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Ethnic differences in the relationships of anthropometric measures to metabolic risk factors in Asian patients at risk of atherothrombosis

Results from the REduction of Atherothrombosis for Continued Health (REACH) Registry

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Abstract

The aim of the study is to examine the relationships between 4 anthropometric indices and metabolic risk factors (hypertension, atherogenic dyslipidemia, and glucose intolerance) in different Asian ethnic groups of patients at risk of atherothrombosis. We analyzed the baseline data of 11 017 Asian patients with established atherothrombotic cardiovascular diseases or at least 3 atherothrombotic risk factors. In East and South Asians, the graded relationships of body mass index (BMI) with the presence of at least 2 metabolic risk factors remained significant after adjustment for waist circumference (top vs bottom quartile—East Asians: odds ratio, 2.02; 95% confidence interval, 1.67-2.45; South Asians: 3.24, 1.18-8.95), whereas the graded relationships of waist circumference decreased or became nonsignificant after adjustment for BMI (East Asians: 1.64, 1.35-1.99; South Asians: 0.68, 0.20-2.30). In Southeast Asian men, the graded relationship of waist circumference with metabolic risk factors (2.27, 1.42-3.63) was stronger than that of BMI (1.34, 0.84-2.12), whereas in Southeast Asian

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women, there was a trend toward a stronger association between BMI and metabolic risk factors. In East Asians and in Southeast Asian women, the waist-to-BMI ratio decreased with the number of metabolic risk factors. The optimal cutoff points for BMI and waist circumference with regard to the presence of at least 2 metabolic risk factors were lowest in East Asians (men: 24 kg/m^2 and 86 cm; women: 24 kg/m^2 and 82 cm). Our findings suggest that both BMI and waist circumference, rather than waist circumference alone, should be included in metabolic risk assessment in this high-risk multiethnic Asian population. Uniform anthropometric cutoff values for all Asian ethnic groups are not appropriate to assess obesity-related metabolic complications, even in patients with established atherothrombotic disease.

1. Introduction

The metabolic syndrome is a combination of metabolic risk factors, including hypertension, atherogenic dyslipidemia, glucose intolerance, and obesity, and is a major public health challenge worldwide [1]. There is now consensus that obesity may be central to the clustering of these risk factors [1,2]. Both body mass index (BMI) and waist circumference are well-established anthropometric measures of obesity. However, different diagnostic guidelines recommend different anthropometric measurements and cutoff values to define obesity [3-7]. In white populations, waist circumference is generally more strongly related to metabolic risk factors than BMI [8-10]. In Asian populations, results are conflicting [11-13].

Although waist circumference provides a crude measure of intraabdominal visceral fat, now considered a main cause of the metabolic syndrome [3,4], one recent study indicated that BMI was correlated with intraabdominal fat as strongly as waist circumference [14]. In some Asian ethnic groups, truncal subcutaneous fat is also an important factor for the development of insulin resistance and the metabolic syndrome [15,16]. Moreover, the associations between metabolic risk factors and other anthropometric indices such as waist-to-height ratio and waist-to-BMI ratio, which adjust central obesity for body height or general obesity, respectively, have not been fully explored.

For the same BMI or waist circumference, Asians, compared with whites, have a higher percentage of body fat and a higher prevalence of hypertension, diabetes, dyslipidemia, and clustering of these risk factors [17-20]. Although there are now ethnic-specific definitions for general and central obesity [3,4,17], these cutoff points have not taken into consideration the possible interethnic differences in body build and body fat distribution among different Asian ethnic groups [19-21].

It has been shown that metabolic risk factors confer an increased cardiovascular risk, not only in individuals without known heart disease, but also in those with established atherothrombotic cardiovascular diseases [9,10]. However, the relationship between measures of obesity and metabolic risk factors in high-risk populations has not been thoroughly examined. In this study, we analyzed the baseline data of 11 017 Asian patients with atherothrombosis enrolled in the international REduction of Atherothrombosis for Continued Health (REACH) Registry [22,23] to investigate (1) the relationships between 4 anthropometric indices (BMI, waist circumference, waist-to-height ratio, and waist-to-BMI ratio) and individual as well as clustering of metabolic risk factors (hypertension, atherogenic dyslipidemia, and glucose intolerance), (2) the relative contributions of BMI and waist circumference to clustering of metabolic risk factors, and (3) the optimal cutoff points for BMI and waist circumference with regard to the constellation of metabolic risk factors in different Asian ethnic groups. The term *atherothrombosis* is used instead of *atherosclerosis* because it encompasses the concepts of both atherosclerosis and disruption of atherosclerotic plaque with superimposed thrombosis, the primary cause of acute ischemic insults in arterial beds [22].

2. Methods

The design and methodology of the international, prospective, observational REACH Registry have been published previously [22,23]. Briefly, consecutive eligible outpatients aged at least 45 years with established coronary artery disease, cerebrovascular disease, or peripheral arterial disease, or with at least 3 atherothrombotic risk factors were enrolled worldwide between December 2003 and June 2004. The risk factors consisted of those that were documented in the medical record or for which patients were receiving treatment at the time of study enrollment: treated diabetes mellitus, diabetic nephropathy, ankle-brachial index less than 0.9, asymptomatic carotid stenosis of at least 70%, carotid intima media thickness of 2 times or more that of adjacent sites, systolic blood pressure of at least 150 mm Hg despite therapy for at least 3 months, hypercholesterolemia treated with medication, current smoking of more than 15 cigarettes per day, men aged at least 65 years, or women aged at least 70 years. The protocol of the REACH Registry was submitted to the institutional review board in each country according to local requirements, and signed informed consent was obtained for all patients.

Among the 69 055 patients enrolled in the registry, 11 111 (16.1%) were from countries in Asia and formed the cohort for this study. Data on demographic characteristics, risk factors, physical examination, and medications were collected centrally using a standardized international case report form completed at the study enrolment visit. The determination of ethnic origin was based on self-reported ethnicity. Patients with an ancestral origin from China or Japan were

Table 1
Distribution of sex and nationality among the 3 Asian ethnic groups in the REACH Registry

	Percentage of Asian ethnic groups											
	Women	Men	China	Hong Kong	Indonesia	Japan	Korea	Malaysia	Philippines	Singapore	Taiwan	Thailand
East Asian (n = 8348)	31.4	68.6	8.2	1.5	0.1	62.2	5.7	2.0	0.5	7.7	11.9	0.2
Southeast Asian (n = 2333)	40.1	59.9	0.5	1.7	20.5	0.1	1.3	7.9	41.3	3.2	2.9	20.6
South Asian (n = 336)	29.2	70.8	1.8	1.5	1.2	0	0.3	44.3	4.2	42.3	0	4.4

defined as having an ethnic origin from *East Asia*, whereas those with an ancestral origin from India were defined as having an ethnic origin from *South Asia*. Patients with an ancestral origin from countries in Southeast Asia were denoted as having an ethnic origin from *Southeast Asia*. Those patients with mixed ethnic origins were asked to choose the ethnic origin with the strongest influence.

Baseline height, weight, waist circumference, seated systolic and diastolic blood pressures, and most recent available fasting plasma glucose, total cholesterol, and triglycerides levels were obtained. *Body mass index* was defined as weight in kilograms divided by the square of height in meters. Waist circumference was recorded as the average of 2 measurements taken while the patient was standing (one taken after inspiration and the other after expiration) at midpoint between the lowest rib and the iliac crest. Waist-to-height and waist-to-BMI ratios were obtained by dividing the waist circumference by body height or BMI, respectively. Three metabolic risk factors (hypertension, atherogenic dyslipidemia, and glucose intolerance) were defined as follows: patients were classified as *hypertensive* if they were receiving treatment of hypertension or had a seated systolic blood pressure of at least 140 mm Hg or a diastolic blood pressure of at least 90 mm Hg; *atherogenic dyslipidemia* was defined as fasting plasma triglycerides of at least 150 mg/dL or hypercholesterolemia treated with medication (high-density lipoprotein cholesterol levels were not obtained in the REACH Registry); and *glucose intolerance* was defined as treated diabetes or a fasting plasma glucose of at least 100 mg/dL.

2.1. Statistical analyses

Continuous variables are expressed as mean (standard deviation) and categorical variables as percentages. Comparisons of categorical variables among different ethnic groups

Table 2
Baseline characteristics of Asian populations by sex and ethnic origin in the REACH Registry

	Women (n = 3653)				Men (n = 7364)			
	East Asian (n = 2620)	SE Asian (n = 935)	South Asian (n = 98)	*P*	East Asian (n = 5728)	SE Asian (n = 1398)	South Asian (n = 238)	*P*
Age (y)	70.4 (8.8)	66.7 (9.8)	66.0 (9.4)	<.0001	67.6 (9.4)	63.2 (10.0)	63.1 (10.4)	<.0001
Weight (kg)	56.4 (10.2)	59.0 (13.7)	61.9 (12.4)	<.0001	65.8 (11.0)	67.8 (12.2)	70.7 (12.0)	<.0001
BMI (kg/m^2)	24.4 (3.8)	24.3 (5.0)	26.8 (5.2)	<.0001	24.2 (3.5)	24.9 (4.0)	25.7 (3.8)	<.0001
Waist circumference (cm)	83.7 (12.0)	86.6 (15.4)	89.5 (13.3)	<.0001	87.8 (10.6)	90.7 (11.5)	93.1 (14.6)	<.0001
Waist-to-height ratio	55.2 (8.0)	55.9 (10.2)	59.0 (9.1)	<.0001	53.4 (6.3)	55.0 (7.2)	56.2 (8.7)	<.0001
Waist-to-BMI ratio	3.46 (0.45)	3.64 (0.66)	3.40 (0.45)	<.0001	3.66 (0.41)	3.70 (0.54)	3.67 (0.66)	.0110
Overweight (BMI 25 to <30 kg/m^2) (%)	32.4	33.2	38.8	<.0001	33.0	36.2	39.9	<.0001
Obese (BMI ≥30 kg/m^2) (%)	7.5	8.5	23.5	<.0001	4.7	8.2	13.9	<.0001
Hypertension[a] (%)	78.3	87.2	84.7	<.0001	71.0	77.3	75.6	<.0001
Hypercholesterolemia[b] (%)	58.8	67.9	73.5	<.0001	45.4	64.3	77.7	<.0001
Diabetes[c] (%)	46.8	54.7	74.5	<.0001	35.5	43.5	55.9	<.0001
Smoking history (%)				<.0001				<.0001
Ex-smoker	8.0	6.3	2.1		53.9	42.9	40.7	
Smoker	5.6	2.2	4.2		21.6	13.0	11.9	
Coronary artery disease (%)	38.1	40.2	55.1	.0022	51.4	55.7	71.4	<.0001
Cerebrovascular disease (%)	43.0	46.3	34.7	.0425	40.8	40.9	24.8	<.0001
Peripheral arterial disease (%)	5.5	5.6	6.1	.9566	10.9	6.2	13.9	<.0001
≥3 Risk factors (%)	23.4	18.9	23.5	.0169	10.7	11.1	7.6	.2634
Systolic blood pressure (mm Hg)	139 (19)	141 (21)	143 (21)	.0338	136 (18)	137 (21)	137 (20)	.0326
Diastolic blood pressure (mm Hg)	77 (11)	82 (11)	82 (11)	<.0001	78 (11)	82 (12)	80 (12)	<.0001
Fasting glucose (mg/dL)	127 (47)	136 (56)	152 (72)	<.0001	122 (43)	129 (54)	138 (63)	<.0001
Fasting total cholesterol (mg/dL)	204 (39)	213 (56)	204 (48)	<.0001	190 (38)	197 (49)	189 (52)	<.0001
Fasting triglycerides (mg/dL)	146 (87)	166 (91)	140 (62)	<.0001	146 (90)	161 (92)	162 (94)	<.0001

Values are means (standard deviation) unless stated otherwise. SE indicates Southeast.

[a] Patients currently treated with antihypertensive agents.

[b] Patients currently treated with lipid-lowering agents.

[c] Patients with type 1 or 2 diabetes mellitus currently treated with hypoglycemic agents or with a history of diabetes.

were performed using the Pearson χ^2 test. The 1-way analysis of variance, followed by post hoc analyses using the Bonferroni test, was used to compare continuous variables between groups. For comparison of values of BMI, waist circumference, waist-to-height ratio, and waist-to-BMI ratio between patients with and without individual metabolic risk factors, a multiple logistic regression model was computed by sex and ethnicity, adjusting for age and smoking status, as well as waist circumference (for BMI) or BMI (for waist circumference and waist-to-height ratio). To assess linear trends in BMI, waist circumference, waist-to-height ratio, and waist-to-BMI ratio for increasing numbers of metabolic risk factors (hypertension, atherogenic dyslipidemia, and glucose intolerance), a multinomial logistic (polytomous) regression model was computed by sex and ethnicity with adjustments for age and smoking status. To determine the relative contributions of BMI and waist circumference to clustering of metabolic risk factors,

Table 3
Anthropometric indices in Asian patients with and without each individual metabolic risk factor

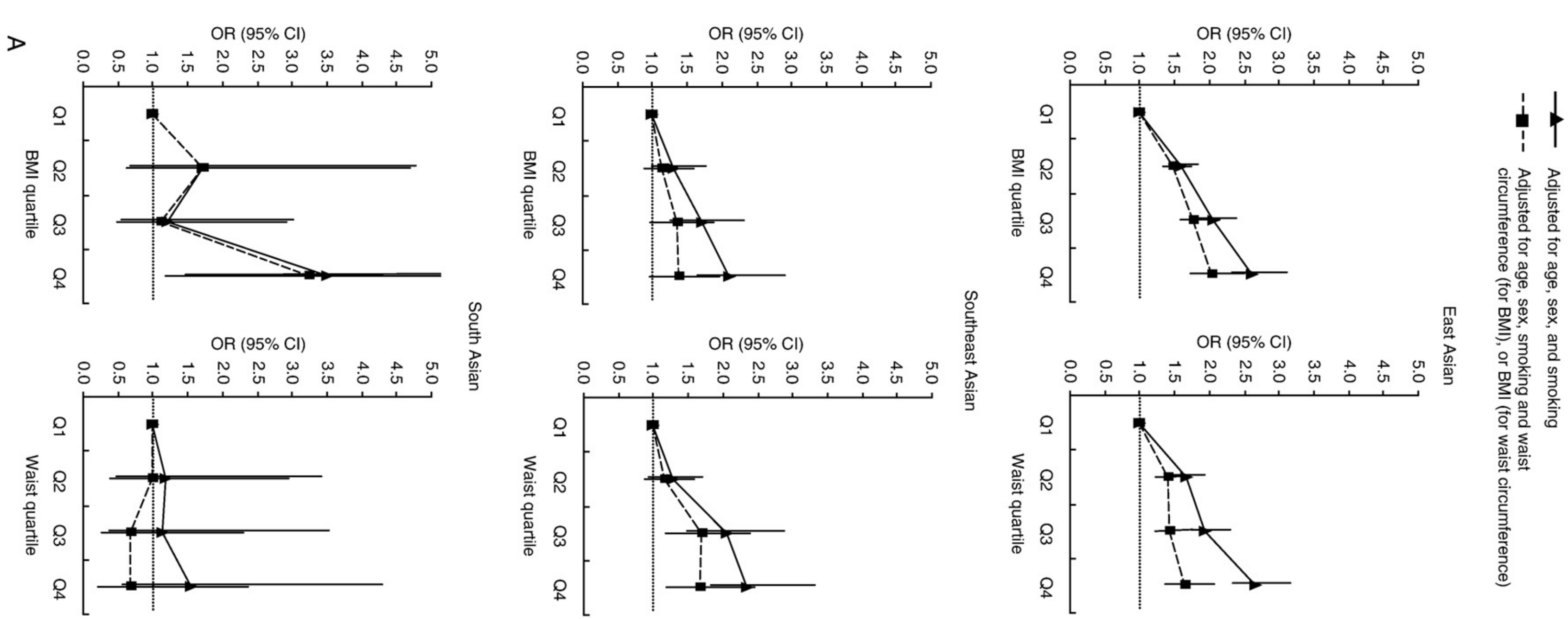
		East Asian (n = 8348)		SE Asian (n = 2333)		South Asian (n = 336)	
		Women (n = 2620)	Men (n = 5728)	Women (n = 935)	Men (n = 1398)	Women (n = 98)	Men (n = 238)
BMI (kg/m^2)							
Hypertension[a]	Yes	24.4 (0.1)	24.3 (0.1)	24.5 (0.4)	24.8 (0.1)	27.2 (1.1)	25.8 (0.3)
	No	23.8 (0.2)	23.7 (0.1)	24.3 (0.6)	24.5 (0.3)	26.1 (1.8)	24.7 (0.6)
	P^d	.0004	<.0001	.6115	.1812	.4561	.0822
Atherogenic dyslipidemia[b]	Yes	24.5 (0.1)	24.4 (0.1)	24.6 (0.4)	24.9 (0.1)	27.0 (1.1)	25.8 (0.3)
	No	23.9 (0.1)	23.9 (0.1)	24.1 (0.5)	24.4 (0.2)	27.8 (1.4)	24.8 (0.6)
	P^d	<.0001	<.0001	.1256	.0135	.4055	.1359
Glucose intolerance[c]	Yes	24.4 (0.1)	24.3 (0.1)	24.7 (0.4)	25.0 (0.1)	27.6 (1.1)	25.4 (0.3)
	No	24.0 (0.1)	24.1 (0.1)	23.8 (0.4)	24.4 (0.2)	26.0 (1.3)	25.9 (0.4)
	P^d	.0057	.0010	.0026	.0047	.1284	.2217
Waist circumference (cm)							
Hypertension[a]	Yes	84.2 (0.4)	87.9 (0.1)	86.1 (1.2)	91.2 (0.4)	87.8 (2.9)	92.8 (1.2)
	No	83.2 (0.6)	87.6 (0.3)	84.0 (1.8)	90.5 (0.7)	86.2 (4.5)	91.9 (2.2)
	P^e	.0515	.2676	.1569	.3775	.6590	.7158
Atherogenic dyslipidemia[b]	Yes	83.9 (0.4)	88.0 (0.2)	86.4 (1.2)	91.7 (0.4)	87.7 (2.9)	92.9 (1.2)
	No	84.2 (0.5)	87.7 (0.2)	84.5 (1.4)	89.4 (0.6)	88.0 (3.6)	91.7 (2.3)
	P^e	.5363	.1726	.0699	.0003	.9064	.6322
Glucose intolerance[c]	Yes	84.3 (0.4)	88.2 (0.2)	85.7 (1.2)	91.6 (0.4)	86.6 (2.9)	93.8 (1.3)
	No	83.4 (0.5)	87.4 (0.2)	86.4 (1.4)	90.0 (0.5)	90.5 (3.3)	90.7 (1.6)
	P^e	.0207	.0008	.4835	.0053	.1221	.0869
Waist-to-height ratio							
Hypertension[a]	Yes	55.2 (0.2)	53.4 (0.1)	55.5 (0.8)	55.2 (0.2)	58.4 (1.9)	56.1 (0.7)
	No	54.9 (0.4)	53.3 (0.2)	53.9 (1.2)	55.2 (0.4)	58.1 (2.9)	55.3 (1.3)
	P^e	.2896	.3431	.1140	.9114	.9074	.5975
Atherogenic dyslipidemia[b]	Yes	55.1 (0.2)	53.5 (0.1)	55.6 (0.8)	55.5 (0.2)	58.2 (1.9)	56.0 (0.7)
	No	55.2 (0.3)	53.3 (0.1)	54.5 (0.9)	54.4 (0.3)	59.5 (2.4)	55.5 (1.4)
	P^e	.7392	.4284	.1039	.0050	.4283	.7184
Glucose intolerance[c]	Yes	55.3 (0.2)	53.6 (0.1)	55.1 (0.8)	55.5 (0.2)	57.5 (1.9)	56.8 (0.8)
	No	54.8 (0.3)	53.1 (0.1)	55.8 (0.9)	54.7 (0.3)	60.3 (2.2)	54.5 (0.9)
	P^e	.0515	.0017	.2725	.0202	.1004	.0414
Waist-to-BMI ratio							
Hypertension[a]	Yes	3.48 (0.02)	3.65 (0.01)	3.59 (0.06)	3.71 (0.02)	3.33 (0.13)	3.66 (0.06)
	No	3.51 (0.03)	3.71 (0.01)	3.60 (0.09)	3.74 (0.04)	3.42 (0.21)	3.71 (0.11)
	P^f	.2146	<.0001	.8843	.4572	.6113	.6494
Atherogenic dyslipidemia[b]	Yes	3.47 (0.02)	3.64 (0.01)	3.58 (0.06)	3.71 (0.02)	3.34 (0.13)	3.65 (0.06)
	No	3.53 (0.02)	3.70 (0.01)	3.62 (0.07)	3.74 (0.03)	3.28 (0.17)	3.71 (0.11)
	P^f	.0005	<.0001	.4645	.4863	.5982	.6719
Glucose intolerance[c]	Yes	3.49 (0.02)	3.66 (0.01)	3.56 (0.06)	3.71 (0.02)	3.28 (0.14)	3.72 (0.06)
	No	3.49 (0.02)	3.67 (0.01)	3.68 (0.07)	3.74 (0.03)	3.47 (0.16)	3.57 (0.08)
	P^f	.7792	.3779	.0145	.3209	.1113	.0851

Values are means (standard deviation).
[a] Treated hypertension or systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg.
[b] Patients currently treated with lipid-lowering agents or fasting triglycerides of at least 150 mg/dL.
[c] Patients with type 1 or 2 diabetes mellitus currently treated with hypoglycemic agents, with a history of diabetes, or with fasting glucose of at least 100 mg/dL.
[d] Adjusted for age, smoking status, and waist circumference.
[e] Adjusted for age, smoking status, and BMI.
[f] Adjusted for age and smoking status.

Table 4
Anthropometric indices in relation to the number of metabolic risk factors clustered in Asian patients

No. of metabolic risk factors clustered[a]	East Asian					SE Asian					South Asian				
	n	BMI (kg/m^2)	WC (cm)	Waist-to-height ratio	Waist-to-BMI ratio	n	BMI (kg/m^2)	WC (cm)	Waist-to-height ratio	Waist-to-BMI ratio	n	BMI (kg/m^2)	WC (cm)	Waist-to-height ratio	Waist-to-BMI ratio
Women															
0	66	23.1 (3.5)	79.8 (10.4)	52.7 (7.3)	3.50 (0.48)	12	20.8 (4.5)	80.0 (13.7)	51.3 (8.7)	3.99 (1.11)	1	21.5	76.0	53.2	3.53
1	472	23.4 (3.6)	81.0 (13.1)	53.5 (8.7)	3.49 (0.47)	130	23.1 (4.9)	83.2 (13.2)	53.7(9.1)	3.68 (0.62)	6	24.6 (4.7)	91.1 (8.6)	59.6 (6.3)	3.80 (0.70)
2	978	24.1 (3.6)	83.3 (11.9)	54.9 (7.8)	3.48 (0.46)	319	24.1 (5.1)	86.4 (16.8)	55.7 (10.6)	3.65 (0.70)	32	27.3 (5.4)	90.7 (15.7)	60.8 (10.8)	3.36 (0.42)
3	1104	25.2 (4.0)	85.5 (11.3)	56.3 (7.6)	3.43 (0.43)	474	24.9 (4.9)	87.9 (14.9)	56.6 (10.1)	3.60 (0.62)	59	26.8 (5.1)	89.0 (12.4)	58.0 (8.3)	3.38 (0.42)
P for trend[b]		<.0001	<.0001	<.0001	.0080		<.0001	.0014	<.0059	.0413		.4926	.8580	.3799	.1905
Men															
0	263	22.8 (3.2)	84.6 (14.9)	51.7 (8.9)	3.75 (0.64)	40	23.3 (3.1)	87.6 (10.9)	53.4(6.2)	3.78 (0.39)	3	24.8 (5.2)	89.7 (13.0)	54.1 (10.6)	3.62 (0.20)
1	1414	23.4 (3.2)	85.8 (10.4)	52.2 (6.2)	3.70 (0.41)	247	24.0 (4.1)	87.5 (11.0)	53.2 (6.8)	3.70 (0.52)	34	24.3 (2.8)	90.3 (7.7)	54.3 (4.3)	3.75 (0.40)
2	2321	24.3 (3.4)	87.7 (9.7)	53.3 (5.8)	3.65 (0.36)	526	24.6 (3.9)	90.1 (11.8)	54.7 (7.4)	3.72 (0.57)	92	25.8 (3.9)	91.5 (11.2)	55.4 (6.5)	3.53 (0.43)
3	1730	25.1 (3.5)	90.2 (10.8)	54.8 (6.4)	3.63 (0.43)	585	25.6 (4.0)	92.7 (11.1)	56.2 (7.0)	3.68 (0.52)	109	26.1 (3.8)	95.5 (18.2)	57.6 (11.0)	3.60 (0.77)
P for trend[b]		<.0001	<.0001	<.0001	<.0001		<.0001	<.0001	<.0001	.1904		.0300	.0281	.0246	.7450

Values are means (standard deviation). WC indicates waist circumference.
[a] Including hypertension, atherogenic dyslipidemia, and glucose intolerance.
[b] Adjusted for age and smoking status.



we compared the odds ratios (ORs) and 95% confidence intervals (CIs) for the presence of at least 2 metabolic risk factors across quartiles of BMI and waist circumference using the logistic regression model in different ethnic groups. Analyses adjusted for waist circumference (for BMI) or adjusted for BMI (for waist circumference) were also performed. The receiver operating characteristic curve analyses were used to determine the optimal cutoff points for BMI and waist circumference with regard to the presence of at least 2 metabolic risk factors. Statistical analyses were performed using the SAS (Chicago, IL) software version 8.01. A P value <.05 was considered to be significant (2-tailed).

3. Results

Among the 11 111 patients enrolled from countries in Asia, 94 did not belong to the 3 predefined Asian ethnic groups and were excluded from the analysis. Of the 11 017 patients studied, 76% were of East Asian origin, 21% were of Southeast Asian origin, and the remaining 3% were of South Asian origin. The distribution of nationality among the 3 Asian ethnic groups is shown in Table 1. Table 2 shows the baseline characteristics of patients stratified by ethnicity and sex. East Asians were older and had a lower prevalence of hypertension, hypercholesterolemia, diabetes, and coronary artery disease than Southeast or South Asians. East Asians

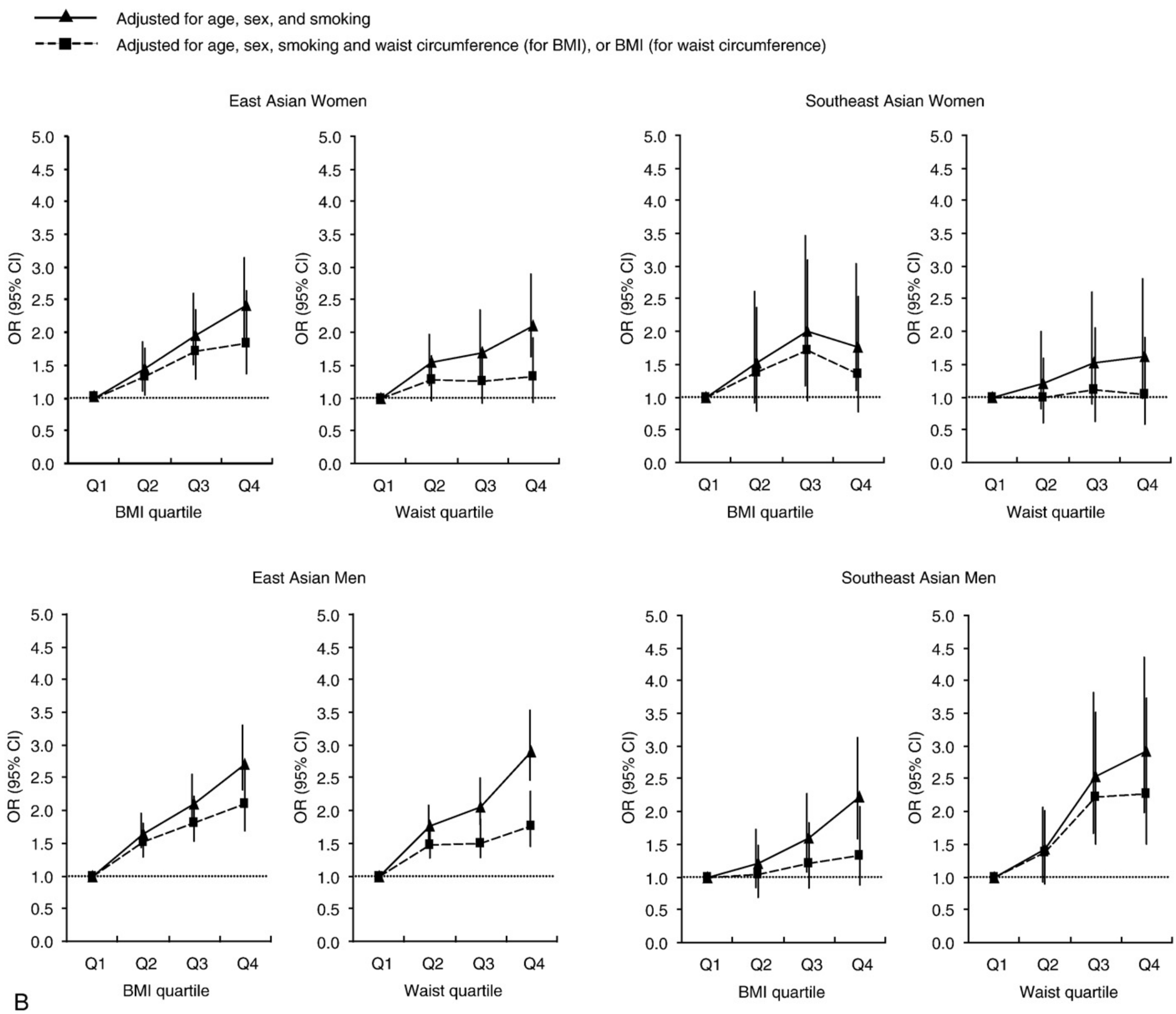


Fig. 1. A, Associations of BMI and waist circumference with at least 2 metabolic risk factors in Asian patients stratified by ethnicity. Vertical bars signify 95% CIs. The cutoff points for BMI quartiles are 22.0, 24.2, and 26.5 kg/m^2. The cutoff points for waist quartiles are 80, 87, and 94 cm. B, Associations of BMI and waist circumference with at least 2 metabolic risk factors in patients of East or Southeast Asian origin stratified by sex. Vertical bars signify 95% CIs. The cutoff points for BMI quartiles are 22.0, 24.2, and 26.5 kg/m^2. The cutoff points for waist quartiles are 80, 87, and 94 cm.

had the lowest BMI, waist circumference, and waist-to-height ratio, followed by Southeast Asians and South Asians. The Southeast Asians had the highest waist-to-BMI ratio among the 3 Asian ethnic groups.

3.1. Effects of sex and ethnicity on the relationships between anthropometric indices and metabolic risk factors

Table 3 summarizes the relationships between different anthropometric indices and metabolic risk factors in the 3 Asian ethnic groups. In East Asians, for both men and women, the mean values of BMI, waist circumference, and waist-to-height ratio were significantly higher in patients with either of 3 individual metabolic risk factors than those without, after adjustment for age and smoking status (data not shown). After further adjustment for each of the other factors (BMI adjusted for waist circumference; waist circumference and waist-to-height ratio adjusted for BMI), only BMI was associated with all 3 individual metabolic risk factors. The mean values of waist-to-BMI ratio were significantly lower in men with hypertension and in both men and women with atherogenic dyslipidemia.

In Southeast Asians, high BMI was associated with atherogenic dyslipidemia in men and with glucose intolerance in both men and women. The mean values of waist circumference and waist-to-height ratio were significantly higher in men with atherogenic dyslipidemia or glucose intolerance. Overall, waist-to-BMI ratio tended to be lower in patients with individual metabolic risk factors than those without. This association reached significance in women with glucose intolerance. In South Asians, BMI tended to be higher in men with hypertension, whereas waist circumference tended to be higher in men with glucose intolerance.

The mean values of BMI, waist circumference, and waist-to-height ratio increased in parallel with the number of metabolic risk factors clustered in both men and women across the different ethnic groups, except for female patients of South Asian origin (Table 4). It is noteworthy that the waist-to-BMI ratio decreased significantly with the increasing number of metabolic risk factors clustered in men and women of East Asian origin and in women of Southeast Asian origin.

3.2. Relative contributions of BMI and waist circumference to clustering of metabolic risk factors

With increasing BMI or waist circumference values, the risk for the presence of at least 2 metabolic risk factors rose progressively, with no distinct threshold, in all 3 Asian ethnic groups (Fig. 1A). In East Asians, the strength of the relationships between waist circumference and metabolic risk factors diminished more substantially when adjusted, than was observed for BMI. The association became nonsignificant in East Asian women after adjustment (Fig. 1B). Compared with the lowest quartile, the OR of the waist circumference top quartile was attenuated from 2.65 (95% CI, 2.28-3.09) to 1.64 (95% CI, 1.35-1.99) after adjustment for BMI. The respective ORs for BMI before and after adjustment for waist circumference were 2.62 (95% CI, 2.25-3.05) and 2.02 (95% CI, 1.67-2.45), respectively. Therefore, BMI correlated dominantly with clustering of metabolic risk factors in East Asians, particularly in women.

In men of Southeast Asian origin, the OR of the top quartile of waist circumference (2.27; 95% CI, 1.42-3.63 after adjustment for BMI) was stronger than that for BMI (1.34; 95% CI, 0.84-2.12 after adjustment for waist circumference). In Southeast Asian women, the graded relationship between BMI and metabolic risk factors was stronger than that for waist circumference after adjustment for age and smoking status. However, the relationships of BMI (OR, 1.36; 95% CI, 0.75-2.45) and waist circumference (OR, 1.03; 95% CI, 0.57-1.89) became nonsignificant after additional adjustment for each other (Fig. 1B).

In South Asians, the graded relationship between BMI and metabolic risk factors remained significant after adjustment for waist circumference (adjusted OR, 3.24; 95% CI 1.18-8.95), whereas that of waist circumference was not significant before (OR, 1.55; 95% CI 0.57-4.21) or after adjustment for BMI (OR, 0.68; 95% CI, 0.20-2.30; Fig. 1A). Sex-specific analysis was not performed in the South Asian group because of the limited case number.

3.3. Cutoff points for BMI and waist circumference with regard to the constellation of metabolic risk factors

Table 5 shows the optimal cutoff points for BMI and waist circumference with regard to the presence of at least 2 metabolic risk factors using the receiver operating

Table 5
Cutoff points for BMI and waist circumference with regard to the presence of at least 2 metabolic risk factors

	Cutoff points	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
BMI (kg/m^2)					
East Asian					
Women	24	55.0	61.5	84.7	26.0
Men	24	55.8	59.2	76.7	35.7
Southeast Asian					
Women	23	62.0	54.0	88.4	20.1
Men	24	59.2	54.4	83.4	25.6
South Asian					
Women	25	63.7	57.1	95.1	10.8
Men	25	56.2	59.5	88.3	20.0
Waist circumference (cm)					
East Asian					
Women	82	58.8	55.6	83.7	25.8
Men	86	62.5	52.2	75.7	36.9
Southeast Asian					
Women	84	55.2	55.5	87.5	18.0
Men	88	63.5	53.9	84.2	27.5
South Asian					
Women	88	53.8	57.1	94.2	8.7
Men	92	54.0	62.2	88.5	20.0

characteristic analyses. The optimal BMI cutoff points were highest in South Asians (25 kg/m^2 in both men and women) and similar between East (24 kg/m^2 in both men and women) and Southeast Asians (24 kg/m^2 in men and 23 kg/m^2 in women). The optimal waist circumference cutoff points were lowest in East Asians (86 cm in men and 82 cm in women), followed by Southeast Asians (88 cm in men and 84 cm in women), and were highest in South Asians (92 cm in men and 88 cm in women). All these results remained similar when patients with established atherothrombotic cardiovascular diseases and those with at least 3 atherothrombotic risk factors were analyzed separately (data not shown).

4. Discussion

In this relatively large data analysis of multiethnic Asian patients at risk of atherothrombosis, we have demonstrated interethnic differences in the distribution of anthropometric indices and in the relationships and relative contributions of BMI and waist circumference to clustering of metabolic risk factors.

In the International Collaborative Study of Cardiovascular Disease in Asia study, BMI and waist circumference were both independently associated with the metabolic syndrome in 15 540 Chinese adults aged 35 to 74 years [11]. Moreover, in our analysis, BMI was found to be a better correlate with metabolic risk factors than waist circumference in East Asians (mainly composed of Chinese and Japanese), particularly in women. Likewise, one recent study showed that, compared with BMI, waist circumference was not effective in identifying the existence of metabolic syndrome in Japanese women aged 35 to 59 years [12]. Taken together, our data and others strongly indicate that measurement of waist circumference alone is insufficient to assess metabolic risk and that the contribution of BMI appears to be incremental. The importance of BMI in conferring risk was further supported by the inverse relationship between waist-to-BMI ratio and the number of metabolic risk factors clustered in East Asians.

As shown in our East Asian patients, we also observed a sex effect in Southeast Asians, with BMI being more important in women, whereas waist circumference was a stronger correlate of metabolic risk factors in men. Similarly, waist-to-BMI ratio decreased with increasing number of metabolic risk factors only in Southeast Asian women and not in men. There is a relative paucity of comparable data in Southeast Asian populations. In the International Collaborative Study of Cardiovascular Disease in Asia study, waist circumference was associated more strongly with fasting plasma glucose and diabetes than BMI in 5302 Thai adults [24]. However, no sex-specific analysis was performed. In contrast to East and South Asians, Southeast Asians had higher waist-to-BMI ratios, suggesting that, for a given BMI, Southeast Asians were more prone to develop abdominal obesity than their East or South Asian counterparts.

We found ethnic-specific cutoff points for waist circumference, suggesting that uniform criteria might not be appropriate for Asian populations. Furthermore, our findings indicate that the current definitions of central obesity for Asians (90 cm in men and 80 cm in women) [1,5] might underestimate the risk for metabolic syndrome in men of East or Southeast Asian origin at risk of atherothrombosis. Although we found a higher cutoff point for waist circumference in South Asians (88 cm in women and 92 cm in men) than a previous report of 10 025 adult Asian Indians (80 cm in women and 85 cm in men) [18], the mean age of the latter group was 40 years compared with 65 years in the REACH cohort.

There are several limitations to our study. The present study design is cross-sectional, which means that we cannot infer causality. Future prospective studies are required to determine the predictive power of different anthropometric indices on the future risk of metabolic syndrome, cardiovascular events, and all-cause mortality in a large multiethnic cohort. Patients enrolled in the REACH Registry were at high risk of atherothrombosis and therefore did not represent the general population. However, given the prognostic value of metabolic risk factors in these high-risk patients, our results should be of value in refining risk assessment and management strategies. The awareness of the high atherothrombotic risk might have motivated our study participants for lifestyle changes. These lifestyle changes, like increasing physical activity and reducing caloric intake, may exert a greater impact on waist circumference than on BMI as a result of decreasing fat mass and increasing lean muscle mass [25]. This may therefore attenuate the correlations between anthropometric measures (especially waist circumference) and metabolic risk factors. High-density lipoprotein cholesterol levels were not obtained in the REACH Registry. Therefore, we have modified the definition of atherogenic dyslipidemia to that of “fasting plasma triglycerides of at least 150 mg/dL or hypercholesterolemia treated with medication.” Indeed, compared with definitions like “fasting triglycerides of at least 150 mg/dL,” “treated hypercholesterolemia alone,” or “fasting total cholesterol of at least 200 mg/dL,” our present definition of atherogenic dyslipidemia exhibited the strongest association with BMI and waist circumference (data not shown). In addition, because of the relatively small number of South Asians in our cohort, the findings in this ethnic group require validation in a larger population. As subjects with similar BMI and waist circumference can have different fat distribution in their subcutaneous and visceral compartments, further studies are needed to elucidate these ethnic-specific relationships using standard methods, such as computed tomography or magnetic resonance imaging.

Given the global epidemic of obesity, with Asia at the forefront, our data suggest that both BMI and waist circumference should be included in metabolic risk assessment in these high-risk multiethnic Asian populations. The varied cutoff points for BMI and waist circumference in different Asian ethnic groups suggest that uniform anthropometric index cutoff values for all Asian ethnic groups are not appropriate to assess obesity-related metabolic complications, even in patients with established atherothrombotic diseases.

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