As already reported, there are marked gender differences in the proportions of subcutaneous fat and visceral fat in the Japanese,<sup>41</sup> and so in the present study, we determined the appropriate cut-off points by using the regression line relating to VFA. In terms of guidelines, a practical and universally acceptable value is essential for screening and on this basis, the W value of 85 cm in men and 90 cm in women satisfies the requirement.

We have established guidelines for diagnosing 'obesity disease' that requires weight reduction for medical reasons. Two points were taken into consideration. First, the degree of obesity in most Japanese subjects is mild. Second, the distribution of fat, particularly the VFA, is very important. The guidelines have 3 major changes. First, the lowered cut-off point for obesity from a BMI of 26.4 to a BMI of 25. Second, the use of the waist circumference to estimate the amount of visceral fat, and third, measuring VFA more accurately as a final diagnosis. Because the prevalence of obesity is increasing, it is necessary to identify patients with 'obesity disease'. However, the waist circumference is not routinely measured in every clinic, so it should be incorporated in clinical and epidemiological studies of obesity as a screening tool to highlight its utility. Currently there are approximately 13,000 CT scanners in Japan, which is sufficient numbers for the precise measurement of the amount of visceral fat in those patients who need further diagnosis. More studies are required to validate this approach and to develop easier methods for defining 'obesity disease'.

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## Appendix 1

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