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Original Investigation

Body composition in patients with rheumatoid arthritis is not different than healthy subjects

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Abstract

Objective: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease (CVD). Increased body fat, particularly its central distribution, is a well-known risk factor for CVD. A change in body composition in RA has been described previously. However, in most of these studies, age- and sex- but not body mass index (BMI)-matched controls were used. The aim of this study was to evaluate body composition in RA patients and compare it with age-, sex-, and BMI-matched controls.

Material and Methods: Sixty-five RA patients (55 females and 10 males; mean age 54.9 ± 10.8) and 31 healthy controls (25 females, 6 males; 53.8±8.6) were included in this study. Mean disease duration was 9.2±9.6 years. Body composition was assessed by anthropometric methods (skinfold thicknesses, body circumferences), bioimpedance analysis, and dual-energy X-ray absorptiometry (DXA). Visceral adipose tissue (VAT) was assessed with computed tomography.

Results: There were no significant differences for total body fatness, regional fat distribution, and total body water and fat-free mass between RA patients and control subjects. Bone mineral content (BMC), assessed by DXA, was significantly lower in RA patients (p=0.004). Clinical disease activity indices and steroid treatment do not affect soft tissue body composition or BMC.

Conclusion: At least some RA patients do not have soft tissue composition alterations and may have similar health risks in comparison with subjects with similar age, sex, and total adiposity.

Key words: Arthritis, rheumatoid, body composition, visceral adipose tissue

Introduction

Rheumatoid arthritis (RA) is the most common inflammatory rheumatic disease. Several studies reported increased mortality and morbidity in RA patients (1-3), and some community- and hospital-based studies showed that the rates of cardiovascular disease (CVD) are increased and may contribute to increased mortality and morbidity (4-6). Some studies evaluated CVD risk factors in patients with RA, and their results were sometimes contradictory (7). Therefore, this increased CVD risk in RA can not be explained entirely by traditional risk factors (6, 7).

Obesity, characterized by increased body fat mass, is a well-known risk factor for CVD and is described based on body mass index (BMI). However, BMI is insensitive to body fatness, at particularly low BMI, as well as in above-normal muscle development conditions (8). Besides, in moderate obesity, regional distribution of fat mass appears to be a more important indicator of CVD, since an inconsistent correlation between BMI and CVD has been found (9, 10). In RA patients, a study aiming to determine incident cardiovascular events and to assess the role of well-known risk factors has also found that increased cardiovascular events were independent of obesity based on BMI (6).

Increased visceral adiposity has been found to be related with CVD risk. This effect was found to be independent of BMI and as a stronger predictor in some studies (11-13). Subcutaneous adipose tissue and lean body mass showed a contradictory association with metabolic diseases and cardiovascular risk factors (14).

Changes in body composition in RA patients have been reported previously. In these reports, loss of lean body mass, increased fat mass, and decreased bone mineral density were found (15-23). The possible explanations for the reduced lean body mass were inflammation, perhaps via cytokines, such as tumor necrosis factor and interleukin-1; reduced physical activity; and changing pattern of hormone production, like growth hormone (GH) and insulin-like growth factor-1 (IGF-1) (7, 16, 18, 19, 24). However, in most of these studies, patients and controls were matched for age and sex but not for body mass index.

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In this study, we examined several adiposity measures, including total adiposity (fat mass) and body fat distribution (waist circumference, visceral adipose tissue, subcutaneous adipose tissue), in patients with RA and compared them with age-, sex-, and BMI-matched controls.

Material and Methods

Sixty-five ambulatory patients with RA according to the 1987 criteria of the American College of Rheumatology (ACR) and 31 healthy controls were included in this study. Subjects with a disease or condition that could affect body composition or hydration status-namely, pregnancy, renal failure, congestive heart failure, malignancy, obvious thyroid dysfunction, steroid myopathy, and peripheral neuropathy-were excluded (25).

All subjects were fasted from midnight, and blood samples were drawn on the following morning. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured according to standard procedures.

Anthropometric measurements

Body height was measured to the nearest 0.5 cm in subjects in the erect posture without shoes, and body weight was measured to the nearest 100 gr in subjects wearing indoor clothes but no shoes. Body mass index was calculated as weight/height^2 (kg/m^2).

Skinfold thickness was determined to the nearest 0.1 mm at the triceps, biceps and suprailiac and subscapular areas on the right side using a standard skinfold caliper. All skinfold measurements recorded were the average of three readings. Waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. All anthropometric measurements were made in the standing position by the same observer using the same equipment for each patient.

Bioelectrical impedance analysis

Bioelectrical impedance analysis was performed using a single-frequency (50 kHz) Bodystat 1500 analyzer with tetrapolar electrode placement and subjects in the supine position. Using a bioelectrical impedance analyzer, total body water (%) and lean body mass (%) were assessed.

Dual-energy X-ray absorptiometry (DXA)

A total body scan was performed using a Hologic QDR-4500W (S/N 49106; Hologic, Waltham, Massachusetts) densitometer. Using DXA percentage of total body fat mass (body fat %), percentage of fat mass at the extremities and total body bone mineral content (BMC) were assessed.

Table 1. Demographic and clinical characteristics of study participants (data shown as mean±SD)

	RA	Controls	P*
N	65	31	
Age (yr)	54.9±10.8	53.8±8.6	0.608
Sex (F/M)	55/10	25/6	0.625
Height (cm)	156.2±6.6	158.0±8.2	0.252
Weight (kg)	67.3±12.2	70.7±10.5	0.193
BMI (kg/m^2)	27.5±4.8	28.1±4.8	0.607
No. of RF positive (%)	48/61 (79%)		
Disease duration (yr)	9.2±9.6		
No. taking steroids	45 (69.2%)		
Mean steroid dose (mg/day)	7.4±5.0		
Morning stiffness (min)	41.0±67.2		
No. of swollen joints	9.1±10.3		
No. of tender joints	8.6±8.0		
ACR functional class	2.3±1.0		
ESR (mm/h)	43.0±32.1	17.2±8.3	0.000
CRP (mg/L)	15.4±19.8	5.1±2.8	0.000

*RA vs controls
RA: rheumatoid arthritis; F: female; M: male; BMI: body mass index; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; ACR: American college of rheumatology

Computed tomography (CT)

To determine the visceral (intra-abdominal) fat area (VAT) and total fat areas, a simple CT scan was taken at the level of the L4-L5 vertebrae by using a 9800 CT scanner (General Electric, Milwaukee, WI). Subcutaneous fat area (SAT) was calculated by subtracting the visceral fat area from the total fat area. All CT measurements were made manually. The ratio of VAT to the SAT (V/S) was also estimated.

This study was approved by the local ethics committee. Informed consent was obtained from all subjects before participation.

Statistical analysis

Since the primary objective of the present study was to compare the body fat content between RA patients and controls, the sample size was estimated by using the results of a previous study that investigated cachexia in RA (26). Based on the findings of body fat % in RA (40.5±10.3) and controls (36.0±8.2) in the study mentioned above, the sample size was calculated as 23 for both samples.

Data were expressed as mean±standard deviation (SD). Differences of means were assessed using student's t-test if the variable was normally distributed. The Mann-Whitney U-test was used if these data were not normally distributed. Group differences in categorical variables were assessed using the χ^2 or Fisher's exact test, where appropriate. The relationships between different variables were analyzed by the Spearman r-test. Statistical evaluation was carried out using a computer package (SPSS Inc., Chicago, IL, USA). Two-sided tests of hypotheses were used, and a p value <0.05 was considered to be statistically significant.

Results

Demographic, clinical characteristics, and inflammatory markers of the patients and controls are shown in Table 1. There were no significant difference between groups concerning age, sex, height, weight, and BMI. The number of postmenopausal women in the two groups was not statistically different, either (p=0.24). However, as expected, ESR and CRP were higher in the patient group (p=0.000).

The results of the anthropometric measurements can be seen in Table 2. Triceps and suprailiac skinfold thickness were higher in the control group.

The results of the bio-electrical impedance analysis are shown in Table 3. As can be seen, there was no statistically significant difference between the groups in terms of total body water.

Total body fat and percentage of fat at the extremities (data not shown) as assessed by DXA were not significantly different, but BMC was significantly higher in the control group (Table 3).

Computed tomography assessment was performed in 44 RA patients and 26 control subjects. Visceral and subcutaneous fat areas, as well as V/S ratio, were quiet similar between the RA patients and the age-, sex-, and BMI-matched controls (Table 4).
Analyses of all variables above between patients and controls in a sex-specific manner revealed the same results (data not shown). This is may be due to the inclusion of a small number of male patients and controls in this study.

Table 2. The results of the anthropometric measurements

	RA			Controls			
	Female	Male	Total	Female	Male	Total	p*
Biceps (mm)	12.0±4.5	5.9±2.5	11.0±4.8	13.0±6.9	5.7±2.3	12.0±6.9	0.426
Triceps (mm)	19.8±6.5	8.9±3.3	18.1±7.2	23.6±6.7	11.5±3.1	21.9±7.5	0.021
Subscapular (mm)	22.4±7.9	15.2±4.4	21.3±7.9	25.0±7.8	16.0±4.3	23.7±8.0	0.175
Suprailiac (mm)	20.7±6.9	14.2±7.2	19.7±7.3	28.3±7.6	16.0±7.6	26.6±8.6	0.000
Waist circumference (mm)	92.8±13.0	91.8±6.0	92.6±12.2	91.7±9.8	97.0±8.2	92.4±9.6	0.928

RA: rheumatoid arthritis
*RA vs controls

Table 3. The results of the bio-electrical impedance analysis and dual-energy X-ray absorptiometry

	RA			Controls			
	Female	Male	Total	Female	Male	Total	p*
[a]Total water (%)	47.4±6.3	58.2±2.9	49.0±7.0	46.9±4.4	56.1±4.9	48.7±5.7	0.833
[b]Body fat %	38.7±6.2	24.5±5.9	36.3±8.0	38.6±4.1	23.0±6.8	35.4±7.8	0.668
bBMC (g)	1746.5±331.2	2105.0±362	1805.2±358.8	1999.4±263.2	2372.5±244.3	2074.0±295.8	0.004

[a]Data from bio-electrical impedance analysis.
[b]Data from DXA scan (n=55 for RA and n=20 for controls).
*RA vs controls
RA: rheumatoid arthritis

Table 4. The results of computed tomography measurements

	RA (n=44)			Controls (n=26)			
	Female	Male	Total	Female	Male	Total	p*
Visceral fat area (cm^2)	144.56±39.9	142.74±52.3	144.27±41.5	141.37±49.7	165.37±48.8	145.98±49.5	0.877
Subcutaneous fat area (cm^2)	380.38±113.8	193.15±62.7	350.59±127.3	342.1±110.1	211.54±86.6	316.95±116.9	0.275
Vis/Subcutan fat area	0.41±0.18	0.75±0.16	0.47±0.21	0.53±0.6	0.83±0.18	0.58±0.55	0.218

RA: rheumatoid arthritis
*RA vs controls

Rheumatoid factor positivity and number of tender and swollen joints at the time of the study did not influence any of the parameters of body composition described above (data not shown). ESR was only weakly correlated with total body water (%) (r=0.22, p=0.045). CRP was found to be positively correlated with total body water (%) (r=0.24, p=0.040) and negatively correlated with weight (r=-0.67, p=0.025) and BMC (r=-0.29, p=0.016). We found no relation between steroid use and body composition parameters, including BMC (data not shown).

Discussion

In some studies, it has been shown that CVD rate is increased in RA (4, 6, 27, 28). However, the evaluation of risk factors for CVD in this group of patients was restricted. In the present study, we investigated the soft tissue body composition, which may have an effect on the CVD risk of RA patients, and found that body fat mass and regional distribution were not altered in RA patients.

Studies about body composition assessment have become more interesting because of the association of excess fat mass-in particular, its distribution-with CVD risk. Following complete dissection of adult human bodies, it has been shown that chemical composition of the body's tissues is relatively constant. These data have served as the reference for the development of various methods for body composition analysis. In the classical two-compartment model of body composition, the body is divided into two parts: the body fat mass and the remaining fat-free (lean) mass (29, 30). However, simple measures, like BMI, that are often used to estimate body composition, take into account total body weight, but they do not distinguish between different tissues that constitute it. Various methods are available for the assessment of body composition, and each may have several advantages and limitations (30, 31). Therefore, in body composition analysis, it is suggested that repetitive or overlapping methods be used in the confirmation of normal or abnormal status. If only one method is used, then there are technical or model limitations, resulting in increased uncertainties associated with that method (29). In the present study, we evaluated the body composition of RA patients by means of various methods, some of which have overlapping results.

BIA is an easy, safe, and non-invasive method for determining body water content. In bioelectrical impedance, a small alternating current is applied to the body, and resistance or impedance of the body to that current is measured. Since only water is able to conduct the current, total body impedance is a measure of total body water. If water is assumed to be a constant part of the lean body mass, then bioelectrical impedance can be predictive of lean body (fat-free) mass (8, 32, 33). Fluid imbalances are a significant limitation to the use of BIA in clinical evaluation. Thus, BIA is inaccurate when the extra- to intracellular ratio is altered as a result of disease or treatment, such as diuretic use or dialysis (8). Our patient group was not significantly different from control patients regarding total body water evaluated by BIA. In addition, current steroid use, which may lead to fluid retention, did not seem to affect body water. The only disease-related parameters, CRP and ESR, were found to be related total body water in our patient group.

Although DXA was first developed to measure bone mineral content, it is now considered a useful tool for the evaluation of gross and regional body composition. Total body and regional fat mass can be measured by DXA (34, 35). Potential sources of errors in *in vivo* fat mass measurements by DXA described and in-

cluded differences in body thickness, variations in fat distribution and the fat content of bone marrow, and difficulties in evaluating fat mass in under- or overlying bone (34-36). Because of these possible limitations of body composition assessment by DXA, we tried to confirm our result with additional measurement techniques and found that both total and regional distribution of fat mass through extremities was not changed in RA patients.

Bone mineral density is defined the ratio of BMC to bone area. The primary function of calculating BMD is to decrease the variance in BMC seen in age groups and increase the statistical power of detecting abnormalities (29). Since it was not our primary objective, we did not evaluate bone mineral density. However, we found significantly lower BMC in RA patients and an inverse relation between BMC and CRP values. Increased rates of bone loss have been documented in patients with RA. Disease activity, reduced physical mobility, and steroid treatment have been found to be associated with this increased bone loss. We found an inverse relation between CRP levels and BMC but not with other indices of disease activity, as reported previously (21, 22, 37-41). Steroid therapy may cause bone loss via the suppression of osteoblastogenesis and osteoclastogenesis and the increased apoptosis of osteoblasts and osteoclasts (42). In most but not all studies, use of steroids was associated with lower bone mass (43, 44). In the present study, steroid usage did not have any effect on BMC. This may be due to concomitant calcium and vitamin D3 therapy or to the existence of other confounding factors, like the inflammatory process itself and decreased mobility. In addition, the effects of steroid usage on bone loss in RA may be more pronounced in the early phase of disease and therapy; however, mean disease duration in our study group was approximately 10 years (41). In a recent study, it was also shown that RA patients treated with low-dose prednisolone had a similar BMD compared with patients who had not been treated with prednisolone (45). In this study, the authors hypothesized that the suppressive effect on bone synthesis of low-dose glucocorticoids may be compensated for by its ability to hamper the inflammatory-mediated increase in bone resorption; therefore, the net effect of prednisolone on body composition and bone may be different in inflammatory diseases, such as RA.

Studies examining the prospective association between visceral adipose tissue and incidence of coronary heart disease have shown that visceral adipose tissue is predictive of coronary heart disease independently of BMI (12, 46). Although the mean BMI of our patients indicates that many of them were not obese, the regional and especially central distribution of fat mass was evaluated to reach a more robust conclusion. Adipose tissue stored in the visceral region has some characteristics that may contribute to increased risk of CVD. Compared with subcutaneous adipose tissue, visceral adipose tissue has higher rates of catecholamine-stimulated lipolysis and is connected via the portal venous system to the liver, allowing higher rates of direct free fatty acid influx to the liver (47). These free fatty acids can lead to hyperinsulinemia, accelerated synthesis of triglycerides, and increased hepatic lipase activity (7, 12, 48). In addition, potentially protective proteins for diabetes and CVD, such as adiponectin, leptin, and peroxisome proliferator-activated receptor-gamma, have been shown to be expressed at lower levels in visceral than subcutaneous adipose tissue (49, 50). Thus, assessment of visceral adipose tissue may be important for evaluation of CVD risk. Visceral adipose tissue can be assessed anthropometrically by subscapular skinfold thickness or waist circumference (11, 14). However, changes in waist circumference can also reflect changes in the risk of CVD (51). Thus, waist circumference may be the most useful parameter in daily clinical practice and epidemiologic studies (14). In our study, subscapular skinfold thicknesses and waist circumference measurements were quiet similar in RA patients and BMI-matched controls.

Both subcutaneous and visceral adipose tissue compartments have been well identified by means of CT, which is presently the gold standard technique (14, 48, 52). The association with cardiovascular disease with amount of visceral adipose tissue, assessed by CT or magnetic resonance imaging (MRI), is stronger than the association observed with indirect measures, such as waist circumference or waist-to-hip ratio (53, 54). We found no significant difference in visceral and subcutaneous fat areas measured by CT between RA patients and BMI-matched controls.

Despite its popularity, there are relatively few reports considering the association between RA and body composition. There are also contradictory findings regarding the association of body composition and RA. Some studies, with different techniques, reported that lean body mass (LBM) of RA patients were reduced compared with healthy subjects (18, 19, 24, 55). On the other hand, some studies reported increased visceral fat in RA subjects despite unchanged BMI values compared with controls (15, 18, 56). In the current study, we found no difference between RA and age-, sex-, and BMI-matched controls regarding total body fatness and its distribution, as well as lean tissue mass. The discrepancy between our results and those of others might be due to differences in the age and sex distribution of the patients, treatment and disease duration, and the methods used for the assessment of body composition and, at least in some studies, lack of appropriate controls.

In conclusion, at least some RA patients do not have soft tissue composition alterations that may contribute to increased risk for CVD in comparison with subjects with similar age, sex, and total adiposity.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Local Ethic committee.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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