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Sex dependence of body fat distribution and fluid volumes in hypertension

JOCELYN M. RAISON, MICHEL E. SAFAR, RISH E. ASMAR, APOSTOLOS M. ACHIMASTOS, and GERHARD M. LONDON

Diagnosis Center and Hypertension Research Center, Broussais Hospital, Paris, France

Several epidemiological studies have emphasized the positive correlation observed between body weight and blood pressure in man [1]. However, the correlation coefficients of the different relationships were found constantly small, indicating that the relationship between overweight and blood pressure is somewhat complex. In patients with hypertension, body weight was shown to be positively related with the levels of both blood pressure and extracellular fluid volume [2–4]. On the other hand, patients with overweight and hypertension were found to be principally affected by hypertrophic obesity, as shown by the evaluation of fat cell weight [5]. However, these findings were exclusively observed in males. No solid data were reported in females. Indeed, the relationships between body weight and extracellular fluid, on the one hand, and between body weight and fat cell weight on the other hand are certainly different in males than in females [6, 7]. In females, extracellular fluid volume is submitted to cyclic changes in sodium balance involving the effect of sex steroid hormones. On the other hand, body fat distribution is different in males and females. In males, body fat predominates in the upper part of the body, while in females, adiposity is mainly observed in the lower part of the body. In that regards, body fat distribution was investigated in males and females with obesity and hypertension, with reference to the most important parameters involved in body weight composition: fat cell weight and extracellular fluid volume.

Patients and methods

Twenty men and 20 females with obesity and hypertension were included in the study. Men and women were divided into two groups matched for age, degree of overweight, and blood pressure level. All were untreated or had discontinued their therapy for at least four weeks before the study. All maintained their weight within a 2 to 3-kg range on a stable calorie intake. Patients were considered to have had sustained hypertension when diastolic pressure repeatedly measured by indirect method was superior or equal to 100 mm Hg during the untreated ambulatory period. Blood pressure determinations were performed using a large pressure cuff, according to the arm circumference [1]. On the basis of thorough classical investigations [4, 5], the 40 hypertensive patients were all considered to have uncomplicated sustained essential hypertension. Patients who had diabetes mellitus, cardiac disease, alcoholism, drug addiction, or psychiatric problems were excluded from the study. Mean creatinine clearance rate was 97 ± 9 ml/min/1.73 cm^2 (±1 SEM). Natriuresis was between 80 and 130 mEq/day.

In the 40 patients, the diagnosis of obesity was defined as an excess weight of more than 20 percent above ideal body weight, determined on the basis of age, height, and body build, according to Metropolitan Life Insurance Company guidelines [4, 5]. Age range was between 20 and 60 years in both groups (42 ± 2 and 40 ± 2 years). Mean body weight and mean height were significantly higher in men than in women (99 ± 2 versus 83 ± 2 kg, $P < 0.05$; 175 ± 2 versus 159 ± 2 cm; $P < 0.05$). The range of over weight was similar (between 120 and 180%) in both groups. Mean systolic and diastolic pressures were not significantly different in obese hypertensive males and females (153 ± 5/94 ± 1 versus 150 ± 6/95 ± 2 mm Hg). Informed consent was obtained from the patients after a detailed description of the procedure.

Anthropometric measurements, adipose tissue morphology, and fluid volumes were studied at 9 a.m. during a day hospitalization. Body weight was determined without shoes. Only underclothes were kept on. Six cuff blood pressure determinations (mercury sphygmomanometer) were performed within one hour in the recumbent position after 10 minutes of rest. Blood pressure was the mean of these measurements. Abolition of Koratkoff sounds was used for the evaluation of diastolic blood pressure. The patient being standing and breathing normally, waist circumference at the level of umbilicus and hip circumference at the level of trochanter were measured using a tape. Anthropometric measurements were performed in duplicate by a single experimented observer. Intra-individual reproducibility was 8 ± 3 percent. Body fat distribution was assessed by the waist-on-hip circumferences ratio (W/H ratio) [8]. In females aged for 30 to 40 years, the normal value of W/H was 0.75 ± 0.02; in males aged for 30 to 40 years, 1 ± 0.02. Adipose tissue morphology was studied in the external part of the gluteal region by percutaneous needle biopsy as described elsewhere [5]. Extracellular fluid volume (EFV) was approximated to the distribution volume of inulin as previously validated [3, 4]. Total body water (TBW) was estimated from the distribution volume of antipyrine [4]. Total body fat was evaluated from total body water and body density. Lean body mass [LBM] was calculated as the difference between body weight and total body fat. Standard statistical analysis was used [9].

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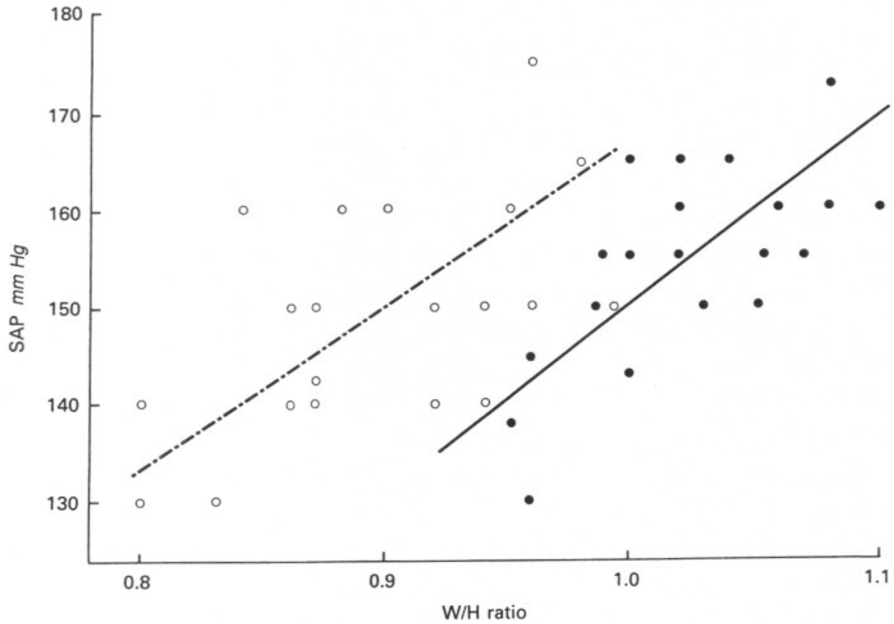

Fig. 1. *Correlation of W/H ratio with systolic arterial pressure (SAP) in obese hypertensive men and women.* Covariance analysis showed that the two curves differed only by the value of intercept. Symbols are: (○— . —) females, $r = 0.50$, $P < 0.05$, $y = 99\times + 66$; (●— . —) males, $r = 0.55$, $P < 0.05$, $y = 122\times + 29$.

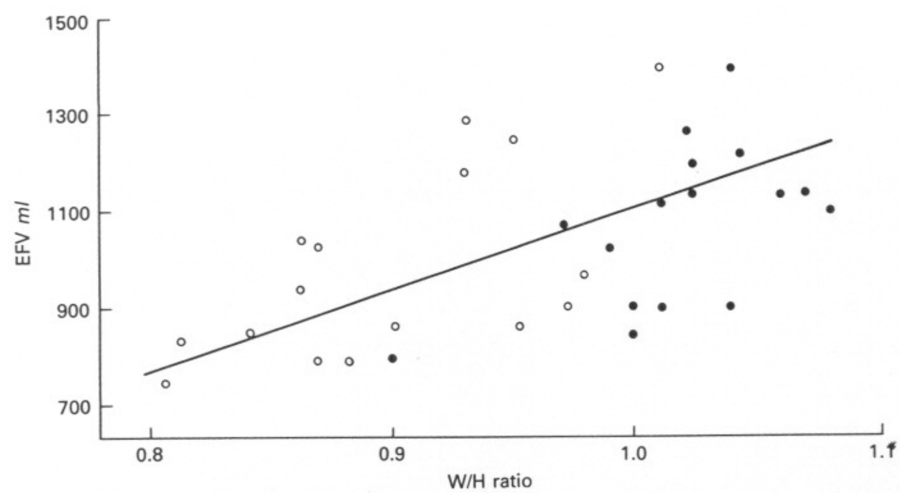

Fig. 2. *Correlations of W/H ratio with extracellular fluid volume (EFV) in obese hypertensive men (●) and women (○)* ($r = 0.51$; $P < 0.01$).

Results

Waist circumference was significantly higher in males than in females (110 ± 2 versus 99 ± 2; $P < 0.01$). Hip circumference was similar (107 ± 1 versus 109 ± 4 cm). The W/H ratio was significantly higher in males than in females (1.02 ± 0.01 versus 0.9 ± 0.01; $P < 0.001$). Gluteal fat cell weight was significantly higher in men (1.07 ± 0.02 μg) than in women (0.79 ± 0.01 μg), $P < 0.05$. TBW, expressed either in absolute values (47,550 ± 1,250 and 36,350 ± 1,280 ml) or in milliliters per kilogram (480 ± 10 and 440 ± 20 ml/kg), was significantly higher in men than in women ($P < 0.001$ and $P < 0.05$). LBM was higher in men than in women (65 ± 2 versus 49 ± 2 kg; $P < 0.001$), while total body fat was similar (34 ± 2 and 34 ± 2 kg). EFV, expressed in milliliters, was similar in men and women (10,400 ± 350 and 9,800 ± 500 ml). When expressed in milliliters per kilogram, EFV was higher in men (120 ± 6 versus 150 ± 4 ml/kg; $P < 0.05$). Systolic arterial pressure was significantly and positively correlated with the W/H ratio in males and in females. Figure 1 shows that, at any given value of the ratio, systolic arterial pressure was higher in females than in males. In men, gluteal fat cell weight was positively correlated with the W/H ratio ($r = 0.55$; $P < 0.05$) and systolic arterial pressure ($r = 0.65$; $P < 0.01$). In women, gluteal fat cell weight was significantly correlated with these parameters ($r = 0.03$ and 0.17). As shown in Figure 2, EFV (ml) was positively and significantly correlated with the W/H ratio both in males and in females. In males, EFV was positively correlated with systolic arterial pressure ($r = 0.51$; $P < 0.05$) and body weight ($r = 0.49$; $P < 0.05$). In females, no significant correlation was found between EFV and systolic pressure or EFV body weight.

Comments

In the present study, distribution of body fat was investigated in a population of obese hypertensive males and females carefully selected on the basis of age, degree of obesity and blood pressure level. The W/H ratio was higher in men than in women, reflecting an abnormal fat predominance in male individuals (6-7). However, the relationship of the W/H ratio with systolic pressure was different in obese hypertensive males and females: for the same W/H ratio and degree of obesity, systolic arterial pressure was higher in females than in males (Fig. 1).

The W/H ratio was found to be directly correlated with gluteal fat cell weight in obese hypertensive men but not in women. In addition, the positive relationship that we have previously observed [5] between blood pressure and fat cell weight was found significant only in men and not in women. Thus, sex influence may partly explain the discrepancies noticed in the literature in the relationship between fat cell weight and blood pressure [10–12]. The relationship between adipose tissue cellularity and blood pressure is probably affected by the regional variations in fat metabolism observed in men and women, and, hence, by the site of biopsy [13]. The role of the latter factor has been emphasized by Kissebach et al [7]. In both sexes, abdominal fat cell weight is associated with metabolic parameters, but gluteal fat is much more dependent of sex steroid hormones than abdominal fat and therefore does not give any indication on metabolic profiles in women [7, 13].

Another important finding of the present investigation was the positive relationship between the W/H ratio and EFV observed both in males and in females (Fig. 2). The result contrasted with the relationships of EFV with body weight and blood pressure which were observed exclusively in men. That upper body fat predominance may be involved in the control of extracellular fluid volume suggests several observations. First, upper body fat predominance is accompanied by enlarged abdominal fat cells and enhanced lipolysis which could be responsible for hyperinsulinemia [7] and, in turn, for a supplementary increase in EFV [14]. Second, predominance of fat in the upper part of the body is also influenced by increased androgenic activity [15], and steroid hormones are known to favor salt and fluid retention [14].

In conclusion, sex difference may influence the complex relationships between blood pressure, body fat, and fluid volumes. Body fat distribution may be an important factor contributing to the heterogeneity of obesity observed in male and female individuals treated for hypertension.

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Reprint requests to Michel Safar, M.D., Centre de Diagnostic, 96 rue Didot, 75674 Paris Cedex 14, France.

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