

Body fat distribution as a risk factor for osteoporosis

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Objective. The aim of this study was to compare the body fat distribution of patients with osteoporosis (OP) with that of an appropriately matched non-OP control group.

Design. Case control study.

Setting. Department of Endocrinology and Metabolism, Tygerberg Hospital.

Participants. A total of 56 patients with histologically proven idiopathic OP, of whom 39 were women (mean age 61 ± 11 years) and 17 men (49 ± 15 years), were compared with 125 age- and sex-matched non-OP (confirmed by dual energy X-ray absorptiometry) subjects, 98 women (60 ± 11 years) and 27 men (51 ± 16 years).

Outcome measures. Anthropometric data, including weight, height, skinfold measurements, mid-upper arm, waist and hip circumferences, as well as elbow breadth.

Results. The men and women with OP were significantly shorter ($P = 0.04$ and $P = 0.03$ respectively) and of lower body mass ($P = 0.04$ and $P = 0.02$ respectively) than the control subjects, although their mean body mass indices were comparable. The OP population had significantly lower skinfold, elbow breadth and arm circumference values, although the majority of subjects in both groups fell within the 15 - 85th percentiles. Despite their lower body mass, both the OP women ($P = 0.009$) and men ($P = 0.002$) had significantly higher waist/hip ratios than corresponding controls.

Conclusion. Whatever the underlying pathogenesis, this new finding suggests that, should these results be confirmed by larger studies, OP can be added to the list of diseases associated with a waist fat distribution.

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Osteoporosis (OP) is an extremely common disorder, characterised by a decrease in bone mineral density (BMD) that results in an increased propensity to fracture which most often involves the spine, hip or wrist.¹⁻³ The pathogenesis and risk factors which predispose to the development of OP, however, remain ill-defined.

In the past, most epidemiological studies that examined the association between obesity and disease considered only total adipose tissue and ignored its distribution. Recently it has become apparent that it is not obesity *per se*, but the regional distribution of adipose tissue, that correlates with many obesity-related morbidities including atherosclerosis, hypertension, hyperlipidaemias and diabetes mellitus.⁴⁻⁸

The anatomical distribution of adipose tissue differs between men and women in both normal and obese individuals, suggesting that sex hormones are involved in the regulation of adipose tissue metabolism.⁹⁻¹⁰ Upper body (android or waist) obesity, which is typically observed in men, is associated with hyperandrogenism, whereas lower body (gynoid or hip) obesity is far more common in women, suggesting an oestrogenic influence.⁹⁻¹² Moreover, upper body obesity has been shown to be associated with hypercortisolism and classically occurs in patients with Cushing's syndrome.¹³ Since hypogonadism and hypercortisolaemia are well-known causes of OP, we questioned whether this disease was also associated with changes in the regional distribution of adipose tissue. The aim of this study was therefore to compare the body fat distribution of patients with proven idiopathic OP with that of an appropriately matched non-OP control group.

Materials and methods

Subjects

All the subjects in the OP group had proven idiopathic OP on dual-energy X-ray absorptiometry (DEXA), as well as a clinical, radiological, biochemical and histological (quantitative histomorphometry after time-spaced tetracycline labelling of undecalcified bone biopsies) work-up, thereby excluding individuals with (i) secondary OP and (ii) metabolic bone diseases other than OP, e.g. osteomalacia, hyperparathyroidism. The group consisted of 56 Caucasian subjects, consecutively admitted to our Endocrine Unit for evaluation of their OP, of whom 17 were men and 39 women. The mean age of the men was 49 (± 15) years and that of the women 61 (± 11) years.

The control group consisted of 125 age- and sex-matched Caucasian subjects of whom 27 were men and 98 women, of mean ages 52 (± 16) years and 60 (± 10) years respectively. The absence of osteopenia in this group was confirmed by DEXA.

Methods

Bone mass was measured by means of DEXA (Hologic QDR-1000) in all the subjects and included the lumbar spine (L1 - L4) and hip. Osteopenia was diagnosed if the BMD was found to be decreased by more than 1.5 standard deviations (SDs) in subjects younger than 40 years, or by more than 2.0 SDs in those over 40 years of age, compared with the BMD of young normal subjects.¹⁴

Anthropometric data were obtained from every subject and included weight, height, skinfold thickness measurements (triceps, biceps, subscapular, supra-iliac), mid-upper arm circumference, waist and hip circumference, as well as elbow breadth determinations.

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The following methods were employed: (i) weight — the subjects were weighed with the minimum of clothes on, to the nearest 0.1 kg;¹⁵ (ii) height was measured with a sliding headpiece to increase the accuracy of the readings, which were taken to the nearest 0.1 cm;¹⁵ (iii) skinfolds were measured with a Harpenden caliper. All measurements were taken to the nearest 0.1 mm on the right side of the body: biceps — over the midpoint of the biceps muscle, triceps — over the triceps muscle, midway between the acromial process of the scapula and the olecranon, subscapular — just below the tip of the scapula, at 45° to the vertical, supra-iliac — just above the iliac crest on the mid-axillary line;¹⁵ (iv) mid-upper arm circumference was measured at the same point as the triceps skinfold;¹⁵ (v) waist circumference was determined in the erect position, around the waist through a point one-third of the distance between the xiphoid process and the umbilicus;⁵ (vi) hip circumference was assessed in the erect position, around the hips through a point 4 cm below the superior anterior iliac spine.⁵ Every effort was made to ensure that the tape was horizontal at the back while waist and hip circumference values were determined. These measurements were taken without clothing; (vii) elbow breadth, the greatest breadth across the elbow joint, was measured with a sliding caliper to the nearest 0.1 cm.¹⁶

All measurements were made in triplicate by the same observer, and the results averaged.

Statistical analysis included the Wilcoxon signed-rank test, the Spearman correlation coefficient and the Cochran-Mantel-Haenszel test to determine odds ratios and to obtain 95% confidence intervals (95% CIs).¹⁷

Results

The BMD of the lumbar spine and various hip areas of both the men and the women with OP was significantly lower than in the corresponding controls (Table I).

Table II lists the anthropometric data of all the subjects. Both the men ($P = 0.04$) and the women ($P = 0.02$) with OP

had a significantly lower body weight than the control subjects. The OP men ($P = 0.04$) and women ($P = 0.03$) were also significantly shorter than controls, although all subjects still maintained an upright posture. Body mass index (BMI) values were, however, comparable. Elbow breadth, an indicator of frame size, was significantly lower in the OP subjects compared with controls, although mean values for both groups were indicative of a medium frame size. The OP group had significantly lower skinfold and circumference values for most of the measurements, although the majority of subjects in both groups fell within the 15 - 85th percentiles. From these data it is clear that both the OP and the control subjects were of normal weight.

Table I. Bone mineral density of subjects (g/cm³) (mean (SD))

| | Women | | Men | |
|-----------------|--------------|-------------|--------------|-------------|
| | OP | Control | OP | Control |
| Vertebrae | | | | |
| L1 - L4 | 0.72 (0.10)* | 1.11 (0.17) | 0.72 (0.13)† | 1.15 (0.13) |
| Femoral | | | | |
| Neck | 0.60 (0.09)* | 0.88 (0.13) | 0.64 (0.12)† | 0.95 (0.08) |
| Ward's triangle | 0.39 (0.11)* | 0.71 (0.17) | 0.39 (0.16)† | 0.69 (0.10) |
| Troch | 0.50 (0.10)* | 0.76 (0.09) | 0.54 (0.08)† | 0.80 (0.06) |
| Total | 0.64 (0.20)* | 1.02 (0.13) | 0.74 (0.12)† | 1.09 (0.06) |

* $P = 0.0001$.

† $P = 0.008$.

The mean waist/hip ratio (WHR) for both control and osteoporotic men was normal (below 1.0). The WHR for control women of 0.81 (0.05) marginally exceeded the accepted upper limit of 0.80, whereas osteoporotic women had a mean WHR of 0.87 (0.1). In fact, both the osteoporotic men ($P = 0.002$) and women ($P = 0.0009$) had significantly higher WHRs than their corresponding controls (Table II). The odds ratio that a man with a waist fat distribution had OP was 8 times higher than that of a man with a hip fat distribution (95% CI: 1.037 - 61.731), whereas for women it was 1.6 times higher (95% CI: 0.751 - 3.588).

Table II. Anthropometric data on subjects (mean (SD))

| Measurements | Women | | | Men | | |
|----------------------------------|-------------|--------------|---------|-------------|-------------|---------|
| | OP | Control | P-value | OP | Control | P-value |
| Body mass (kg) | 64 (12) | 69 (12) | 0.02 | 70 (12) | 77 (12) | 0.04 |
| Height (cm) | 1.62 (0.06) | 1.64 (0.07) | 0.03 | 1.71 (0.07) | 1.77 (0.08) | 0.04 |
| BMI | 24 (5) | 26 (5) | 0.17 | 24 (3) | 25 (3) | 0.22 |
| WHR | 0.87 (0.11) | 0.81 (0.05) | 0.0009 | 0.96 (0.06) | 0.89 (0.06) | 0.002 |
| Middle circumference (cm) | 84.9 (15.3) | 83.9 (10.7) | 0.91 | 85.6 (12.2) | 90.9 (9.6) | 0.18 |
| Hip circumference (cm) | 97.9 (13.4) | 103.9 (10.3) | 0.01 | 89.3 (12.3) | 100.9 (6.5) | 0.001 |
| Elbow breadth (cm) | 6.4 (0.8) | 6.7 (0.4) | 0.03 | 7.1 (0.3) | 7.4 (0.4) | 0.007 |
| Biceps (mm) | 12.0 (5.7) | 12.6 (5.9) | 0.69 | 5.6 (2.9) | 6.5 (2.5) | 0.10 |
| Triceps (mm) | 20.0 (6.4) | 23.4 (6.3) | 0.01 | 10.7 (5.3) | 13.2 (2.9) | 0.01 |
| Subscapular (mm) | 16.3 (6.7) | 16.8 (7.1) | 0.96 | 12.3 (4.6) | 16.4 (6.4) | 0.03 |
| Supra-iliac (mm) | 18.2 (8.5) | 19.9 (9.0) | 0.52 | 13.1 (5.5) | 16.6 (5.3) | 0.07 |
| Mid-upper arm circumference (cm) | 29.0 (4.3) | 31.1 (3.6) | 0.0005 | 29.2 (2.0) | 31.4 (3.0) | 0.008 |

BMI = body mass index; WHR = waist/hip ratio.

Discussion and conclusions

The relationship between body mass and BMD is well established, and a low body mass is classically regarded as a risk factor for the development of OP.^{1-3,18-20} Both weight and adiposity could affect BMD in a number of ways. In heavy subjects, weight imparts a load factor on weight-bearing bones, resulting in the stimulation of osteoblastic bone formation.²¹ In postmenopausal women, adipose tissue serves as the site of peripheral conversion of androstenedione to metabolically more active oestrogens, known to inhibit bone resorption.²⁰⁻²³ Adiposity cannot, however, be regarded as a homogeneous disorder anymore, and the clinical significance of regional fat distribution is now well established.

Because a significant correlation exists between the intra-abdominal/subcutaneous fat ratio and the WHR, the latter has become a useful indirect measure of visceral adiposity and correlates well with many obesity-related morbidities regardless of whether the BMI is high or low.^{13,24}

A number of metabolic abnormalities have been shown to be associated with upper body (android) obesity; many of these may have potentially deleterious effects on skeletal integrity. An upper body fat distribution is associated with increased circulating glucocorticoid levels and Björntorp has hypothesised that it is primarily a maladaptive hypothalamic response to various environmental stressors that results in increased activity along the corticotrophin (ACTH)-cortisol axis in these subjects.²⁵ An android profile of fat deposition is well established in patients with Cushing's syndrome and it has been suggested that the influence of high cortisol levels on abdominal fat cells could be due to the high density of glucocorticoid receptors in this depot.^{26,27} Since glucocorticoid excess is known to inhibit bone formation directly,^{28,29} enhance parathyroid hormone-mediated bone resorption,²⁹ impair renal vitamin D hydroxylation and intestinal calcium absorption,^{2,29} and decrease circulating levels of sex hormones,^{30,31} the association between abdominal obesity and a decreased BMD, noted in the present study, may not be surprising.

Women with upper body obesity have increased serum free testosterone and decreased sex hormone-binding globulin levels.^{8-11,32-34} Conversely, the serum and tissue levels of oestrogens and progesterone seem to be related to lower body fat accumulation with little influence on truncal-abdominal fat.³⁵ Abdominal adiposity is also observed in hyperandrogenic conditions like the polycystic ovary syndrome,³⁴ idiopathic hirsutism^{4,8,34,36} and the menopause.³⁵ In women with an android fat distribution there is evidence of decreased sex steroid secretion, which may result from aberrations of gonadotrophin release.²⁵ Moreover, hypercortisolaemia is known to decrease circulating levels of female sex hormones.³⁰ In men, central obesity is associated with ageing, low levels of testosterone^{37,38} and increased peripheral aromatisation of androgens to oestrogens.^{11,35} In both sexes, upper body obesity therefore seems to be associated with relative hypercortisolism and decreased sex hormone levels. Oestrogen deficiency is a known risk factor for the development of OP in women. The effect of oestrogen on bone was initially thought to be indirectly mediated via its activation of vitamin D metabolism, stimulation of intestinal calcium absorption, or increase in

circulating levels of the anti-resorptive hormone, calcitonin, and protection against parathyroid hormone-mediated bone resorption.¹⁻³ Recently, however, oestrogen receptors have been noted in human bone cells.³⁹ Hypogonadism is also a well-known cause of osteoporosis in men, and androgens have potent anabolic effects on skeletal tissue.⁴⁰

We acknowledge that vertebral compression fractures can result in decreased height and a change in posture. However, even though the osteoporotic subjects were significantly shorter than the controls, no posture changes resulting from clinical kyphosis, which might give rise to a subsequent relatively larger abdominal circumference, were observed in this group. We do not believe, therefore, that the findings are in any way influenced by anatomical posture changes caused by kyphosis.

Finally, we should take cognisance of the fact that regional fat distribution, like OP, also has significant genetic determinants.³⁵ In this regard, the recent observation that relative truncal adiposity is influenced by a major locus and polygenic inheritance is of interest.⁴¹ Speculation on the pathophysiological basis of the observed association between osteoporosis and regional fat distribution is therefore not difficult — further studies are needed, however, before the findings of the present study can be placed in their proper perspective.

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