Published in final edited form as:
Arthritis Care Res (Hoboken). 2013 January ; 65(1): 62–70. doi:10.1002/acr.21810.

Gender Differences in Assessment of Obesity in Rheumatoid Arthritis

Patricia PKatz, PhD, **Jinoos Yazdany, MD**, **Laura Trupin, MPH**, **Garbriela Schmajuk, MD**, **Mary Margaretten, MD**, **Lindsey A. Criswell, MD, MPH**, and **Edward H. Yelin, PhD**
University of California, San Francisco

Abstract

Objective—Determine prevalence of obesity and how accurately standard anthropometric measures identify obesity among men and women with RA.

Methods—Dual-energy x-ray absorptiometry (DXA) was performed for 141 persons with RA (56 men, 85 women). Two anthropometric proxies of obesity (body mass index [BMI], waist circumference [WC]) were compared to a DXA-based obesity criterion. Receiver operating characteristic (ROC) curves determined optimal cut-points for each anthropometric measure, relative to DXA. Association of body fat and anthropometric obesity measures with disease status and cardiovascular risk was assessed in multiple regression analyses, controlling for age and glucocorticoid use. All analyses were performed separately for men and women.

Results—20%, 32%, and 44% of women, and 41%, 36%, and 80% of men were classified as obese by BMI, WC, and DXA, respectively. Cut-points were identified for anthropometric measures to better approximate DXA estimates of percent body fat (BMI: women, ≥26.1 kg/m^2; men ≥24.7 kg/m^2. WC: women, ≥83 cm; men, ≥96 cm). For women and men, higher % fat was associated with poorer RA status. Anthropometric measures were more closely linked to RA status for women, but identified cardiovascular risk for both women and men.

Conclusions—A large percentage of this RA sample was overfat; DXA-defined obesity was twice as common in men than in women. Utility of revised BMI and WC cut-points compared to traditional cut-points remains to be examined in prospective studies, but results suggest that lower, sex-specific cut-points may be warrented to better identify individuals at risk for poor RA and/or cardiovascular outcomes.

Until recently, most studies of body composition in rheumatoid arthritis (RA) have focused on low lean mass or cachexia that may be caused by chronic inflammation(1,2). However, newer studies suggest that a substantial portion of individuals with RA may be obese or overfat(3-5), which may in part explain the increased cardiovascular (CV) disease risk seen in RA. Visceral fat appears to carry the greatest CV risk(6-8), and a high prevalence of central or abdominal obesity has been found in RA (9,10). The strong association between central obesity and cardiovascular outcomes suggests that waist circumference, often used as a proxy measure for central obesity or visceral fat mass, may be useful in RA, but this has not been confirmed.

Corresponding author: Patricia Katz, PhD, University of California, San Francisco, 3333 California Street, Suite 270, San Francisco, California 94143-0920, Phone: 415-476-5971, Fax: 415-476-9030, patti.katz@ucsf.edu.

The authors did not have any financial support or other benefits from commercial sources for the work reported on in this manuscript, or any other financial interests that could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

In most large-scale studies, obesity is estimated from body mass index (BMI; $weight_{kg}/height_m^2$). BMI may not accurately reflect the amount of body fat in persons with RA (4,9), however, because rheumatoid cachexia may occur with little or no weight loss, so that an individual may have a BMI within a normal range, but have greater fat mass than suggested by the BMI. As an example, one recent study reported that about one-third of an RA cohort was obese by BMI, a proportion that is roughly equivalent to the proportion of obese in the general population(5). Yet, using a more sensitive measure of body composition, over half of this same sample was determined to be over-fat. Use of RA-specific BMI criteria for defining obesity has been suggested(4), but little validation of revised BMI criteria has occurred.

Additionally, there is preliminary evidence of sex differences in the impact of RA on body composition. Giles reported that women with RA had significantly greater total body fat than women in a BMI-matched control group, but no differences in total fat were noted between men with RA and controls(5). Perhaps most important, however, men with RA appeared to accumulate greater visceral fat(10).

The goals of these analyses were to (1) determine the proportion of a cohort of men and women with RA who were obese using DXA and two common anthropometric proxy measures: BMI and waist circumference; (2) evaluate the accuracy of the standard obesity criteria for anthropometric measures for men and women with RA compared to DXA determinations of obesity, and identify criteria that best reflect DXA results; and (3) examine association of body fat and obesity with measures of RA symptoms and disease activity and cardiovascular risk.

Methods

Data source

The majority of research participants were drawn from the University of California, San Francisco (UCSF) RA Panel. The RA Panel was constructed in 1982 from a random sample of rheumatologists practicing in Northern California and originally consisted of 822 patients. There were subsequently four additional enrollment periods in 1989-90, 1995, 1999, and 2003, during which 203, 131, 122, and 169 individuals were enrolled, respectively. The principal data source for the RA Panel is an annual structured telephone interview that includes questions on demographics, RA symptoms, comorbidities, and functioning. Annual retention from year to year has averaged 93%; the 7% attrition includes deaths.

At the end of the telephone interviews in study years 2007-2009, RA Panel participants who lived in the greater San Francisco Bay Area and were willing to travel to UCSF were recruited for in-person assessments at the UCSF Clinical and Translational Science Institute's Clinical Research Center (CRC) that included measurement of body composition. Exclusion criteria were non-English-speaking, younger than age 18, current daily oral prednisone dose ≥50 mg, current pregnancy, uncorrected vision problems that interfered with reading, and joint replacement within one year.

A total of 101 participants were recruited from the RA Panel. There were no significant differences between eligible RA Panel members who participated compared to those who did not participate in terms of sex, race/ethnicity, education, RA duration, Health Assessment Questionnaire (HAQ) scores(11), pain severity ratings, depressive symptom scores, or BMI from self-reported height and weight. Participants were, however, significant younger than non-participants (mean age 61 years vs. 67 years, $p<.0001$). In 2009, an additional 44 subjects were recruited from the UCSF rheumatology clinic and from individuals who had participated in another study of RA. Data were not available to compare

characteristics of participants recruited from these sources to individuals who declined to participate.

Of 242 eligible individuals, 97 (40.1%) declined participation, primarily because of transportation (n=36) and scheduling difficulties (n=38), and 145 individuals completed study visits. Four participants were excluded from analysis because they did not complete the body composition assessment. Of the remaining 141, 85 (60.3%) were women and 56 (39.7%) were men.

The study was approved by the UCSF Committee on Human Research.

Measures

Body composition

Anthropometric measures: Height was measured with a wall-mounted stadiometer. Weight was measured with subjects wearing light indoor clothing and no shoes. Body mass index (BMI) was calculated as weight (Kg) divided by height (meters^2). Obesity by BMI was initially defined as BMI ≥30 kg/m^2 (12). Waist circumference (WC) was measured with a non-stretch measuring tape that applies a consistent amount of tension to the tape (Gullick II Tape Measure) at the mid-point between the lower border of the ribs and the iliac crest. Two measurements were taken, and the average measure used. Women with WC ≥88 cm and men with WC ≥102 cm were initially classified as obese(12).

Dual Energy X-ray Absorptiometry (DXA): Body composition and regional body fat distribution were assessed in the CRC using a Lunar Prodigy™ Dual Energy X-ray Absorptiometry (DXA) system. DXA has been validated as a method of assessing body composition in both younger and older persons, has good reported reproducibility, and is sensitive to small changes in body composition(13-16). Precision errors (1SD) for percent fat are 1.4%, for fat mass 1.0 Kg, and for lean tissue mass 0.8 Kg(14). DXA has previously been successfully used to assess body composition in RA (5,17-22).

There is no agreed-upon standard definition of obesity based on percent body fat (23). We used a standard that linked percent fat to the National Institutes of Health BMI guidelines defining obesity (24). To develop obesity criteria, average percent fat for individuals with BMI between 30-35 kg/m^2 (obese, but not morbidly obese) from three samples from the US, UK, and Japan was ascertained by DXA, and aggregated by sex, age, and racial group. Obesity definitions thus derived ranged from 38% fat for African American women aged 20-39 to 43% for white women aged 60-79, and from 26% for African American and white men aged 20-39 to 31% for white men aged 69-79 (24). We used those percentages as the criteria for defining obesity from DXA total percent fat, based on individuals' sex, age, and race. Other definitions of obesity based on percent fat have been suggested, but those specify lower fat percentages as obese (25,26).

Other variables—Socio-demographic characteristics (e.g., age, race/ethnicity, education, smoking status) were obtained from self-report. Glucocorticoid use was ascertained at the time of the visit by self-report.

Disease status: Self-reported RA disease activity was assessed at the visit with the Rheumatoid Arthritis Disease Activity Index (RADAI)(27,28). RADAI scores range from 0-10, with higher scores reflecting greater disease activity. The RADAI has been shown to be reliable and valid (27,28). Pain was rated on an 11-point numeric rating scale, from 0-10 (no pain-extreme pain) (29). The fatigue severity subscale from the Multi-Dimensional Assessment of Fatigue was used; scores range from 0-10 (no fatigue-severe fatigue)(30,31).

Functional limitations were assessed with the HAQ (scores range from 0-3, with higher scores reflecting greater limitations)(11). Blood was drawn and processed through a commercial laboratory to ascertain erythrocyte sedimentation rate (ESR).

Cardiovascular risk factors: Data were collected at the clinic visit that permitted calculation of the Framingham cardiovascular risk score (32). Blood pressure was measured by registered nurses while subjects were seated. Serum lipids and high-sensitivity C-reactive protein (hsCRP) were obtained through non-fasting blood draws. Although fasting measurements of blood lipids are ideal, non-fasting measures of total cholesterol and HDL have been found to very closely approximate fasting levels (33). Serum samples were processed by a commercial laboratory. Because hsCRP values were not normally distributed, log values were used in analyses.

Analysis

Differences in sociodemographic, disease, and body composition characteristics between men and women were assessed with t-tests and chi-square analyses. Receiver operating characteristic (ROC) curves were calculated to determine optimal cut-off points for each anthropometric measure, relative to DXA-determined obesity. Two threshold selection methods were used: the Youden and a second technique that determines the proximity to perfect correspondence (referred to in this paper as a “Distance to Perfect” index) (34). Briefly, the Youden Index determines maximum vertical distance from the ROC curve to the diagonal reference, or ‘chance’ line; the “optimal” cut-off point corresponds to the point on the ROC curve farthest from the reference line, which has also been used as a measure of the accuracy of a diagnostic test in clinical epidemiology (35). The Distance to Perfect Index selects the point on the ROC curve that is closest to the upper left-hand corner of the graph (0,1), which represents perfect classification (36), thereby minimizing misclassification. We calculated sensitivity, specificity, and positive and negative predictive value of both established and new criteria for each anthropometric measure compared to the DXA-based obesity classification.

To examine the potential usefulness of original and revised obesity criteria, we first examined the relationship of DXA-based body composition measures (total % body fat, obesity classification, and % total body mass from truncal fat) with disease status measures and cardiovascular risk using multivariate linear regression, controlling for age, glucocorticoid use, RA duration, and smoking. (The exception was for Framingham Risk Scores. Because smoking status is used to calculate the risk score, smoking was not included as a covariate in these regression analyses.) Next, we examined the relationship of anthropometric measures to the same disease and cardiovascular measures, also controlling for age, glucocorticoid use, RA duration, and smoking. These analyses were intended to identify relationships with DXA-defined body fat estimates, and then determine if anthropometric proxies of obesity were sensitive to these same associations.

Because body composition differences exist between racial and ethnic groups at the population level, we repeated all analyses including only white, non-Hispanic subjects (excluding 7 men and 7 women). Results from these analyses did not yield results substantively different from those obtained with the total sample, and are therefore not shown.

Results

Characteristics of the sample are shown in Table 1. There were no significant gender differences in sociodemographic or clinical variables, with the following exceptions: disease duration was greater for women (21.6 years vs. 16.1 years, p=.001), a greater proportion of

men were positive for anti-citrullinated peptide antibodies (100% vs. 81.2%, p=.0002), and mean Framingham Risk score was higher for women (11.5 vs. 9.1, p = .006).

Body composition and obesity

Mean BMI for the total sample was 27.1±6.0 (Table 2), and 28.4% were obese by BMI. Mean BMI for men was significantly higher than that of women (28.6 vs. 26.2, p=.02), and more men than women were obese by BMI (41.1% vs. 20.0%, p=.008). Overall, 33.8% (n=47) met the WC obesity criterion, but there was no difference in the proportion of men and women classified as obese by WC.

There were no significant sex differences in total % fat (men: 39.9%; women: 40.5%; p=.68) or % truncal fat. Over half of the total sample (58.2%, n=82) met the DXA criterion for obesity, with significantly more men than women classified as obese (80.4% vs. 43.5%, p<. 0001).

Analysis of obesity definitions

ROC analyses identified new gender-specific obesity definitions for each anthropometric measure, using DXA-defined obesity as the criterion. In each case, the new criteria were lower and more subjects were classified as obese. In addition, correspondence between DXA-defined obesity and anthropometric measures improved for each revised definition, although some improvements were slight.

Revised BMI obesity definitions were ≥24.7 for men and ≥26.1 for women (Table 3). For men, sensitivity and specificity of the original BMI definition of obesity were 0.47 and 0.82, respectively; the revised BMI definition produced a sensitivity of 0.73 and specificity of 0.73. For women, the original BMI definition yielded sensitivity and specificity of 0.46 and 1.00, respectively; the revised BMI definition produced sensitivity of 0.76 and specificity of 0.85. Using the revised obesity criteria, 73.2% of men and 81.2% of women were correctly classified.

For WC, men's revised obesity definition was ≥96 cm, which yielded sensitivity of 0.50 and specificity of 0.73 (in contrast to 0.41 and 0.82 from the original definition). Women's revised WC obesity definition was ≥83 cm, which yielded sensitivity of 0.78 and specificity of 0.77 (compared to 0.57 and 0.87 from the original). Using revised WC criteria, 53.6% of men and 76.5% of women were correctly classified compared to DXA classifications.

Association of DXA-based body composition with disease status and cardiovascular risk factors

For men, total % fat was significantly associated with higher pain ratings, greater disease activity by RADAI, and greater fatigue after adjustment for age, glucocorticoid use, disease duration, and smoking (Table 4). Percent truncal fat was also associated with pain rating and fatigue. However, when the DXA obesity cut-point was applied to % fat, no significant associations were noted between obesity and disease status.

Among women, greater total % fat and greater % truncal fat were each significantly associated with higher pain ratings, higher RADAI scores, and greater fatigue. Women who were obese by DXA had significantly greater pain, RADAI scores, and fatigue.

DXA-derived body fat measures were not associated with Framingham Risk scores or hsCRP for men. Among women, both higher total % fat and higher % truncal fat were associated with higher levels of hsCRP. Obesity by DXA and higher % truncal fat were also associated with higher Framingham Risk scores among women.

Association of anthropometric measures with disease status and cardiovascular risk factors

We examined associations of the same disease status measures with original and revised BMI and WC obesity definitions. Obesity defined by both original and revised BMI definitions was associated with significantly greater pain ratings and higher RADAI scores for men, and significantly greater fatigue ratings for women (Table 4). Obesity by the original, but not revised, BMI definition was associated with higher fatigue ratings, higher HAQ scores, higher ESR, and higher Framingham risk scores for men, and with higher pain ratings, RADAI scores, ESR values, Framingham Risk scores, and hsCRP levels for women.

No disease status measure was associated with WC-defined obesity for men, but central obesity by both original and revised WC definitions was significantly associated with higher Framingham risk scores for men. For women, however, both original and revised WC obesity were associated with greater pain, higher RADAI scores, and greater fatigue; higher HAQ scores and elevated ESR were associated with WC obesity by original definition only. Central obesity defined by both the original and revised WC criteria was associated with elevated Framingham risk score.

Discussion

A large portion of this RA sample was obese -- over one quarter using the standard BMI definition, one third using standard WC definitions, and over half using % fat from DXA. These rates are similar to those reported in other RA samples; e.g., Giles reported 33% of women and 36% of men with RA were obese by BMI and 57% were obese by DXA(5), and a UK study reported a BMI-defined prevalence of obesity of 31%(37).

Differences between rates of obesity in men and women were striking. Using both BMI and DXA criteria, twice as many men than women were classified as obese. DXA results showed that 80% of men in this RA sample were overfat. Of particular note, there was no significant difference in the total % fat between men and women in our sample, a finding that is at odds with population studies(38,39). Other published studies have noted differences in adiposity between men and women with RA. For example, Giles found that abdominal visceral adiposity was 51% higher in men with RA compared to men without RA, while there was no difference between women with and without RA(10). On the other hand, women with RA had more subcutaneous abdominal fat. Stavropoulos-Kalinoglou also noted relatively higher fat distributions in men with RA compared to men without RA(4). Men with RA had total fat percentages 49% higher than controls, while total percent fat for women with RA was 19% higher than controls. For truncal fat, men with RA were 43% higher than controls, while women with RA were 23% higher. However, none of these studies reported disparities in the prevalence of obesity between men and women with RA of the size we found. Additional study with larger samples will be needed to shed light on this unexpected finding.

We identified much lower BMI criteria to define obesity, as well as different cut-points criteria for men and women (men, 24.7; women 26.1). Stavropoulous-Kalinoglou previously suggested that the BMI cut-point for obesity be reduced by 2 kg/m^2 (i.e., to 28) for individuals with RA; our analyses support cut-points that are even lower. Other investigators have also noted in non-RA populations that the current obesity cut-point of BMI≥30 is too high, has low sensitivity to detect adiposity in the general population, and is not appropriate for specific ethnic groups, and have identified alternate BMI obesity cut-points very similar to those we identified, ranging from 25-25.8(40-45).

Relationships between DXA body fat measures and RA disease status measures existed for both men and women. Greater total percent fat was associated with higher pain ratings, higher disease activity ratings, and greater fatigue for men and women. Greater truncal fat was also associated with higher pain ratings and greater fatigue for both men and women. Framingham Risk scores were associated with DXA-defined obesity and truncal fat for women, but not for men. Among women, inflammatory biomarkers were also associated with % truncal fat; a similar association was not noted for men. There were few non-obese men, though, which may have limited our ability to find these associations, although Giles also noted different patterns of association of fat with CRP for men and women(22): adiposity was significantly associated with CRP for women, but not for men, similar to our findings.

We expected associations between anthropometric obesity proxies and RA disease status and cardiovascular risk measures to parallel those seen with measures of body fatness obtained through DXA, and there were important consistencies as well as inconsistencies. BMI appeared to function satisfactorily as a proxy for DXA-derived obesity in these analyses. Men and women who met the standard BMI obesity criterion had significantly greater pain, disease activity, fatigue, and ESR levels. Only a few associations were noted with the revised BMI criterion, calling its usefulness into question.

The revised WC cut-points improved correspondence with DXA over the original WC cut-points, but only marginally. Substantial differences existed between men and women in the associations between central obesity and RA disease measures. There were no significant differences in RA disease measures for men using either WC criterion. In contrast, women who met the original WC obesity criterion exhibited worse RA status on all measures, and differences remained for pain, RADAI, and fatigue when the revised WC criterion was used.

The relationship between WC and cardiovascular risk was more robust. Both men and women who met either WC obesity criterion had significantly higher Framingham risk scores. The revised WC definitions we derived are similar to those proposed by International Diabetes Federation(46) for whites as low risk for metabolic syndrome (men: 94 cm for men; women: 80 cm). Further study is needed to establish the usefulness of WC as a proxy of obesity in RA and the appropriate criteria to define obesity.

Our revised obesity criteria for both BMI and WC improved sensitivity to detect obesity over the traditional definitions, but decreased specificity. As BMI and WC might be used as screening tests to identify individuals with potentially harmful levels of body fat, a condition treatable by fairly benign means but associated with heighted risk of a number of poor health outcomes, the trade-off of high sensitivity for lower specificity, particularly when specificity is still at an acceptable level, seems appropriate.

This study has several limitations. The sample was relatively small, and, we may have lacked statistical power in some cases. These analyses present cross-sectional associations; no causal attributions can be made. Clearly, these analyses need to be repeated with larger, longitudinal samples. The range of disease severity may have limited our findings. Few participants had very active RA, but the restricted range of disease activity should have biased our findings toward the null. Population-based studies have demonstrated racial and ethnic differences in the correspondence of BMI with body fatness. Our sample was primarily white, which limits the extent to which our results, particularly the revised obesity definitions, can be extended to other groups; at the same time, however, our more homogenous sample limited the variability due to racial or ethnic differences. We have only measures of total truncal fat, and were not able to differentiate between subcutaneous and visceral fat. Sex differences in preponderance of visceral fat have previously been noted in

an RA sample, with men having greater visceral fat, and visceral fat is, in turn, most strongly linked to cardiovascular events and outcomes(6-8). Glucocorticoid use has often been linked to body composition; cumulative prednisone dose has been linked to visceral fat(10,47). While we were able to control for glucocortioid use during the year prior to data collection, we do not have a good estimate of cumulative glucocorticoid use.

Our results do not provide a clear picture of the mechanism whereby obesity might be associated with worse RA disease or cardiovascular risk, although we can make a proposal based on results of the inflammatory biomarker results. Elevated ESR is often linked to active or severe RA; likewise, elevated CRP is associated with longitudinal risk of cardiovascular disease. It seems reasonable to project that greater amounts of adipose tissue are a source of inflammation, which then may lead to heighted disease activity and cardiovascular risk (3,22,48-50). This mechanism has been proposed by several investigators, and our cross-sectional associations provide supportive evidence, but future longitudinal studies are needed to further elucidate these pathways. While a paradoxical relationship has been found in which obesity is associated with less severe joint damage in RA, other health effects of obesity in RA appear to parallel those seen in the general population -- increased cardiovascular risk, greater functional limitations, and worse disease status.

These findings provide further evidence of a high prevalence of obesity or overfatness among individuals with RA. Sex differences existed in this sample, with men having higher rates of obesity, which may place them at particularly high risk of cardiovascular disease and events. Findings from this study indicate that consideration of separate BMI obesity critiera for men and women may be warranted, although this proposal should be confirmed in other samples. The revised BMI and WC cut-points identified for women with RA are very similar to those identified for women with SLE using the same methodology (BMI: 26.8; WC: 84.75)(51). Nonetheless, these revised obesity criteria may be overly stringent; those suggested by Stavroupoulous-Kalinoglou (BMI≥28)(4) may be more realistic. However, these results do underscore the issue of importance of considering overfatness in RA.

Future research is needed to determine if relationships noted in these two rheumatic conditions are unique; if lower obesity criteria should be considered for connective tissue diseases, in general; or if these lower cut-points are reflective of changes in body composition in the general population. Regardless, these results suggest that use of more stringent criteria for proxy measures such as BMI among individuals with RA, as has been previously suggested, may be warranted, because more stringent methods appear to identify risk for poor RA outcomes, as well as heightened CV risk. Furthermore, anthropometric measures may provide proxy estimates of body composition that are as effective in identifying risk for poor RA and CV outcomes as DXA, but are much less costly and can easily be implemented in clinical settings.

Acknowledgments

We gratefully acknowledge the important contributions of Sandi Kaplan, Holly Wing, and Rachel Diskin, who conducted all of the study assessments

This research was supported by NIH/NIAMS grant P60 AR053308 and by NIH/NCRR UCSF-CTSI Grant Number UL1 RR024131.

References

1. Roubenoff R. Exercise and inflammatory disease. Arthritis Rheum (Arthritis Care Res). 2003; 49:263–266.
2. Walsmith J, Roubenoff R. Cachexia in rheumatoid arthritis. Int J Cardiol. 2002; 85:89–99. [PubMed: 12163213]
3. Stavropoulos-Kalinoglou A, Metsios G, Koutedakis Y, Kitas G. Obesity in rheumatoid arthritis. Rheumatology. 2011; 50:450–462. [PubMed: 20959355]
4. Stavropoulos-Kalinoglou A, Metsios G, Koutedakis Y, Nevill A, Douglas K, Jamurtas A, van Zanten J, Labib M, Kitas G. Redefining overweight and obesity in rheumatoid arthritis patients. Ann Rheum Dis. 2007; 66:1316–1321. [PubMed: 17289757]
5. Giles J, Ling S, Ferrucci L, Bartlett S, Andersen R, Towns M, Muller D, Fontane K, Bathon J. Abnormal body composition phenotpes in older rheumatoid arthritis patients: association with disease characteristics and pharmacotherapies. Arthritis Care Res. 2008; 59:807–815.
6. Koster A, Stenholm S, Alley D, Kim L, Simonsick E, Kanaya A, Visser M, Houston D, Nicklas B, Tylavsky F, et al. Body fat distribution and inflammation among obese older adults with and without metabolic syndrome. Obesity. 2010; 18:2354–2361. [PubMed: 20395951]
7. Rosito G, Massaro J, Hoffmann U, Ruberg F, Mahabadi A, Vasan R, O'Donnell C, Fox C. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcificaton in a community-based sample: the Framingham Heart Study. Circulation. 2008; 117:605–613. [PubMed: 18212276]
8. Mahabadi A, Massaro J, Rosito G, Levy D, Murabito J, Wolf P, O'Donnell C, Fox C, Hoffmann U. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease buden: the Framingham Heart Study. Eur Heart J. 2009; 30:850–856. [PubMed: 19136488]
9. Elkan A, Engvall I, Cederholm G, Hafström I. Rheumatoid cachexia, central obesity, and malnutrition in patients with low-active rheumatoid arthritis: feasibility of anthropometry, Mini Nutritional Assessment and body composition techniques. Eur J Nutr. 2009; 48:315–322. [PubMed: 19333642]
10. Giles J, Allison M, Blumenthal R, Post W, Gelber A, Petri M, Tracy R, Szklo M, Bathon J. Abdominal adiposity in rheumatoid arthritis. Arthritis Rheum. 2010; 62:3173–3182. [PubMed: 20589684]
11. Fries J, Spitz P, Kraines R, Holman H. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980; 23:137–145. [PubMed: 7362664]
12. World Health Organization. Obesity: preventing and managing the global epidemic. World Health Organization; Geneva: 2000.
13. Heymsfield S. Dual photon absorptiometry: comparison of bone mineral and soft tissue mass measurements in vivo with established methods. Am J Clin Nutr. 1989; 49:1283–1289. [PubMed: 2729167]
14. Mazess R. Dual-energy x-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. Am J Clin Nutr. 1990; 51:1106–1112. [PubMed: 2349926]
15. Wang J. body fat from body density: underwater weighing vs dual-phon absorptiometry. Am J Physiol. 1989; 256:E829–E834. [PubMed: 2735405]
16. Visser M, Pahor M, Tylavsky F, Kritchevsky S, Cauley J, Newman A, Blunt B, Harris T. One- and two-year change in body composition as measured by DXA in a population-baesd cohort of older men and women. J Appl Physiol. 2003; 94:2368–2374. [PubMed: 12598481]
17. Westhovens R, Nijs J, Taelman V, Dequeker J. Body composition in rheumatoid arthritis. Br J Rheumatol. 1997; 36:444–448. [PubMed: 9159537]
18. Rall L, Walsmith J, Snydman L, Reichlin S, Veldhuis J, Kehayias J, Abad L, Lundgren N, Roubenoff R. Cachexia in rheumatoid arthritis is not explained by decreased growth hormone secretion. Arthritis Rheum. 2002; 46:2574–2577. [PubMed: 12384914]
19. Roubenoff R, Walsmith J, Lundgren N, Snydman L, Dolnikowski G, Roberts S. Low physical activity reduces total energy expenditure in women with rheumatoid arthritis: implications for dietary intake recommendations. Am J Clin Nutr. 2002; 76:774–779. [PubMed: 12324290]

20. Walsmith J, Abad L, Kehayias J, Roubenoff R. Tumor necrosis factor-α production is associated with less body cell mass in women with rheumatoid arthritis. J Rheumatol. 2004; 31:23–29. [PubMed: 14705214]
21. Giles J, Bartlett S, Andersen R, Fontaine K, Bathon J. Association of body composition with disability in rheumatoid arthritis: impact of appendicular fat and lean tissue mass. Arthritis Rheum (Arthritis Care Res). 2008; 59:1407–1415.
22. Giles J, Bartlett S, Andersen R, Thompson R, Fontaine K, Bathon J. Association of body fat with C-reactive protein in rheumatoid arthrits. Arthritis Rheum. 2008; 58:2632–2641. [PubMed: 18759279]
23. Expert WHO Committee on Physical Status. Technical Report Series No 854. 1995. Physical status: the use and interpretation of anthropometry: report of a WHO expert committee.
24. Gallagher D, Heymsfield S, Heo M, Jebb S, Murgatroyd P, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. Am J Clin Nutr. 2000; 2000:72.
25. Schutz Y, Kyle U, Pichard C. Fat-free mass index and fat max index percentiles in Caucasians aged 18-98y. Int J Obesity. 2002; 26:953–960.
26. Heyward, V.; Wagner, D. Applied body composition assessment. 2nd edn. Human Kinetics; Champaign, IL: 2004.
27. Stucki G, Liang M, Stucki S, Bruhlmann P, Michel B. A self-administered rheumatoid arthritis disease activity index (RADAI) for epidemiologic research. Arthritis & Rheumatism. 1995; 38(6): 795–798. [PubMed: 7779122]
28. Fransen J, Langenegger T, Michel B, Stucki G. Feasibility and validity of the RADAI, a self-administered rheumatoid arthritis disease activity index. Rheumatology. 2000; 39(3):321. [PubMed: 10788543]
29. Hawker G, Mian S, Kendzerska T, French M. Measures of adult pain. Arthritis Care Res. 2011; 63(suppl):S240–S252.
30. Hewlett S, Dures E, Almeida C. Measures of fatigue. Arthritis Care Res. 2011; 63(suppl):S263–S286.
31. Multidimensional Assessment of Fatigue (MAF) User's Guide
32. D'Agostino R, Vasan R, Pencina M, Wolf P, Cobain M, Massaro J, Kannel W. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008; 117:743–753. [PubMed: 18212285]
33. The Emerging Risk Factors Collaboration. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009; 302:1993–2000. [PubMed: 19903920]
34. Youden W. Index for rating diagnostic tests. Cancer. 1950; 3:32–35. [PubMed: 15405679]
35. Kraemer, H. Evaluating medical tests: objective and quantitative guidelines. Sage Publications; Newbury Park, CA: 1992.
36. Coffin M, Sukhatme S. Receiver operating characteristic studies and measurement errors. Biometrics. 1997; 53:823–837. [PubMed: 9333348]
37. Armstrong D, McCausland E, Quinn A, Wright G. Obesity and cardiovascular risk factors in rheumatoid arthritis. Rheumatology. 2006; 45:782. [PubMed: 16632480]
38. Borrud L, Flegal K, Looker A, Everhart J, Harris T, Shepherd J. Body composition data for individuals 8 years of age and older: U.S. population, 1999-2004. Vital Health Stat 11. 2010; (250):1–87. [PubMed: 20812448]
39. Chumlea W, Guo S, Kuczmarski R, Flegal K, Johnson C, Heymsfield S, Lukaski H, Friedl K, Hubbard V. Body composition estimates from NHANES III bioelectrical impedance data. Int J Obes. 2002; 26:1596–1609.
40. Rahman M, Berenson A. Accuracy of current body mass index obesity classification for white, black, and hispanic reproductive-age women. Obstet Gynecol. 2010; 115:982–988. [PubMed: 20410772]
41. Romero-Corral A, Somers V, Sierra-Johnson J, Thomas R, Collazo-Clavell M, Korinek J, Allison T, Batsis J, Sert-Kuniyoshi F, Lopez-Jimenez F. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obesity. 2008; 2008:959–966.

42. Okorodudu D, Jumean M, Montori V, Romero-Corral A, Somers V-J,J, Erwin P, Lopez-Jimenez F. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obesity. 2010; 34:791–799.
43. Blew R, Sardinha L, Milliken L, Teixeira P, Going S, Ferreira D, Harris M, Houtkooper L, Lohman T. Assessing the validity of body mass index standards in early postmenopausal women. Obes Res. 2002; 10:799–808. [PubMed: 12181389]
44. Evans E, Rowe D, Racette S, Ross K, McAuley E. Is the current BMI obesity classification appropriate for black and white postmenopausal women? Int J Obes. 2006; 30:837–843.
45. Chen Y, Ho S, Lam S, Chan S. Validity of body mass index and waist circumference in the classification of obesity as compared to percent body fat in Chinese middle-aged women. Int J Obes. 2006; 30:918–925.
46. Alberti K, Zimmer P, Shaw J. Metabolic syndrome -- a new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med. 2006; (23)
47. Kirwan, J. Systemic glucocorticoids in rheumatology. In: Hochberg, M.; Silman, A.; Smolen, J.; Weinblatt, M.; Weisman, M., editors. Rheumatology. 3rd edn. Mosby; New York, NY: 2003.
48. Lago F, Gómez R, Conde J, Scotece M, Gómez-Reino J, Gualillo O. Cardiometabolic comorbidities and rheumatic diseases: focus on the role of fat mass and adipokines. Arthritis Care Res. 2011; 63:1083–1090.
49. Neumann E, Frommer K, Vasile M, Müller-Ladner U. Adipocytokines as driving forces in rheumatoid arthritis and related inflammatory diseases? Arthrits Rheum. 2011; 63:1159–1169.
50. Rho Y, Solus J, Sokka T, Oeser A, Chung C, Gebretsadik T, Shintani A, Pincus T, Stein C. Adipocytokines are associated with radiographic joint damage in rheumatoid arthritis. Arthritis Rheum. 2009; 60:1906–1914. [PubMed: 19565493]
51. Katz P, Gregorich S, Yazdany J, Trupin L, Julian L, Yelin E, Criswell LA. Obesity and its measurement in a community-based sample of women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011; 63(2):261–268. [PubMed: 20824801]

Significance and Innovation

- Obesity is associated with numerous negative health effects, including heightened cardiovascular risk.
- The prevalence of obesity is high in RA; there appear to be substantial sex differences in prevalence, with obesity more common in men than women with RA.
- Obesity defined by anthropometric proxy measures identifies poor RA-specific outcomes, as well as cardiovascular risk.
- Lower, sex-specific cut-points to define obesity by both BMI and waist circumference may be warranted.

Table 1

Subject characteristics

	Total (n = 141)	Men (n = 56)	Women (n = 85)	p
Sociodemographic				
Age, mean ± SD	58.0 ± 10.8	56.6 ± 11.1	58.9 ± 10.5	.21
White, % (n)	90.1 (127)	87.5 (49)	91.8 (78)	.41
Education < 12 years, % (n)	3.6 (5)	3.6 (2)	3.5 (3)	.99
Disease-related				
RA duration, mean ± SD	19.4 ±11.2	16.1 ± 8.3	21.6 ± 12.3	.002
Current glucocorticoid use, % (n)	35.5 (50)	36.5 (31)	33.9 (19)	.86
Current dose*, mg, mean ± SD	6.3 ± 5.2	7.1 ± 7.3	5.7 ± 3.3	.42
Highest dose in past year*, mg, mean ± SD	17.1 ± 19.4	13.6 ± 13.8	19.9 ± 22.7	.18
Pain rating, mean ± SD (range 0-10)	2.6 ± 2.2	2.8 ± 2.3	2.5 ± 2.1	.38
RADAI score, mean ± SD (range 0-10)	2.6 ± 1.7	2.7 ± 1.8	2.5 ± 1.7	.48
Fatigue severity, mean ± SD (range 0-10)	5.0 ± 2.5	5.4 ± 2.7	4.8 ± 2.4	.14
HAQ, mean ± SD (range 0 – 3)	0.94 ± 0.67	0.95 ± 0.65	0.94 ± 0.69	.96
Anti-citrullinated peptide antibody (ACPA) positive	88.7 (125)	100 (56)	81.2 (69)	.0002
Other				
Current smoker, % (n)	5.7 (8)	7.1 (4)	4.7 (4)	.71
Framingham Risk Score, mean ± SD	10.5 ± 5.1	9.1 ± 5.0	11.5 ± 5.0	.006
High sensitivity C-reactive protein	4.8 (7.9)	4.5 ± 6.5	5.1 ± 8.8	.66

RADAI = Rheumatoid Arthritis Disease Activity Index

HAQ = Health Assessment Questionnaire

*Current glucocorticoid use n = 50; any use in past year n = 61 (43.3%).

Table 2

Body composition characteristics of sample

	Total	Men	Women	P
BMI, mean ± SD	27.1 ± 6.0	28.6 ± 6.6	26.2 ± 5.4	.02
Obese by BMI≥30, % (n)	28.4 (40)	41.1 (23)	20.0 (17)	.008
Obese by waist circumference, % (n)	33.8 (47)	36.4 (20)	32.1 (27)	.71
% Total fat from DXA, mean ± SD	40.3 ± 8.7	39.9 ± 9.5	40.5 ± 8.2	.68
% Trunk fat[1], mean ± SD	20.6 ± 5.4	21.0 ± 5.3	20.4 ± 5.5	.53
% Appendicular fat[2], mean ± SD	18.4 ± 4.7	17.7 ± 5.7	18.9 ± 4.0	.17
% Appendicular lean mass[3], mean ± SD	25.2 ± 4.1	26.0 ± 4.3	24.7 ± 3.8	.08
Obese by DXA, % (n)	58.2 (82)	80.4 (45)	43.5 (37)	<.0001

[1] percent of total mass from trunk fat (trunk fat/total mass)

[2] percent of total mass from appendicular fat

[3] percent of total mass from appendicular lean mass

Table 3

Results of receiver operating curve analyses to estimate revised BMI and waist circumference obesity criteria for men and women with RA

	BMI				Waist circumference			
	Men		Women		Men		Women	
	Original	New	Original	New	Original	New	Original	New
Cutpoint	≥30	24.7	≥30	26.1	102	96	88	83
% classified as obese	41.1	64.3	20.0	41.2	36.4	45.5	32.1	47.6
% correctly classified	53.6	73.2	76.5	81.2	48.2	53.6	72.9	76.5
Sensitivity	0.47	0.73	0.46	0.76	0.41	0.50	0.57	0.78
Specificity	0.82	0.73	1.00	0.85	0.82	0.73	0.87	0.77
Positive predictive value	0.91	0.92	1.00	0.80	0.90	0.88	0.78	0.73
Negative predictive value	0.27	0.40	0.71	0.82	0.26	0.27	0.72	0.82

Table 4

Relationship between body fat/obesity measures and disease status and cardiovascular risk factors*

	DXA			BMI		Waist circumference	
	Total fat % (Total fat mass/ total mass)§	**Obese by DXA**	**Trunk fat % (Trunk fat mass/ total mass§**	**Original**	**New**	**Original**	**New**
Men							
Disease status							
Pain rating (0 – 10)	**0.8 (0.2, 1.4)** ††	0.9 (−0.7, 2.4)	**1.2 (0.1, 2.3)** †	**1.4 (0.02, 2.6)** †	**1.3 (0.1, 2.7)** †	0.8 (−0.4, 2.1)	0.7 (−0.6, 1.9)
RADAI score	**0.6 (0.1, 1.1)** †	0.5 (−0.7, 1.7)	0.8 (−0.1, 1.7)	**1.2 (0.2, 2.2)** †	**1.0 (0.0, 2.0)** †	0.6 (−0.4, 1.6)	0.4 (−0.6, 1.4)
Fatigue	**1.1 (0.4, 1.7)** ††	0.7 (−1.0, 2.5)	**1.6 (0.3, 2.9)** †	**1.5 (0.02, 2.9)** †	1.3 (−0.1, 2.8)	0.7 (−0.7, 2.2)	0.8 (−0.6, 2.2)
HAQ	0.1 (−0.04, 0.3)	−0.2 (−0.7, 0.2)	0.2 (−0.1, 0.5)	**0.4 (0.05, 0.8)** †	0.2 (−0.2, 0.5)	0.2 (−0.2, 0.6)	0.2 (−0.1, 0.6)
ESR	1.2 (−4.5, 6.9)	1.8 (−11.4, 15.1)	4.4 (−5.6, 14.4)	**11.6 (0.9, 22.4)** †	1.9 (−9.1, 12.9)	9.6 (−1.0, 20.3)	10.1 (−0.2, 20.4)
Cardiovascular risk factors							
Framingham Risk Score	0.1 (−0.5, 0.7)	0.8 (−0.6, 2.2)	0.7 (−0.3, 1.8)	**1.8 (0.7, 2.9)** ††	1.1 (−0.1, 2.3)	**1.4 (0.3, 2.5)** †	**1.8 (0.7, 2.8)** ††
hsCRP (log)	0.0 (−0.3, 0.3)	−0.5 (−1.0, 0.1)	0.2 (−0.3, 0.6)	0.4 (−0.1, 0.8)	−0.3 (−0.8, 0.2)	0.4 (−0.1, 0.9)	0.4 (−0.1, 0.9)
Women							
Disease status							
Pain rating (0 – 10)	**0.9 (0.3, 1.4)** ††	**1.3 (0.4, 2.2)** ††	**1.5 (0.7, 2.2)** ††	**2.1 (1.0, 3.2)** ††	0.9 (−0.03, 1.9)	**1.5 (0.6, 2.4)** ††	**1.0 (0.1, 1.9)** †
RADAI score	**0.7 (0.2, 1.1)** ††	**0.9 (0.1, 1.6)** †	**1.2 (0.5, 1.8)** ††	**1.7 (0.8, 2.6)** ††	0.6 (−0.2, 1.4)	**1.2 (0.4, 1.9)** ††	**0.9 (0.1, 1.6)** †
Fatigue	**0.9 (0.3, 1.5)** ††	**1.2 (0.3, 2.2)** †	**1.7 (0.9, 2.5)** ††	**2.4 (1.3, 3.6)** ††	**1.4 (0.4, 2.4)** ††	**2.0 (1.2, 2.8)** ††	**1.5 (0.6, 2.5)** ††
HAQ	0.1 (−0.1, 0.3)	0.1 (−0.1, 0.4)	0.2 (−0.1, 0.5)	0.2 (−0.2, 0.5)	−0.1 (−0.3, 0.2)	0.3 (0.03, 0.6)†	0.1 (−0.2, 0.4)
ESR	3.3 (−1.8, 8.4)	4.0 (−4.5, 12.5)	**7.5 (0.1, 14.9)** †	**11.6 (0.6, 21.5)** †	0.4 (−8.5, 9.2)	**11.0 (2.3, 19.6)** ††	6.3 (−2.1, 14.7)
Cardiovascular risk factors							
Framingham Risk Score	0.7 (−0.02, 1.4)	**1.2 (0.1, 2.4)** †	**1.3 (0.3, 2.3)** †	**1.8 (0.4, 3.2)** ††	0.5 (−0.7, 1.7)	**1.8 (0.7, 3.0)** ††	**1.5 (0.3, 2.6)** †
hsCRP (log)	**0.3 (0.1, 0.5)** †	0.3 (−0.1, 0.6)	**0.4 (0.1, 0.8)** †	**0.5 (0.1, 1.0)** †	0.2 (−0.2, 0.6)	0.3 (−0.1, 0.7)	0.3 (−0.1, 0.7)

*Values in table are beta 95% confidence) from multivariate regression analyses, adjusted for age, glucocorticoid use, disease duration, and smoking. (Exception: Framingham risk scores were not adjusted for smoking because smoking in included in the calculation of the risk score.)

§Per 10% increment.

†p<.05;

††p<.01