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Body fat distribution and C-reactive protein — a principal component analysis

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Abstract *Background and Aims:* To assess, using principal component analysis, the independent associations of general, central and peripheral subcutaneous fat with high-sensitivity C-reactive protein (hs-CRP), in men and women from the general population.
Methods and results: We studied 833 women and 486 men, randomly selected from the non-institutionalized population of Porto, Portugal, with information on hs-CRP (≤10 mg/l) and anthropometrics (1999–2003). Body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR) and a skinfold composite index to estimate the proportion of arm subcutaneous fat (PSFA), were ascertained by trained personnel. Beta regression coefficients were obtained from generalized linear models with adjustment for the main confounders.

Direct associations were found between BMI, WC, WHR and hs-CRP. PSFA was inversely associated with hs-CRP in women ($\widehat{\beta} = -0.080$, p-trend $= 0.010$). Since the anthropometric measures were strongly correlated, we used principal component analysis to identify new independent anthropometric factors. The first one, representing a generalized fat distribution (high BMI and WC), was directly associated with hs-CRP ($\widehat{\beta} = 0.226$, p-trend < 0.001 in women; $\widehat{\beta} = 0.138$, p-trend $= 0.002$ in men). The second factor, characterized by a high PSFA, showed an inverse association with hs-CRP in women ($\widehat{\beta} = -0.071$, p-trend $= 0.048$). The third factor, representing a central pattern of fat distribution (low BMI, but high WC and high WHR), was directly associated with hs-CRP in men ($\widehat{\beta} = 0.090$, p-trend $= 0.005$).

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Conclusion: A central pattern of fat distribution is directly associated with hs-CRP levels in men, while a high proportion of peripheral subcutaneous fat seems to be inversely associated with hs-CRP, but only in women.

Introduction

Obesity has been associated with metabolic complications, such as insulin resistance, hypertension and dyslipidemia [1—3]. These effects could be mediated, in part, by the relationship between obesity, mainly total and central obesity, and a state of low-grade chronic inflammation [4—10]. Although its patho-physiologic basis is incompletely understood, it is known that adipose tissue expresses a variety of proinflammatory cytokines, namely interleukin-6, tumor necrosis factor-α, and complement C3 [11,12], which stimulate the production of acute phase proteins, such as C-reactive protein [13].

Measures of central obesity, such as waist circumference (WC) and waist-to-hip ratio (WHR), are stronger and more consistent predictors of inflammation than general obesity which is frequently estimated from the body mass index (BMI) [4—6]. There is an increasing understanding of the metabolic effects of abdominal fat, both visceral and subcutaneous [14—16], but less information is available on the relative contribution of central and peripheral fat (fat accumulated in peripheral depots, such as upper and lower limbs), which seem to confer opposing effects — adverse for central and protective for peripheral fat — on cardiovascular risk [17—20]. In fact, the finding that the adverse effects of a high WHR could be due not only to a larger waist but also to narrower hip or thigh circumferences [21,22], suggests a cardio-protective effect of peripheral fat.

Although peripheral fat was previously associated with different cardiovascular risk markers, to our knowledge very few studies [5,19] have examined the relation between peripheral fat and markers of systemic inflammation. Since men and women have different ranges of variation in levels of body fat, a sex-effect in this relationship could be expected. However, sex differences and the potential confounding effects of lifestyles on the associations between body fat and inflammatory markers are often disregarded. Moreover, it is relatively difficult to distinguish between the effects of abdominal, peripheral and total body fat, due to the strong correlation between the different locations of fat. As a result, traditional regression methods of adjusting the effects of one anthropometric measure for the others might not suffice. The use of principal component analysis to identify uncorrelated measures of obesity could be a useful approach to assess the independent effect of fat location on health outcomes.

This study used principal component analysis to investigate the independent associations of general, central and peripheral subcutaneous fat with high-sensitivity C-reactive protein, in men and women from the general population.

Methods

Study population

Participants were selected between 1999 and 2003, among the 300,000 non-institutionalized inhabitants of Porto, a large urban centre in the north-west of Portugal. Participants were selected by random digit dialling; in each household, permanent residents were characterized according to age and sex, and one subject aged $\geq$18 years was selected by simple random sampling. Eligible participants were invited to visit the Department of Hygiene and Epidemiology of the University of Porto Medical School, for interview and physical examination. Refusals were not substituted and the participation rate was 70% [23].

The study evaluated 2485 participants (1538 women and 947 men). For the present analysis, we excluded 947 individuals without C-reactive protein measurements, 101 with missing information on anthropometric measures, and 40 who lacked data on selected confounders. Seventy eight participants (55 women and 23 men) with C-reactive protein levels >10 mg/l, which might suggest a clinically relevant inflammatory condition [24], were also excluded. Therefore, the final study sample included 1319 subjects (833 women and 486 men).

Data collection

Anthropometrics

Anthropometrics were obtained by trained personnel, according to standard procedures [25], with subjects in light clothing and barefoot. Body weight was measured to the nearest 0.1 kg using a digital scale (SECA®) and height was measured to the nearest cm using a wall stadiometer (SECA®). BMI was calculated as the value of weight (kg) over the height squared (m).

WC was measured midway between the lower limit of the rib cage and the iliac crest, and hip circumference on the maximum circumference over the femoral trochanters; both were measured to the nearest cm using a flexible and non-distensible tape. The WHR was calculated by dividing the waist by the hip circumference.

Triceps, biceps, subscapular and suprailiac skinfold thicknesses were measured with a Harpenden® calliper on the non-dominant side of the body. All the skinfolds were grasped with the thumb and index fingers about 1 cm proximal to the skinfold selected site, and were measured three times at each site to the nearest 0.5 mm; the average value was registered. We used a skinfold (SKF) composite index ($\sum$ triceps and biceps SKF/$\sum$ triceps, biceps, subscapular and suprailiac SKF) to estimate the proportion of subcutaneous fat of the arms (PSFA). Different skinfold