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Relationship between measures of central and general adiposity with aortic stiffness in the general population☆

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ABSTRACT

Objective: Increased aortic stiffness may be one of the mechanisms by which obesity increases cardiovascular risk independently of traditional risk factors. While body mass index (BMI) is generally used to define excess adiposity, several studies have suggested that measures of central obesity may be better predictors of cardiovascular risk. However, data comparing the association between several measures of central and general obesity with aortic stiffness in the general population are inconclusive.
Methods: In 1031 individuals (age 53 ± 13 years, 45% men) without manifest cardiovascular disease randomly selected from population, we tested the association between parameters of central obesity (waist circumference – WC, waist-to-hip-ratio – WHR, waist-to-height ratio – WHtR) and general obesity (BMI) with carotid-femoral pulse wave velocity (cfPWV).
Results: In univariate analysis, WC and WHtR were more strongly associated with cfPWV than BMI in both genders, while WHR showed a stronger association with cfPWV only in women. WHtR was more closely associated with cfPVW than WHR. This difference between obesity measures remained after multivariate adjustment. When the fully adjusted hierarchical regression was used, among central obesity measures, WHtR had the largest additive value on top of BMI, while there was no additive value of BMI on top of WHtR.
Conclusion: Central obesity parameters are more closely associated with aortic stiffness than BMI. Of central adiposity measures, WHtR has the strongest association with aortic stiffness beyond body mass index and cardiovascular risk factors. Our results suggest that WHtR may be the best anthropometric measure of excess adiposity in the general population.

1. Introduction

Obesity has been linked to increased all-cause and cardiovascular mortality [1–3]. This increased mortality risk is at least partially mediated through hypertension, diabetes, and metabolic syndrome [4,5]. However, these traditional risk factors can only partially account for the cardiovascular risk associated with obesity, and the actual mechanisms through which obesity can increase cardiovascular disease beyond traditional risk factors have not been clearly identified [6]. Pulse wave velocity measured between the carotid and femoral arteries (cfPWV), as a measure of aortic stiffness, has been shown to predict all-cause and cardiovascular morbidity and mortality in patients with various levels of cardiovascular risk [7]. Loss of the buffering function of the aorta due to aging and cardiovascular risk factors leads to left ventricular hypertrophy, increased oxygen demand and subendocardial myocardial ischemia [8,9] and, ultimately, to microvascular damage to the

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brain [10–12] and kidneys [13]. Increased aortic stiffness may be a mechanism by which obesity increases total and cardiovascular mortality independently of traditional risk factors. Several studies indicate that obesity, as defined by an increased body mass index (BMI), is independently associated with increased aortic stiffness [14–17]. However, other studies have either failed to confirm this relationship [18–21], or suggest that fat distribution may be more important than the absolute degree of fatness per se [22–25].

The aim of this study was to assess and compare the strength of association of general and central obesity measures with aortic stiffness in a large-scale population-based study and to evaluate the additive value of different measures of obesity.

2. Methods

2.1. Study population

The Czech MONICA and post-MONICA study is a population-based survey studying trends and determinants of cardiovascular risk factors in a random sample of the Czech population. Methods of the Czech post-MONICA study have been described elsewhere [26,27].

A total of six independent cross-sectional surveys for major cardiovascular risk factors were conducted in the Czech Republic. Three (1985, 1988, and1992) were organized within the WHO MONICA project in six districts. One-percent samples stratified by age and sex were randomly selected each year from the National Population Register within an age range of 25–64 years. In 1997/98, 2000/01, and 2007/08, another three screenings for cardiovascular risk factors were organized in nine districts of the Czech Republic, again involving a 1% percent population random sample aged 25–64 years in each district. Selection was made from the General Health Insurance Company registry that keeps, by law, a list of all people insured.

The present study included patients aged over 25 years resident in the Pilsen district, examined between years 2006 and 2009. The response rate was 68%. Of the 1417 individuals examined, 1114 had complete data on cfPWV and anthropometric measures of obesity. We excluded 83 individuals with a history of coronary heart disease. Thus, data from 1031 subjects were used for further analysis. The study was approved by the local ethics committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital, and was in accordance with the Declaration of Helsinki.

Hypertension was defined as a systolic blood pressure (SBP) $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg, or current use of antihypertensive medication. Diabetes was defined as fasting glucose $\geq$ 7.0 mmol/l or treatment by oral antidiabetic drugs and/or insulin. Dyslipidemia was defined as total cholesterol $\geq$ 5 mmol/l or LDL-cholesterol $\geq$ 3 mmol/m, or HDL-cholesterol < 1 mmol/l in men and <1.2 mmol/l in women or use of lipid-lowering drugs. Smoking was defined as any smoking history during the past 1 year preceding the interview. Coronary heart disease was defined as a self-reported history of myocardial infarction or angina or percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

2.2. Body adiposity measures

Height and body weight were measured with participants standing without shoes and heavy outer garments. Height was determined using a wall-mounted stadiometer. The value was rounded to the closest centimeter. Body weight was determined using a homologated electronic scale. Readings were rounded to the nearest 100 g mark. Waist circumference was measured while standing at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, as suggested by the World Health Organization (WHO), ensuring that the tape was adjusted without compressing the skin. The reading was taken at the end of a normal breath. Hip circumference was taken around the widest portion of the buttocks at a level parallel to the floor. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist-to-hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm). Waist-to-height ratio (WHtR) was calculated as waist circumference (cm) divided by height (cm).

2.3. Measurement of carotid-femoral pulse wave velocity

Carotid-femoral pulse wave velocity (cfPWV) as a parameter of aortic stiffness was measured, following an expert consensus, using the SphygmoCor device (AtCor Medical Ltd, West Ryde, New South Wales, Australia) in the recumbent position [28] according to a standardized protocol we have reported previously [29,30]. ECG-gated consecutive registration of the pulse waves at the carotid and femoral arteries was done and the time shift (Δt) between the wave feet was calculated. Traveled distance (D) was calculated by subtracting the distance from the jugular fossa to carotid pulsation from the jugular fossa to the pulsation of the femoral artery in the groin. Pulse wave velocity was calculated as D (m)/Δt (s).

2.4. Laboratory analysis

All laboratory analyses were performed centrally in the Institute for Clinical and Experimental Medicine, Prague, Czech Republic. Lipid analyses were performed in the Lipid Laboratory of the Institute for Clinical and Experimental Medicine using a fully automated enzymatic method (Cobas MIRA S analyzer) with enzymatic kits by the same manufacturer. Accuracy of analysis is continuously monitored and tested by the Centers for Disease Control and Prevention (Atlanta, GA, USA); all analyses of total cholesterol and HDL-cholesterol were within the limit of ±2%. Glycemia and serum creatinine were also determined by enzymatic methods, and urinary albumin excretion in the first morning spot using immunoturbidimetry.

2.5. Statistical analysis

Descriptive statistics are given as mean ± standard deviation, or frequency and percent. In the figures, error bars represent a 95% confidence interval of the mean. The univariate association of parameters of obesity with cfPWV was assessed using Pearson's correlation, correlation coefficient (r). Differences in correlation coefficients were assessed using Steiger's Z statistics for comparison of correlations within a single sample. Equality of correlation coefficients from different subgroups was assessed using Fisher's Z test. To assess independent association of each parameter of obesity with cfPWV, we used separate stepwise linear regression analyses. Inputs of these analyses included age, sex, mean arterial pressure (MAP), heart rate, hypertension, dyslipidemia, and diabetes/treatment for diabetes (oral antidiabetic or insulin). Only treatment for diabetes was included as diabetes defined by fasting glucose and/or use of antidiabetic drugs/insulin was not independently associated with cfPWV in multivariate models. Because smoking or smoking-age interaction term was not independently associated with cfPWV, it was not included into multivariate models. To assess the additive predictive value of each measure of obesity incremental to other measure of obesity, we used hierarchical linear regression. This was done initially without additional adjustments to be later adjusted for age, sex, MAP (Model 1) and, additionally, for hypertension, diabetes, and dyslipidemia (Model 2). The proportion of explained