Low Body Mass Index Is Adversely Associated with Radiographic Joint Damage in Indian Patients with Early Rheumatoid Arthritis

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ABSTRACT. Objective. Various factors affect joint damage in rheumatoid arthritis (RA). The influence of body mass index (BMI) is not adequately known. As BMI is potentially modifiable, we studied its influence on radiological joint damage in patients with RA.

Methods. Treatment-naive patients with early RA (< 24 mo) were included. Demographic data were collected along with swollen joint count (SJC), tender joint count (TJC), erythrocyte sedimentation rate (ESR), and IgM-rheumatoid factor (IgM-RF). Radiographs of hands and feet were obtained. BMI and Disease Activity Score for 28-joint count (DAS28-ESR) were calculated. Joint damage was assessed using the Simplified Erosions Narrowing Score (SENS).

Results. A total of 101 patients were studied (81 women; mean age 41.91 ± 11.99 yrs). Mean disease duration was 10.77 ± 6.73 months; 55 patients (54.5%) were IgM-RF-positive. Mean BMI was 22.82 ± 4.66 kg/m² with 24 (23.8%) patients having low, 42 (41.6%) normal, and 35 (34.7%) high BMI. Mean SENS score was 16.81 ± 11.10; mean DAS28 was 6.23 ± 0.96. Significant correlation was noted between SENS and DAS28 (r = 0.28; p < 0.005). There was significant negative correlation between BMI and SENS (r = -0.509; p < 0.0005). In patients with low BMI, mean SENS (26.62 ± 13.45) was significantly higher than in patients with normal (15.88 ± 8.38; p < 0.001) and high BMI (11.20 ± 7.32; p < 0.001). Patients with normal BMI also had significantly higher SENS scores than those with high BMI (p < 0.05). One-way ANOVA did not reveal significant differences in DAS28 between groups. SENS was significantly higher in the IgM-RF-positive group (19.55 ± 11.36) than in the IgM-RF-negative group (13.54 ± 9.94; p < 0.01); DAS28 was not different between the 2 groups (6.22 ± 0.98 vs 6.26 ± 0.96, respectively). Within the 2 IgM-RF groups, a significant negative correlation was seen between BMI and SENS. Multiple regression analysis revealed RF, DAS28, and BMI were independently associated with SENS. BMI accounted for 23.04% of the variance in SENS independent of DAS28 and IgM-RF.

Conclusion. Low BMI is adversely associated with joint damage in patients with early RA.

Key Indexing Terms:
BODY MASS INDEX    DISEASE ACTIVITY SCORE    RHEUMATOID ARTHRITIS
OBESITY    RADIOLOGICAL DAMAGE    SIMPLIFIED EROSION NARROWING SCORE

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease affecting about 1% of the adult population. The hallmark of this disease is synovial inflammation and its potential to cause cartilage and bone damage, with consequent effects on joint integrity. The mechanisms leading to this destruction remain unclear. Proinflammatory cytokines and activation of osteoclasts appear to have a crucial role1,2,3. The destructive consequences of the disease are evident by the appearance of erosions in 10%–26% of patients within 3 months of disease onset, in over 60% within one year, and in about 75% of patients within 2 years4,5. More recently, RA inflammation has also emerged as an important cause of cardiovascular morbidity and mortality.

The joint damage does not progress predictably in every patient. There are significant interpatient differences in the rate at which the joint damage progresses; various factors associated with it have been studied over years. Unfortunately, most of these factors are nonmodifiable. One that seems to be of clinical significance but has not been adequately studied is the body mass index (BMI), which reflects the nutritional status of an individual. In a general population, high BMI has been associated with increased risk of conditions such as diabetes mellitus, cardiovascular disease, stroke, and osteoarthritis. Interestingly, a few recent studies have paradoxically shown a protective effect of...
higher BMI on cardiovascular disease in patients with RA. A few studies have also shown low BMI to be associated with increased radiographic joint damage in patients with RA. It is an important clinical variable because of the potential to be favorably modified to influence outcomes in patients with RA.

It is known that factors influencing disease processes may not be uniformly applicable across ethnic groups. Indians represent a race with a population distribution of body fat and BMI very different from those of Caucasians. Whether low BMI protects against joint damage in Indian patients with RA is not known. We investigated this concept hoping to establish its generalizability.

**MATERIALS AND METHODS**

This study was conducted in the outpatient clinic of the Department of Rheumatology, Nizam’s Institute of Medical Sciences, Hyderabad, India. The study was approved by the institutional ethics committee. Informed consent was obtained from all participating patients. Treatment-naive patients with early RA (< 24 months) fulfilling American College of Rheumatology criteria were included. Smoking and alcohol abuse at incidence and thereafter were exclusion criteria.

Data were collected on age, sex, height, weight, swollen joint count, tender joint count, erythrocyte sedimentation rate (ESR: Westergren method), and IgM rheumatoid factor (IgM-RF). Radiographs were taken of both hands with wrists (posteroanterior views) and both feet (anteroposterior views). BMI (weight in kg/height in m²) and Disease Activity Score-28 (DAS28 ESR) were calculated in all subjects. Based upon the BMI values, patients were assigned to low, normal, or high BMI groups following the classification criteria of the World Health Organization.

Radiographic joint damage was assessed using the Simplified Erosions Narrowing Score (SENS) as this was considered more feasible. In SENS, joint erosions are scored in 32 joints in both hands and wrists [10 metacarpophalangeal (MCP) joints, 8 proximal interphalangeal (PIP) joints, 2 interphalangeal joints of the thumbs, right and left first metacarpal bone, right and left radius and ulnar bones, right and left trapezium and trapezoid (as one unit; multiangular), right and left scaphoid bones, right and left lunate bones] and 12 joints in both feet [10 metatarsophalangeal (MTP) joints and 2 interphalangeal joints of the big toes]. Joint space narrowing (JSN) is assessed in 30 joints in both hands and wrists [10 MCP joints, 8 PIP joints, right and left third, fourth, fifth carpometacarpal joints, right and left multiangular-scaphoid joints, right and left capitocapitate-scaphoid-lunate joints, right and left radiocarpal joints] and 12 joints in both feet (10 MTP joints and 2 interphalangeal joint of the big toes). A joint is scored as affected “1” if it displays any erosion and as affected “2” for JSN. The score for each joint can therefore range from 0 to 2. The maximum total score of SENS per patient is 86.

Statistical analysis was done using SPSS statistical software, version 15.

**RESULTS**

A total of 101 patients were studied; 81 (80.2%) women and 20 (19.8%) men. The mean age was 41.91 ± 11.99 years (range 19–72 yrs). Mean duration of disease was 10.77 ± 4.66 kg/m², with 24 (23.8%) patients having low BMI (< 18.5), 42 (41.6%) having normal BMI (18.5–24.9), and 35 (34.7%) having high BMI (> 25). The mean SENS score was 16.81 ± 11.10 (range 3–54); the mean DAS28 was 6.23 ± 0.96. There was a significant correlation between SENS and DAS28 (r = 0.28, p < 0.005). Patients’ characteristics have been summarized in Table 1.

The relationship between BMI and SENS was investigated using Pearson correlation coefficients. There was a strong negative correlation between the 2 variables (r = −0.509, p < 0.0005; Figure 1). Also, in patients with low BMI, mean SENS (26.62 ± 13.45) was significantly higher than in those with normal BMI (15.88 ± 8.38) (p < 0.001) and high BMI (11.20 ± 7.32) (p < 0.001). Similarly, patients in the normal BMI group also had significantly higher SENS than those in the high BMI group (p < 0.05). However, there was no correlation between SENS and DAS28 in any of the groups. One-way ANOVA did not reveal significant differences in DAS28 between groups. Post-hoc analysis for multiple comparisons also did not show significant differences in DAS28 between any 2 of the groups. Since our study cohort had a higher proportion of female patients as compared to other reported RA cohorts, in order to exclude the likelihood of this exerting bias on the overall results, we also analyzed the correlation between BMI and SENS in male and female groups separately. There was significant negative correlation between them in both these groups as well (female group, r = −0.449, p < 0.0005; male group, r = −0.678, p < 0.001).

Comparing the IgM-RF-positive and IgM-RF-negative groups, the SENS was significantly higher in the IgM-RF-positive group than in the IgM-RF-negative group; however, the DAS28 was not different in the 2 groups, nor was the BMI (Table 2). Within the IgM-RF-positive and IgM-RF-negative patient groups as well, a significant negative correlation was seen between BMI and SENS (IgM-RF-positive group, r = −0.55, p < 0.0001; IgM-RF-negative group, r = −0.36, p < 0.05).

Multiple regression analysis was further used to investigate the unique contributions of IgM-RF, DAS28, and BMI (as independent variables) to SENS (dependent variable). The result of the multiple regression model (R² = 0.345, p < 0.0005) is summarized in Table 3 and indicates that IgM-RF, DAS28, and BMI were independently associated with SENS. Independent of DAS28 and IgM-RF, BMI accounted for 23.04% of the variance in SENS according to this model.

**DISCUSSION**

Our study shows that BMI significantly influences joint damage in patients with early RA, patients with high BMI having less joint damage than patients with normal or low BMI. These findings are supported by other studies that also show that high BMI protects against joint damage in patients with RA. Whether low BMI protects against joint damage in Indian patients with RA is not known. We investigated this concept hoping to establish its generalizability.
the nutritional status of the population from which the study cohort is derived. It is unlikely to be due to high inflammatory state, as the disease activity was comparable in the low, normal, and high BMI groups. Moreover, a recent study has shown that inflammation does not seem to influence BMI in RA18. This finding is possibly of considerable significance. Since high BMI is found to protect against radiographic damage, it raises an important question — does poor nutritional state (and hence low BMI) in a population predispose RA patients from that community to accrue higher damage?

Our findings of a graded decrease in radiological score from low through normal to high BMI groups in the presence of comparable disease activity supports the concept proposed by Kauffman, et al. of BMI being an “inflammation-independent” factor determining joint damage, which has also been endorsed by the results from Westhoff, et al.8,10.

RF positivity is well known to be associated with higher damage19,20. The same is also evident here. We also found higher BMI to be protective in both RF-positive and negative groups. Although Westhoff, et al.10 did not find BMI to protect against joint damage in an RF-negative group, they have suggested that due to the overall lower joint destruction in the RF-negative patients, the potential association between BMI and joint damage could not be seen in their study. Our results reinforce their suggestion and prove that BMI protects even in an RF-negative group. The lower joint destruction in RF-negative patients might also be the explanation of why the strength of association was weaker in the RF-negative group compared to that in the RF-positive group in our study.

The mechanisms by which high BMI protects against joint damage are not entirely known. One possible link that has been studied is white adipose tissue, which is known to be an active producer of adipokines that play an important role in inflammation and immunity21. Adiponectin is strongly associated with radiographic damage and independently accounts for about 6% of the variability in radiographic scores, which was comparable to RF22. To date no correlation of adiponectin levels and disease activity have been found to support the “inflammation-independent” effects of BMI23. Adiponectin also has various antiinflammatory effects, such as induction of interleukin 10 (IL-10) and IL-1 receptor antagonist production by monocytes-macrophages, inhibition of IL-6 and tumor necrosis factor-α, and other mechanisms24,25,26,27,28. Adiponectin concentrations in plasma of RA patients were found to be higher than in con-

Table 1. Characteristics of patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total, n = 101</th>
<th>Low BMI, n = 24</th>
<th>Normal BMI, n = 42</th>
<th>High BMI, n = 35</th>
<th>p, ANOVA*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, n (%)</td>
<td>81 (80.2)</td>
<td>18 (75)</td>
<td>30 (71.4)</td>
<td>33 (93.4)</td>
<td>NS†</td>
</tr>
<tr>
<td>Age, yrs, mean ± SD</td>
<td>41.9 ± 11.9</td>
<td>39.88 ± 13.02</td>
<td>42.95 ± 12.13</td>
<td>42.06 ± 11.23</td>
<td>NS</td>
</tr>
<tr>
<td>RA disease duration, mo, mean ± SD</td>
<td>10.77 ± 6.73</td>
<td>13.5 ± 7.6</td>
<td>9.3 ± 5.8</td>
<td>10.6 ± 6.7</td>
<td>NS</td>
</tr>
<tr>
<td>IgM-RF-positive, n (%)</td>
<td>55 (54.5)</td>
<td>15 (62.5)</td>
<td>22 (52.4)</td>
<td>18 (51.4)</td>
<td>NS†</td>
</tr>
<tr>
<td>RF, IU/ml</td>
<td>54.44 ± 42.74</td>
<td>57.08 ± 46.67</td>
<td>53.14 ± 39.30</td>
<td>54.17 ± 45.06</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.82 ± 4.66</td>
<td>16.69 ± 1.16</td>
<td>21.94 ± 1.94</td>
<td>27.90 ± 2.39</td>
<td>NA</td>
</tr>
<tr>
<td>SENS, mean ± SD</td>
<td>16.8 ± 11.1</td>
<td>26.62 ± 13.45</td>
<td>16.05 ± 8.34</td>
<td>11.27 ± 7.40</td>
<td>&lt; 0.0005</td>
</tr>
<tr>
<td>DAS28, mean ± SD</td>
<td>6.2 ± 0.9</td>
<td>6.62 ± 0.87</td>
<td>6.04 ± 0.93</td>
<td>6.21 ± 1.01</td>
<td>NS</td>
</tr>
</tbody>
</table>

RF: rheumatoid factor; BMI: body mass index; SENS: Simplified Erosion Narrowing Score; DAS28: Disease Activity Score 28-joint count; NS: nonsignificant; NA: not applicable. * Between low, normal, and high BMI groups. † Kruskal-Wallis test.

Table 2. Comparison of IgM-RF-positive and negative groups.

<table>
<thead>
<tr>
<th></th>
<th>IgM-RF-positive</th>
<th>IgM-RF-negative</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENS</td>
<td>19.55 ± 11.36</td>
<td>13.54 ± 9.94</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>DAS28</td>
<td>6.22 ± 0.98</td>
<td>6.26 ± 0.96</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>23.08 ± 0.64</td>
<td>22.60 ± 0.66</td>
<td>NS</td>
</tr>
</tbody>
</table>

SENS: Simplified Erosion Narrowing Score; DAS28: Disease Activity Score 28-joint count; BMI: Body Mass Index; RF: rheumatoid factor; NS: not significant.

Figure 1. Scatterplot showing negative correlation of natural logarithm (ln) transformation of the Simplified Erosions Narrowing Score (SENS) and body mass index (BMI).

Figure 2. Scatterplot showing negative correlation of natural logarithm (ln) transformation of the Simplified Erosions Narrowing Score (SENS) and body mass index (BMI).
Moreover, same BMI does not correspond to the same degree of fat content in different populations and so may not only be addressed by large population-based studies. With more data supporting the effect of BMI on RA, it is time to incorporate it as a potentially modifiable variable for RA outcomes.

The limitations of our study include its cross-sectional design. A relatively low proportion of RF positives and higher proportion of females compared to other RA cohorts also might limit the generalizability of the results. Moreover, same BMI does not correspond to the same degree of fat content in different populations and so may not be the most appropriate measure to compare the fat content. This may have a bearing on the influence of BMI on joint damage.

REFERENCES


