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Impact of sex-specific body composition on cardiovascular risk factors: the Hong Kong Cardiovascular Risk Factor Study

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Abstract

The aim of the study was to analyze the effects of sex-specific distribution of adiposity, particularly emphasizing the independent contribution of waist and hip circumferences relative to body mass index (BMI), on cardiovascular risk factors in a Chinese population. Blood pressure and anthropometric and biochemical parameters were measured in 2510 population-based Chinese subjects. The relative contributions of waist and hip circumferences to the presence of cardiovascular risk factors were determined. The Chinese men were significantly larger than women, with greater BMI and central adiposity. Waist and hip circumferences were both positively associated with the presence of hypertension, dyslipidemia, and diabetes. However, after adjustment for BMI and age, hip circumference exhibited a significant dose-dependent inverse relationship with dyslipidemia and diabetes in women, but not men. Sex-specific differences exist. After adjustment for age and BMI, hip circumferences independently and inversely contribute to cardiovascular risk in women, but not in men. Increasing adjusted waist circumference was associated with increased risk of hypertension and diabetes in Chinese and dyslipidemia in women only.

1. Introduction

Sex-specific anthropometric differences have been well reported in white populations and are associated with differential risk of cardiovascular disease. Premenopausal women typically have a lower body adipose distribution (gynoid) characterized by fat deposition in the gluteofemoral region. However, in men, an upper body adipose distribution (android) develops, which is characterized by central fat deposition in the abdominal intraperitoneal and subcutaneous regions. Android, compared with gynoid, adiposity is associated with increased prevalence of cardiovascular risk factors, including hypertension, type 2 diabetes mellitus [1,2] and subsequent atherosclerotic vascular disease [3], and contributes to the differences in the prevalence of vascular disease between men and women. However, extrapolation of data derived from white populations may not be applicable to those of Chinese origin. Data have shown a greater cardiovascular risk at a given level of adiposity in Chinese compared with whites, and this has led the World Health Organization to introduce lower criteria for general and central obesity in Asian subjects [4]. Similarly, for a given body mass index (BMI), Chinese have been reported to have greater percentage body fat compared with whites [5,6], further suggesting ethnicity may influence the relationship between obesity and cardiovascular risk. In this population-based study, we examine

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how sex-specific adiposity may influence the development of cardiovascular risk, and particularly emphasize the independent contribution of waist and hip circumferences relative to BMI.

2. Methods

2.1. Subject selection

In a cardiovascular risk factors prevalence study, 7730 Chinese, aged 25 to 74 years, were randomly selected for telephone interviews in Hong Kong from 1994 to 1996, with a response rate of 78%. One household member, who was a Chinese Hong Kong resident, was randomly selected for an interview. Pregnant women and those with serious diseases such as cancer or who were hospitalized were excluded. A standardized questionnaire modified from the questionnaire used in the 1992 Singapore National Health Survey was used, with the addition of the WHO Rose-Angina Questionnaire (previously translated into Chinese and validated in a study of elderly Chinese). Information collected included demographic characteristics, lifestyle factors, and history of cardiovascular diseases and diabetes mellitus. The method of telephone interview was validated in a morbidity survey in Hong Kong [7]. At the end of the interview, the respondent was invited to come to the Clinical Biochemistry Unit of Queen Mary Hospital, a teaching hospital of the Faculty of Medicine, the University of Hong Kong, for physical examination and blood testing. One to 2 days before the appointment to the hospital, the subjects were reminded to fast for 12 hours before their visit. On arrival, the subjects' identity was checked, an information sheet provided, and a consent form signed. The study complied with the Declaration of Helsinki and was approved by the University of Hong Kong Faculty of Medicine Ethics Committee. The clinic attendees closely matched the overall Hong Kong population because there was no difference in age distribution or socioeconomic characteristics between subjects attending for laboratory tests, those who participated in the telephone interview, and the population as a whole as described in the 1996 Hong Kong by-census, and thus, nonattendance bias should be small [8]. The detailed methods of measurement had been reported elsewhere [8,9].

2.2. Measurements

A total of 2510 subjects had physical examinations, including blood pressure, anthropometry, and blood tests (fasting and 2-hour post–75-g anhydrous glucose load), and had fasting insulin results available.

2.2.1. Anthropometry measurements

Height was measured to the nearest 0.5 cm and weight to the nearest 0.1 kg (Detecto Instrument, Webb City, MO), without shoes and in light clothing. Participants fasted for 12 hours before attending the survey center.

2.2.2. Blood pressure measurement

Seated blood pressure was measured in duplicate after 10 minutes of rest, 2 to 3 minutes apart. If the readings differed by 4 mm Hg or higher, then a third reading was taken. Extreme blood pressures were confirmed on a subsequent visit.

2.3. Laboratory accreditation

The biochemical parameters were measured in the Clinical Biochemistry Unit of Queen Mary Hospital. The laboratory used standard methods and met international quality control standards. The laboratory participates in the Murex External Quality Control Program for glucose and in the Royal College of Pathologist of Australasia/Australasian Association of Clinical Biochemists Quality Control Program for Lipids and Lipoproteins. The laboratory has met the criteria of the Centers for Disease Control, National Heart, Lung, and Blood Institute Standardization Program for Cholesterol.

2.4. Biochemical measurements

A venous sample of blood was then taken for the measurement of fasting biochemical parameters. Afterward, 75 g of anhydrous glucose was dissolved in 200 mL of distilled water and drunk over 2 to 3 minutes. The subjects remained seated in the center, and after 2 hours, a further sample was taken for glucose estimation. Fasting (12 hours) glucose (intra-assay coefficient [CV] of variation, 1.8% at 4.4 mmol/L), cholesterol (CV, 2.9% at 3.3 mmol/L and 2.5% at 7.0 mmol/L), triglycerides (CV, 3.3% at 0.63 mmol/L), and high-density lipoprotein cholesterol (HDL-C) (CV, 4.2% at 1.64 mmol/L) were carried out in the Clinical Biochemistry Unit of Queen Mary Hospital using standardized procedures. Fasting plasma insulin was measured in 2510 subjects, but data describing the 2-hour post–75-g anhydrous oral glucose load insulin levels were only available in a subset of the subjects ($n = 839$).

2.5. Disease classification criteria

Subjects were considered hypertensive if their systolic and/or diastolic blood pressures were 140/90 mm Hg or higher or if they were receiving blood pressure–lowering drugs [10]. Subjects were classified as having a normal glycemic profile if their fasting plasma glucose was less than 6.1 mmol/L and oral glucose tolerance test (OGTT) level was less than 7.8 mmol/L. Diabetes was classified as a fasting glucose of 7.0 or higher or postload glucose of 11.1 mmol/L or higher or were receiving hypoglycemic medication, whereas glucose intolerance in the nondiabetic subjects was classified as ≥ 6.1 and <7.0 mmol/L or ≥ 7.8 and <11.1 mmol/L, respectively [11]. For the indexes of insulin resistance we used the fasting insulin-glucose product, which if divided by 22.5 is numerically equivalent to the homeostasis model assessment [12], which has been shown to correlate well with the results of the euglycemic

Table 1
Anthropometric characteristics, blood pressure characteristics, and prevalence of metabolic abnormalities in the male and female subjects

	Male subjects	Female subjects	*P*
n	1231	1279	–
Age (y)	46.0 ± 13.2	45.0 ± 12.3	NS
Weight (kg)	66.2 ± 10.5	56.4 ± 9.2	<.001
Height (m)	1.65 ± 0.06	1.54 ± 0.06	<.001
BMI (kg/m^2)	24.3 ± 3.4	24.0 ± 3.8	.037
Waist circumference (cm)	83.0 ± 9.6	75.4 ± 9.5	<.001
Hip circumference (cm)	94.3 ± 6.3	93.7 ± 6.9	.010
Waist-to-hip ratio	0.88 ± 0.07	0.80 ± 0.08	<.001
Hip-to-height ratio	0.57 ± 0.04	0.61 ± 0.04	<.001
Systolic blood pressure (mm Hg)	122 ± 17	117 ± 21	<.001
Diastolic blood pressure (mm Hg)	77 ± 10	73 ± 11	<.001
Mean arterial pressure (mm Hg)	92 ± 12	88 ± 14	<.001
Dyslipidemia: cholesterol/ triglyceride/either (%)	27.4/11.2/31.9	19.2/5.1/20.7	All <.001
Hypertension (%)	18.3	17.8	NS
Obesity by BMI/ waist/either (%)	37.9/21.5/39.6	33.6/29.0/37.7	.027/ <.001/NS
Hyperglycemia GI/ diabetes/total	13.8/9.5/23.3	15.4/10.0/25.4	all NS

Values are mean ± SD. GI indicates glucose intolerance; NS, nonsignificant by *t* test.

hyperinsulinemic clamp in population-based studies [13] and the glucose and insulin results of the OGTT. Hypertriglyceridemia was classified as either fasting plasma triglycerides of 2.3 mmol/L or higher. Hypercholesterolemia was classified as total cholesterol of 6.2 mmol/L or higher or between 5.2 and 6.2 mmol/L with a total-to–HDL-C ratio of more than 5.0 or if the subjects were receiving treatment to lower lipid levels [14,15]. General obesity was classified as a BMI of 25.0 kg/m^2 or higher [4] and central obesity as a waist circumference of 80 cm or more in women or 90 cm or more in men [4].

2.6. Statistical analyses

2.6.1. Univariate analyses

Data from normally distributed parameters are presented as mean ± SD, whereas skewed data (triglycerides, fasting and OGTT glucose and insulin, and the fasting insulin-glucose product) were logarithmically transformed and expressed as geometric mean with 95% confidence intervals. The Statistics Package for Social Sciences (SPSS for windows, version 11.0.1, 2001, SPSS, Chicago, IL) was used for the following analyses. Student *t* test was used to determine differences in continuous variables between the male and female groups. The χ^2 test was used to determine differences in the prevalence rates of the categorical cardiovascular risk factors between the tertile groups and sexes.

2.7. Multivariate analyses

Following an approach previously described by Seidell et al [16], we used linear regression in sex-specific analyses with waist and hip circumferences as dependent variables to determine age-adjusted residuals (model 1) and also BMI and age-adjusted residuals (model 2). In addition, as a relationship between hip size and lifestyle factors have been reported in white populations, we performed a further analysis that adjusted for smoking and alcohol usage and physical activity and also waist circumference [17]. Tertiles of these residuals were then determined. The lowest tertile represents subjects with relatively small hip or waist circumferences for their body size, whereas the upper tertile represents those with excessive hip or waist circumferences. The use of residuals in these analyses allows the evaluation of the independent contributions of correlated parameters such as the anthropometric parameters included in the current study [16]. We then used logistic regression analyses to determine the odds ratios for the presence of hypertension, glucose intolerance/diabetes, or dyslipidemia for the tertile groups of hip and waist circumference residuals. The residual tertile group representing the lowest waist or hip circumferences for body size was used as the reference group. The effects of menopausal status were also investigated by subdividing the female subjects based on the mean menopausal age in Hong Kong (51 years), and the above analyses were repeated in each group.

3. Results

3.1. Sex-specific differences

Despite being of similar age, there were large sex differences between the male and female Chinese subjects. The Chinese male subjects had a larger mean waist circumference than the females (Table 1), but more females were classified as centrally obese than the males (29.0% vs 21.5%, $P < .001$), yet the degree of generally obese subjects (by BMI) was greater in men (37.9% vs 33.6%, $P = .027$). The overall combined proportion (by BMI and/or waist circumference) of obese male and female subjects was similar

Table 2
Plasma biochemical characteristics in the male and female subjects

	Men	Women	*P*
n	1231	1279	–
Age (y)	46.0 ± 13.2	45.0 ± 12.3	NS
Total cholesterol (mmol/L)	5.1 ± 1.0	5.0 ± 1.0	.012
HDL-C (mmol/L)	1.16 ± 0.30	1.34 ± 0.32	<.001
LDL-C (mmol/L)	3.3 ± 0.8	3.2 ± 0.9	<.001
Triglyceride (mmol/L)	1.23 (1.17-1.30)	1.01 (0.96-1.05)	<.001
Apolipoprotein A-I (mmol/L)	1.35 ± 0.26	1.40 ± 0.27	<.001
Apolipoprotein B (mmol/L)	1.01 ± 0.27	0.92 ± 0.30	<.001
Fasting glucose (mmol/L)	5.3 (5.2-5.4)	5.1 (5.1-5.2)	.001
Fasting insulin (pmol/L)	5.1 (4.9-5.5)	5.8 (5.5-6.1)	<.001
OGTT 2-h glucose (mmol/L)	6.5 (6.3-6.8)	6.9 (6.8-7.1)	<.001
OGTT 2-h insulin (pmol/L)	48.7 (44.8-53.0)	57.8 (54.2-61.5)	.002
Fasting insulin-glucose product	27.3 (25.4-29.4)	29.8 (28.1-31.6)	.001

Values are mean ± SD or geometric mean (geometric 95% confidence intervals of the mean). LDL-C indicates low-density lipoprotein cholesterol.

Table 3
Age-adjusted odds ratios with 95% confidence intervals from logistic regression analyses for the independent variables hip and waist circumferences

Dependent variables (model 1)	Male subjects				Female subjects			
	First	Second	Third	P for trend	First	Second	Third	P for trend
Hip circumference age-adjusted tertiles								
Hypertension	1.0	1.32 (0.86-2.03)	3.04 (2.02-4.59)	<.001	1.0	2.66 (1.65-4.28)	4.38 (2.80-6.86)	<.001
GI/DM	1.0	1.58 (1.09-2.31)	3.12 (2.16-4.49)	<.001	1.0	1.04 (0.72-1.49)	1.86 (1.33-2.60)	<.001
Dyslipidemia	1.0	1.95 (1.42-2.69)	3.15 (2.30-4.33)	<.001	1.0	1.81 (1.23-2.67)	1.99 (1.37-2.88)	<.001
Waist circumference age-adjusted tertiles								
Hypertension	1.0	2.50 (1.54-4.06)	4.36 (2.76-6.89)	<.001	1.0	2.02 (1.07-3.79)	6.83 (3.80-12.26)	<.001
GI/DM	1.0	2.39 (1.56-3.67)	5.42 (3.62-8.11)	<.001	1.0	1.69 (1.09-2.60)	5.04 (3.32-7.63)	<.001
Dyslipidemia	1.0	2.42 (1.74-3.39)	4.19 (3.01-5.82)	<.001	1.0	2.17 (1.34-3.51)	4.54 (2.85-7.21)	<.001

GI/DM indicates glucose intolerance/diabetes mellitus.

(39.6% vs 37.7%). Male subjects had significantly higher hip circumferences than females in this Chinese population (Table 1), although after adjustment for height using the hip-to-height ratio the situation was reversed ($P < .001$). The male subjects had higher values for blood pressure (Table 1), lipid profile, and glucose control, but otherwise significantly better insulin resistance parameter levels (Table 2). However, there was a similar prevalence of glucose intolerance (13.8% vs 15.4%) and type 2 diabetes mellitus (9.5% vs 10.0%) in the Chinese men and women, respectively (Table 1).

3.2. Relationship between metabolic abnormalities and anthropometry in the Chinese subjects

In both the male and female Chinese subjects, there was a clear positive relationship with increasing odds ratios for having hypertension, glucose intolerance/diabetes, or dyslipidemia, except for hypercholesterolemia in the females, and increasing age-adjusted tertiles of waist or hip circumference (model 1, Table 3).

In contrast, in the female Chinese subjects, increasing hip circumferences adjusted for age and BMI were significantly associated with decreasing proportion of diabetes and the dyslipidemias, reducing the risk by 49% and 47% when the extreme tertiles were compared (model 2, Table 4). This finding was not observed in the male subjects. There was no evidence that the age- and BMI-adjusted hip size effect in model 2 differed by women's menopausal status (data not shown). The relationship between increasing tertiles of waist circumference adjusted for age and BMI with increasing risk for the presence of hypertension, glucose intolerance/diabetes, or the dyslipidemias was similar, but of less strength, to the results without adjustment for BMI. Only dyslipidemia in the male subjects did not reach significance. In female subjects, there were lower odds ratios of each condition, but there was a significant increase when the upper adjusted waist circumference tertile was compared with the lowest (Table 4). Age- and BMI-adjusted tertiles of hip circumference for both male and female subjects were significantly associated with lower levels of education. For instance, in the lowest adjusted hip circumference tertile, the prevalence of those receiving at most primary school education was 43.6% and 33.0% compared with the prevalence of 9.7% and 21.3% of those reaching at least matriculation-level education for women and men, respectively, whereas in the highest adjusted hip circumference tertile, the prevalence of primary school education or below was 38.4% and 22.0%, respectively, for at least matriculation-level education, it was 16.0% and 27.6%, respectively, for women (χ^2 = 7.97, P = .019) and men (χ^2 = 13.3, P = .001). The odds ratios after adjustment of the analyses for lifestyle factors and waist circumference were similar to those reported in Tables 3 and 4, and as such the data are not shown.

Table 4
Age- and BMI-adjusted odds ratios with 95% confidence intervals from logistic regression analyses for the independent variables hip and waist circumferences

Dependent variables (model 2)	Male subjects				Female subjects			
	First	Second	Third	P for trend	First	Second	Third	P for trend
Hip circumference age- and BMI-adjusted tertiles								
Hypertension	1.0	0.87 (0.60-1.26)	1.30 (0.92-1.84)	.072	1.0	0.70 (0.49-1.0)	0.91 (0.65-1.28)	NS
GI/DM	1.0	0.97 (0.70-1.34)	0.92 (0.66-1.28)	NS	1.0	0.71 (0.52-0.96)	0.51 (0.37-0.71)	<.001
Dyslipidemia	1.0	0.92 (0.68-1.24)	1.07 (0.80-1.43)	NS	1.0	0.53 (0.38-0.74)	0.53 (0.38-0.74)	<.001
Waist circumference age- and BMI-adjusted tertiles								
Hypertension	1.0	1.07 (0.74-1.56)	1.66 (1.16-2.36)	.008	1.0	0.82 (0.56-1.19)	1.46 (1.03-2.05)	.005
GI/DM	1.0	1.38 (0.98-1.94)	1.77 (1.26-2.47)	.004	1.0	0.82 (0.56-1.19)	1.46 (1.03-2.05)	.005
Dyslipidemia	1.0	1.03 (0.76-1.39)	1.31 (0.98-1.76)	NS	1.0	0.94 (0.66-1.33)	1.55 (1.12-2.15)	.004

4. Discussion

As expected, there were clear sex-specific differences in a range of metabolic parameters, with the larger Chinese male subjects having worse blood pressure and lipid profiles, but the Chinese female subjects having more adverse fasting insulin and postprandial insulin and glucose levels, although not all differences are likely to be clinically significant. Similar findings have been reported in white populations, such as in the DECODE study, although in that study, women had higher total cholesterol levels [18]. These differences will in part be the result of the concomitant sex-specific differences in anthropometric indexes, with men having a larger BMI and being more centrally obese. For a given BMI, Chinese subjects have been reported to have a greater proportion of body fat [5], which contributes to an increased risk of cardiovascular risk factors [4]. Chinese women had a significantly greater proportion of central obesity when compared with the Chinese men. In Chinese women, central obesity has been associated with hyper-androgenicity and increasing testosterone [19] and cortisol and decreased growth hormone levels that contribute to the development of centrally deposited fat depots [20].

The relationship between increasing waist circumference, whether directly or after adjustment for age and BMI, and increasing prevalence of cardiovascular risk factors is clearly evident. The pivotal role of central adiposity, which incorporates elevated visceral fat levels, in the pathogenesis of cardiovascular disease has been reported in studies involving both Chinese and white subjects and links hypertension, insulin resistance and type 2 diabetes mellitus, and the dyslipidemias, particularly hypertriglyceridemia [1,4,16,21-27]. Central adiposity is likely to contribute to the development of cardiovascular disease risk factors in a number of ways. It is an important determinant of insulin resistance [1,28] that limits insulin-mediated antilipolytic action promoting free fatty acid production. Free fatty acids subsequently increase gluconeogenesis, yet reduce glucose uptake, as free fatty acids enter the Randle cycle oxidation in preference to glucose [29] and reduce insulin clearance, further promoting insulin resistance [30]. Resistance decreases lipoprotein lipase activity [31] and increases activity of cholesteryl ester transfer protein [32] and triglyceride lipase [31], which results in increased triglyceride and decreased HDL-C levels. Similarly, the resultant hyperinsulinemia promotes sodium reabsorption and vascular smooth muscle hypertrophy that may contribute to increases in blood pressure [33,34]. Obesity also contributes to adverse blood pressure and lipid profiles independently [1,28], through factors such as adipocyte-secreted leptin and renin-angiotensin system components [33,35,36].

Hip circumference was similarly associated with the presence of cardiovascular risk factors in the unadjusted analyses, as we and others have reported previously [1,21]. It is likely that the positive relationship in the Chinese population between cardiovascular risk factors and hip circumference in the unadjusted analyses reflects increasing adiposity that is being deposited both peripherally as indicated by increasing hip circumference and centrally, particularly visceral fat depots, as measured by waist circumference. However, we also examined the relationship between hip circumference and cardiovascular risk factors after adjustment for age and BMI, which removes much of the effect of increasing adiposity from the relationship, enabling the elucidation of the independent contribution of hip or waist circumference. In these analyses, there was a clear inverse relationship between decreasing hip circumference and increasing glucose intolerance and the dyslipidemias in the female subjects, but not the males. In white subjects, similar findings have been reported, but in contrast, those studies also reported the relationship in men [16,23,24,37,38]. Adjusted hip circumferences were inversely associated with hypertension in both white men and women, but the relationship was weaker and less consistent [24,37].

Other developing Oriental populations have also reported associations between anthropometry and cardiovascular risk factors that contrast with those from white populations. For instance, in Koreans, the inverse relationship between height and coronary heart disease observed in whites was absent [39]. In Hong Kong, women with low socioeconomic status have increased cardiovascular risk, as seen in modern societies, but the reverse is true in men, who are at increased risk in high socioeconomic settings, as observed in the West before the 1970s [40]. Similar transitional secular changes are currently visible in modern societies where the male-to-female sex ratio for coronary heart disease is high and results from increased disease in men, not women [41]. These large sex disease ratios are not observed in societies with low levels of disease [41], suggesting the high level of disease in men may be a result of inadequate or maladaptation in men, but not women, to their environment, or unaccounted for lifestyle or environmental factors.

Overall, these data suggest that those female subjects with a relatively small hip circumference are at increased risk of developing diabetes and dyslipidemia and that a larger hip circumference for a given body size is protective. In whites, the inverse association between adjusted hip circumference and risk factors has been associated with a range of lifestyle factors including smoking, alcohol consumption, and level of physical activity [17], which may in part mediate the differences. These lifestyle factors may contribute to the inverse association between adjusted hip circumference and visceral fat levels in white men, although not in women [24]. Visceral fat is a major determinant of a number of metabolic abnormalities, including in Chinese subjects [25-27]. Thus, a relationship between adjusted hip circumference and visceral fat may account for the observed differences.

In addition to a possible relationship with body fat, particularly that surrounding the viscera, relatively small hip circumferences may also reflect, at least in part, a relatively small leg muscle mass [16,42], a major site of glucose disposal that may predispose individuals to the deleterious effects of insulin resistance [43]. However, other studies have reported either no difference in mid-thigh skeletal muscle cross-sectional area [27] or increased lean mass in postmenopausal obese women with or without metabolic abnormalities [26]. In addition, a possible explanation is that relatively small hip size may be a marker of poor childhood development, which, through other proxy markers, such as leg length [44], has been associated with the development of type 2 diabetes mellitus [45], higher blood pressure [46], and associated biological risk factors [46,47]. The absence of the relationship between height and coronary heart disease in Koreans also supports differences in the relationship between anthropometric parameters and risk factors in populations undergoing secular transition later than in developed Western populations [39]. These transitional changes in Oriental populations, particularly the Chinese, are likely to be more extreme than those in Western populations. For instance, in China, more than 10 million died during World War II, and during the Cultural Revolution, in the Great Leap Forward of 1959 to 1961, 16 to 30 million people were reported to have died of starvation [48]. It is possible that differences in transitional status between men and women could account for differences in the association with adjusted hip circumferences and cardiovascular risk factors.

In summary, after adjustment for BMI, hip circumference independently and inversely contributes to cardiovascular risk in women but not in men, unlike in white populations where the relationship was identified in both sexes.

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