Original Article

Central obesity and risk of cardiovascular disease in the Asia Pacific Region

Asia Pacific Cohort Studies Collaboration[1]

This paper compares body mass index, waist circumference, hip circumference, and waist-hip ratio as risk factors for ischaemic heart disease and stroke in Asia Pacific populations. We undertook a pooled analysis involving six cohort studies (45 988 participants) and used Cox proportional hazards regression to assess the associations of the four anthropometric indices with stroke and ischaemic heart disease by age, sex and region. During a mean follow-up of six years, 346 stroke and 601 ischaemic heart disease events (fatal and non-fatal) were documented. Overall, a one-standard deviation increase in index was associated with an increase in risk of ischaemic heart disease of 17% (95% CI 7-27%) for body mass index, 27% (95% CI 14-40%) for waist circumference, 10% (95% CI 1-20%) for hip circumference, and 36% (95% CI 21-52%) for waist-hip ratio. There were no significant differences between age groups, sex, and region. None of the four anthropometric indices had a strong association with risk of stroke. These data indicate that measures of central obesity such as waist circumference and waist-hip ratio are strongly associated with risk of ischaemic heart disease in this region. Therefore, we suggest that, along with calculation of body mass index, measures of central obesity such as waist circumference and waist-hip ratio should be undertaken routinely.

Key Words: abdominal obesity, waist circumference, waist hip ratio, cardiovascular diseases, cohort studies, Asia

Introduction

The risk of heart disease and stroke increases continuously with increasing body mass index (BMI)[1,2] but the relative importance of total and central obesity is still debated. There are uncertainties over what anthropometric index, BMI, waist circumference (WC), hip circumference (HC), or waist-hip ratio (WHR), is the most important risk factor for cardiovascular events. Previous prospective studies comparing the importance of various anthropometric indices in determining risk of CVD have been mainly conducted in North America,[3,4] Europe,[5-7] and more recently Australia.[8] There is a lack of similar prospective data from the greater Asia Pacific region, despite frequent assertions that lower cut-offs should be used to define overweight and obesity in Asian populations.[9,10] Data collected with the Asia Pacific Cohort Studies Collabora-tion allow comparison of four anthropometric indices as risk factors for both stroke and ischaemic heart disease (IHD) in the Asia Pacific region.

Methods

Identification of studies and collection of data

The Asia Pacific Cohort Studies Collaboration (APCSC) is an individual participant data overview (meta-analysis) involving prospective cohort studies in the Asia Pacific region. As reported elsewhere,[11] studies are eligible for inclusion in the collaboration if they satisfied the following criteria; 1) a study population from the Asia Pacific region: 2) prospective cohort design; 3) at least 5 000 person-years of follow-up recorded; 4) date of birth or age, sex, and blood pressure recorded at baseline; 5) date of death or age at death recorded during follow-up. Studies are identified by literature searches (Medline and EMBASE), scrutiny of abstracts from proceedings of meetings, and enquiry among collaborators and colleagues. There are no language restrictions.

In addition to these inclusion criteria, data sought on individual participants include date of baseline survey, height, weight, WC, HC, and smoking habit. As height, weight, WC, and HC were not essential for inclusion in the collaboration not all studies could contribute to the analyses reported here. Measurements of indices were variably standardized and not uniform in the different studies. Outcome data for these analyses included fatal and non-fatal stroke and IHD events, where fatal events were defined as death occurring within 28 days of the event. All data provided to the secretariat were checked for completeness and consistency and were recoded where necessary to maximize comparability across cohorts. Summary reports were referred back to principal investigators of each collaborating study for review and confirmation.

Statistical methods

In eligible cohorts, analyses were restricted to participants aged 20 years or older who had data on baseline height, weight, WC and HC. BMI was calculated as weight (kg) divided by the square of height (m), and WHR was calculated as WC (cm) divided by HC (cm). Participants with values outside the following ranges were excluded since it was assumed that they were due to recording errors: $12 \leq BMI \leq 59$, $50 \leq WC \leq 150$ and $50 \leq HC \leq 200$ ($N = 17$). Analyses were undertaken for total (fatal and non fatal

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combined) events and performed separately for two endpoints: IHD and stroke.

Cox proportional-hazards analyses[12] were used to regress time until first event against anthropometric index at baseline within individual participant data collected in all cohorts. Regression coefficients and standard errors were calculated with adjustment for smoking (current vs. non-current). Analyses were also adjusted for age, and stratified by sex and cohort to control for confounding and reduce statistical heterogeneity. Age at risk (age at time of event) was treated as a time-dependent covariate[12] in order to assess change in hazards as an individual's age increases.

Analyses assessed the relationship of the four individual anthropometric indices to cardiovascular endpoints. Hazard ratios and 95% confidence intervals were estimated for a one standard deviation (SD) increase in each index. This 'standardized' comparison of hazard ratios was necessary as each index is measured on a different scale. The change in likelihood ratio χ^2 was used as a measure of the improvement of goodness of fit,[12] or 'informativeness', between a model containing each anthropometric index compared with a model that contained age and smoking status, stratified by sex and cohort, but no anthropometric index (the 'base model').

Age-specific analyses included age at risk categories of <65 and 65+ years, and analyses were also conducted by sex and region (Asia vs. Australia). Sensitivity analyses were undertaken excluding the first three years of follow-up in order to determine the potential impact on observed associations of confounding by prevalent disease at baseline. Further sensitivity analyses investigated the impact of limiting the analyses to fatal events only in order to determine if there was a differential effect on risk of non-fatal and fatal events, and the effect of excluding the study with the largest number of events (Western Australia AAA Screenees Study) from the analyses.

Results

Study sample

The analyses are based on data from six cohort studies from APCSC that provided data on height, weight, WC and HC at baseline (Table 1). In total there are 45 988 participants with 278,680 person years of follow-up. There are two cohorts from mainland China (14% of participants), one from Hong Kong (4%), and three from Australia (82%). The mean age of participants at baseline was 54 years, and 48% were female. During a mean follow-up of 6.1 years, a total of 346 strokes (155 fatal) and 601 IHD events (506 fatal) were recorded. The mean (standard deviation) for each anthropometric measure was: BMI 26.2 (4.2) kg/m^2; WC 86.4 (12.3) cm; HC 101.0 (8.4) cm; and WHR 0.85 (0.08). The table demonstrates expected variability in anthropometry between the Asian and non-Asian cohorts.

Ischaemic heart disease

After allowing for age, sex, cohort and smoking, there was a significant log-linear association between each of the anthropometric indices and IHD (Fig. 1). A one SD increase in the index is associated with an increase in risk of total IHD of 17% (95% CI 7-27%) for BMI, 27% (95% CI 14-40%) for WC, 10% (95% CI 1-20%) for HC, and 36% (95% CI 21-52%) for WHR (Fig. 1). Most frequently, the hazard ratios are highest for WHR and WC, and HC consistently has the weakest association. Examination of results by age, sex, and region sub-groups (Fig.1) suggests that associations are stronger in those aged less than 65 years, in males, and in the Australian cohorts. However, the confidence intervals of the hazard ratios within the subgroups overlap so differences may not be statistically significant.

The change in likelihood ratio χ^2 statistic comparing each anthropometric index with the base model for total IHD is shown (Fig. 1). Overall WHR is the most informative, followed closely by WC. The only exception is for those aged less than 65 years where WC is the better predictor. HC consistently ranks as the least important index, whereas BMI is usually intermediate between HC and WC or WHR.

The same patterns were found when analyses were restricted to fatal IHD events (data not shown). Sensitivity analyses excluding the first three years of follow-up also produced similar results (data not shown), and demonstrated stronger associations with IHD than those seen in the main analyses, suggesting that pre-existing disease at baseline may have confounded the associations. Exclusion of the largest study from the analyses also produced similar results (data not shown), and the associations were again stronger than those seen in the main analyses.

Stroke

The association between each of the anthropometric measures and total stroke events is weak, with a one SD increase in the index being associated with an increase in the risk of total stroke of 3% (95% CI -9, 16%) for BMI, 5% (95% CI -9, 20%) for WC, 0% (95% CI -11, 13%) for HC and 9% (95% CI -8, 28%) for WHR. No clear associations between any of the anthropometric measures and stroke were seen across the age, sex, and region subgroups.

Discussion

These analyses demonstrate that while there are clear associations for all measures of obesity with risk of IHD in these Asia Pacific populations, the associations are typically stronger for BMI, WC and WHR than for HC. In particular, WHR and WC, which measure central obesity, have the strongest associations with risk of IHD: a one quarter to one third increase in risk is associated with one SD increase in each index. In contrast, there is no clear association between any of the measures and risk of stroke.

The finding that WC and WHR appear to be more important predictors of coronary risk than BMI and HC in these Asia-Pacific populations is consistent with results from European and North American populations. Cohort studies in the United States have found that higher WHR or WC are strongly associated with increased risk of IHD[4] in women, and stroke in men.[3] Swedish cohort studies have also found that the relationship with acute myocardial infarction,[6] and stroke and IHD,[5] is stronger for WHR than for other anthropometric measures such as BMI and sum of skinfold thicknesses. Similar findings

Table 1. Characteristics of the study cohorts

Study name	Country	Sample Size	Start Year	Mean Follow-up (years)	% Females	Age (Years) mean	SD	BMI (kg/m^2) mean	SD	WC (cm) mean	SD	HC (cm) mean	SD	WHR mean	SD	Total Stroke	Total IHD
Anzhen02	China	4 153	1992	2.8	51	47	8	24.0	3.3	80.1	9.3	96.7	6.5	0.83	0.07	16	1
CISCH	China	2 163	1992	3.3	51	44	7	24.7	3.5	80.8	9.6	97.0	7.0	0.83	0.09	9	14
Hong Kong	Hong Kong	1 872	1991	2.0	50	79	7	22.0	3.8	83.3	10.6	92.7	8.5	0.90	0.07	40	57
Western Australia AAA Screenees	Australia	12 192	1996	3.2	0	72	4	26.9	3.7	99.1	10.4	103.2	7.2	0.96	0.06	227	321
Australian National Heart Foundation	Australia	9 243	1989	8.2	51	43	13	25.4	4.3	83.3	12.9	100.5	8.7	0.83	0.09	17	76
Melbourne	Australia	16 365	1990	8.6	60	55	9	26.8	4.4	85.5	12.9	101.5	8.9	0.84	0.09	37	132
Total or average†		45 988		6.1	48	54	9	26.2	4.2	86.4	12.3	101.0	8.4	0.85	0.08	346	601

BMI=Body mass index, WC=Waist circumference, HC= Hip circumference, WHR=Waist-hip ratio † Weighted by person years of follow-up; Total person years of follow-up=278,680

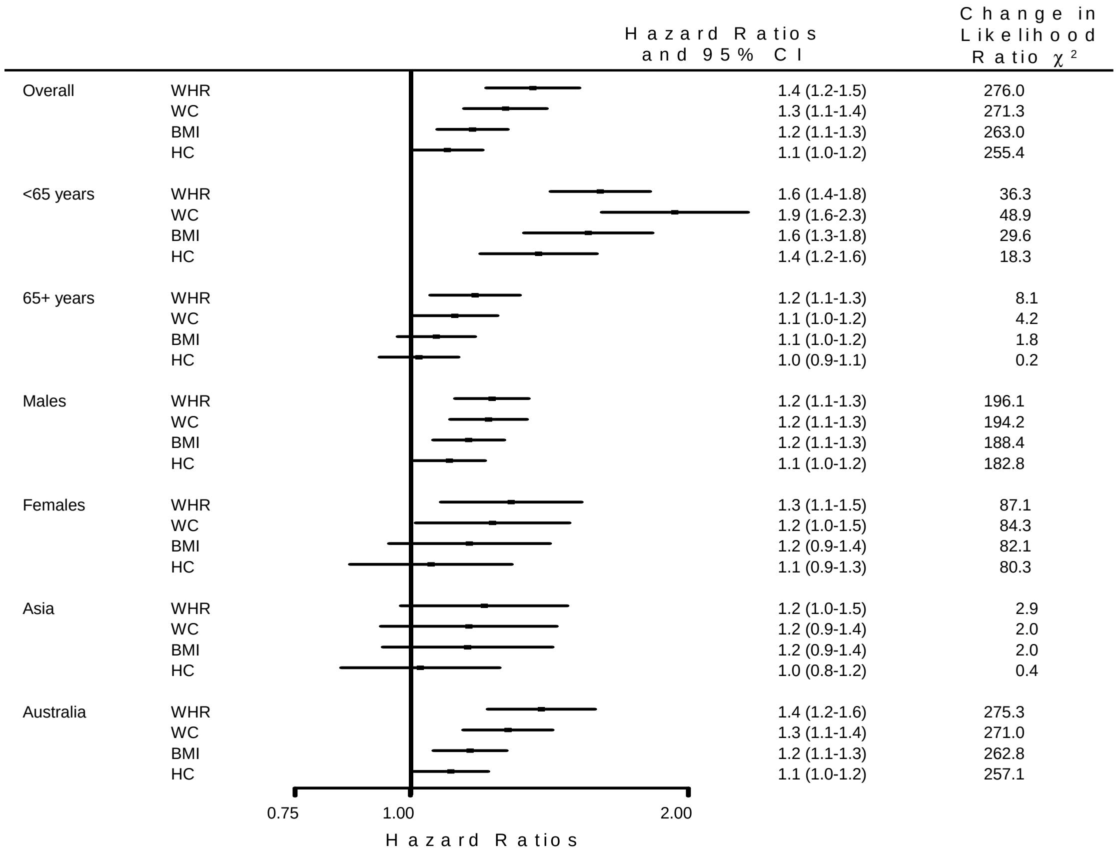

Figure 1. Relationship between anthropometric indices and total ischaemic heart disease events.

The hazard ratios for total ischaemic heart disease events are plotted on a log scale, overall and for age (<65 years, 65+years), sex and region (Asia & Australia) subgroups, for each of the following anthropometric indices: body mass index (BMI), waist circumference (WC), hip circumference (HC) and waist-hip ratio (WHR). The hazard ratios are adjusted for age, sex, cohort and smoking, and have been calculated for a one standard deviation increase in each index. The solid squares are larger where there are more events, as their size is proportional to the inverse of the variance, and the horizontal lines represent 95% confidence intervals. The change in likelihood ratio χ^2 statistic has been calculated by comparing a model containing each anthropometric index with a model that contained age at risk and smoking, stratified by sex and cohort, but no anthropometric index (the 'base model'). The greater the change in likelihood ratio χ^2 statistic, the greater the increase in goodness of fit or "informativeness" of the index.

have been observed in cohort studies that have examined the relationship between various anthropometric measures and risk of diabetes mellitus.[13-15] As larger studies have found associations between BMI and risk of stroke,[16] and other measures of central obesity and stroke,[3,5] the lack of association with risk of stroke seen in these analyses may be due to the small number of stroke events (346) included.

The higher hazard ratios observed for IHD in Australian versus Asian cohorts was statistically non-significant and is likely to be due to the longer mean follow-up periods (3.2–8.6 years) of the Australian studies. Sensitivity analyses demonstrated that exclusion of the first three years of follow-up strengthened associations between the various anthropometric measures and IHD. The Asian cohorts all had mean follow-up periods of 3.3 years or less, and the attenuated associations seen in these studies may be due to confounding by pre-existing disease at baseline.

These analyses have several strengths: they involve a large number of participants, utilize individual participant data, and the anthropometric measures were largely measured rather than self-reported. Most importantly they are based on prospective cohort data rather than cross-sectional data. However, provision of data on anthropometric measures was not a requirement for participation in the Collaboration and many cohorts did not collect or provide data on these risk factors. Our analyses were therefore limited to six of the 44 cohorts in the APCSC. As a result, there were a relatively small number of events available for analysis, and it is possible that despite the apparent lack of significant effects by age, sex or region, some important subgroup effect might have been obscured. In addition, the current analyses are largely dominated by data from the Australian cohorts, which had the larger number of participants, person years of follow-up, and events. Additional data on measures of obesity have been requested from all members of the Collaboration with a view to further analyses.

Several risk factors associated with central obesity may account for the increased risk of IHD. These include changes in lipoprotein levels and lipid transport,[17] insulin resistance,[18] and glucose intolerance and type 2 diabetes.[19] Cross-sectional studies conducted in the Asia Pacific region[20,21] have found a continuous relationship between central obesity and cardiovascular risk factors including blood pressure, plasma glucose, plasma lipids, and insulin levels. However, no prospective data from the region have been available until now.

Our analyses demonstrate that a one SD increase in BMI, WC or WHR is associated with an increased risk of IHD ranging from 17 to 36%. In practical terms, this equates to a 4.2 kg/m^2 increase in BMI, a 12.3 cm increase in WC, or an increase in WHR of 0.08. These are substantial increases of the kind that might be expected to take place within a population only over several years. For example, in New Zealand, mean BMI increased by 1.4 kg/m^2 in men and 1.9 kg/m^2 in women over a period of 26 years (1977 to 2003).[22] Based upon our analyses these changes would equate to a subsequent 5% and 7% increase in risk of IHD.

These analyses demonstrate that BMI, WHR, and WC are important measures in predicting risk of IHD in Asia-Pacific populations. In particular, WHR and WC are the strongest anthropometric predictors of IHD, suggesting that central obesity is an important risk factor for IHD in this region. Measures of central obesity should therefore be undertaken routinely along with measurements of general obesity such as BMI. In situations where time or resources are scarce WHR may be the most appropriate single anthropometric measure of cardiovascular risk.

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Appendix

Asia Pacific Cohort Studies Collaboration

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Original Article

Central obesity and risk of cardiovascular disease in the Asia Pacific Region

Asia Pacific Cohort Studies Collaboration[1]

亚太地区向心性肥胖与心血管疾病的风险

本论文比较作为亚太地区人口缺血性心脏病和脑卒中危险因子的四项指标：身体质量指数，腰围，臀围和腰臀比。我们的合并分析包括对 6 组人群研究（45988 名参与者），使用 Cox 比例危险回归法，通过年龄、性别与地域评估以上四项人体测量指标与缺血性心脏病和脑卒中的相关性。6 年中，诊断出 346 例脑卒中和 601 例缺血性心脏病，其中有致命的也有不致命的。结果显示身体质量指数、腰围，臀围和腰臀比每增加一个标准差，缺血性心脏病危险度分别增加 17% (95% CI 7-27%)、27% (95% CI 14-40%)、10% (95% CI 1-20%)和 36% (95% CI 21-52%)。而年龄、性别和地区组间没有显著性差异。这四项指标与脑卒中也没有显著相关性。数据显示该地区向心性肥胖的测量如腰围和腰臀比与缺血性心脏病危险度显著相关。因此我们建议，在计算身体质量指数的同时，腰围和腰臀比要作为向心性肥胖的常规测量指标。

关键词：肥胖、人体测量学、心血管疾病、亚洲、人群研究。