Low body mass index in long standing rheumatoid arthritis: relation to RA disease activity and functional indices

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SUMMARY

The aim of the work was to study the relationship between the body mass index (BMI) in longstanding rheumatoid arthritis (RA) and RA disease activity and functional indices. This study included 105 RA patients. For all patients, we recorded the presence of erosions on radiographs, the presence of subcutaneous nodules (SCN), the 28-tender joint count (TJC), 28-swollen joint count (SJC) scores, the visual analogue scale (VAS), physicians’ global assessments (PhGA), the erythrocyte sedimentation rate (ESR), and the rheumatoid factor (RF). The disease activity index (DAS28) and BMI were calculated and current treatment was recorded. Patients were divided into two groups: group I: BMI <25, and group II: BMI >25. Group I included 32 (30.5%) patients, whereas group II included 73 (69.5%) patients. There were statistically significant differences between the two groups regarding each of the following: SJC (p=0.006), erosions (p=0.006), DAS28 (p=0.016) and PhGA (p=0.007). All were higher in group I (underweight and normal) than in group II (overweight and obese). No statistically significant differences emerged regarding age (p=0.11), smoking (p=0.69), disease duration (p=0.46), TJC (p=0.14), SCN (p=1.00), HAQ (p=0.26), VAS (p=0.16), ESR (p=0.25), RF (p=0.54) and steroid cumulative dose (p=0.08).

Low BMI in longstanding RA patients may indicate more active and erosive disease and it may be considered as a poor prognostic factor.

Key words: Rheumatoid arthritis; Body mass index; DAS28; Radiological erosions.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder in which polyarticular synovitis is particularly prominent (1). Although some studies have shown that high body mass index (BMI) may be associated with RA (2), and poor RA disease outcome (3), others have reported that there is a paradoxical effect of BMI on survival in people with RA, demonstrating that as BMI decreases, so too does survival probability among RA patients studied (4).

It has been reported that obesity may have a protective effect on the amount of joint destruction in established RA (5), and that weight loss in individuals with RA has been recognized since early observations of the disease (6). It has also been found that low BMI at the beginning of RA is associated with higher radiographic progression (7). Low BMI among people with RA may indicate uncontrolled active systemic inflammation (8). Accordingly, BMI could be of interest as a sensitive and inflammation-independent predictor for the radiological outcome of RA (7).

On the other hand, the influence of BMI and/or body fat on RA and its disease activity is not entirely clear, since there have been conflicting results (2) and other researchers have concluded that there is no association between BMI and disease activity composites of RA (9).

This study aimed to explore the relationship between BMI in longstanding RA and RA prognostic factors.
PATIENTS AND METHODS

A cross-sectional study was conducted involving 105 RA patients (96 women and 9 men). Patients were diagnosed according to the 1987 ACR criteria for RA (10). Patients were recruited from the Rheumatology and Rehabilitation department, Cairo University hospital. Their age ranged from 22 years to 66 years with a mean of 45.92±12.12 years and their disease duration ranged from 1 year to 25 years with a mean of 8.15±6.05 years. Eight patients were smokers.

All patients gave their informed consent prior to their inclusion. Patients with any associated disease which might have affected BMI (e.g., celiac disease) were excluded from this study. The study was approved by the local ethics committee and it conforms to the standards currently applied in Cairo University Teaching Hospitals.

Patients described their tobacco use, and submitted written estimates for their pain (0-10 scale) using a visual analog scale (VAS) (11). Overall functional status was estimated according to the Multidimensional Health Assessment Questionnaire (MD-HAQ; 0-3 scale) (12).

We recorded the presence of erosions on radiographs (13), the presence of subcutaneous nodules (SCN), 28 tender joint count (TJC) scores, 28 swollen joint count (SJC) scores, erythrocyte sedimentation rate (ESR; mm/hour), and physicians’ global assessment (PhGA) (14).

The composite DAS28 score was computed as DAS28 = [0.56*sqrt (number of tender joints) +0.28*sqrt (number of swollen joints) +0.70*ln (ESR) +0.014* (patient global score)] (15).

Body mass index (BMI) was calculated as a continuous variable, from the measured heights and weights, as weight in kilograms divided by the square of the height in meters. BMI values were also categorized into the widely used underweight (<18.5 kg/m²), normal (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²) and obese (≥30 kg/m²) categories, based on the 1998 clinical guidelines (16). In our study, the patients were divided according to their BMI into two groups: Group I including the underweight and normal BMI categories and Group II including overweight and obese BMI categories.

Regarding laboratory measures; serum collected was analyzed to determine rheumatoid factor (RF; positivity at ≥15 IU/mL) and ESR.

In this study, all patients were on current disease modifying anti-rheumatic drugs (DMARD) therapy (methotrexate, leflunomide or sulfasalazine), 48% of patients were on current low dose steroid (3.28±4.13 mg/day), but none of them received biological treatment before or during time of the study.

RESULTS

Group I included the underweight and normal BMI categories. It represented 30.5% (n=32) of the enrolled patients. Group II included the overweight and obese BMI categories. It represented 69.5% (n=73) of the enrolled patients.

Regarding the two groups, there were statistically significant differences in the following parameters: SJC (p=0.006), presence of erosions (p=0.006), DAS28 (p=0.016), and PhGA (p=0.007). There was no statistically significant difference between the two groups regarding each of the following: age, gender, smoking, disease duration, TJC, SCN, HAQ, VAS, ESR, RF and steroid cumulative dose as shown in Tables I-III.

Body mass index (BMI) was significantly positively correlated with age (p=0.046), but was significantly negatively correlated with disease duration (p=0.029) and PhGA (p=0.042).
The relation between BMI and RA is controversial. Fassio and colleagues (17) stated that mean BMI was statistically lower in RA patients (P<0.05). However, Albrecht et al. (18), stated, that compared to the general population, a higher prevalence of obesity was observed in all RA cohorts. Body mass index (BMI) can be considered as a simple anthropometric measure that provides a marker of nutritional status and was shown to interact with radiographic joint damage in a large cohort of patients with early RA (19). Even more, some reports consider low BMI as independent predictor of poor radiological outcome (7). Although obesity is generally considered to be a risk factor for proinflammatory disorders such as atherosclerosis and diabetes, in RA the story may be different. In this study we found that the increase in BMI

**Table I** - Comparison between Group 1 (underweight and normal) and Group 2 (overweight and obese) regarding their epidemiological data.

<table>
<thead>
<tr>
<th></th>
<th>Underweight and normal Group 1</th>
<th>Overweight and obese Group 2</th>
<th>P</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.16±12.46</td>
<td>48.67±9.38</td>
<td>0.11</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>9.55±7.62</td>
<td>7.53±5.17</td>
<td>0.462</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients with</td>
<td>Total number Group 1 (32)</td>
<td>%</td>
<td>Total number Group 2 (73)</td>
<td>%</td>
</tr>
<tr>
<td>Smoking</td>
<td>3</td>
<td>9.3</td>
<td>5</td>
<td>15.6</td>
</tr>
</tbody>
</table>

**Table II** - Comparison between Group 1 (underweight and normal) and Group 2 (overweight and obese) regarding their clinical and treatment data.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=32)</th>
<th>Group 2 (n=73)</th>
<th>P</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SJC</td>
<td>7.56±4.31</td>
<td>5.22±4.04</td>
<td>0.006*</td>
<td></td>
</tr>
<tr>
<td>TJC</td>
<td>8.53±4.91</td>
<td>7.08±4.58</td>
<td>0.141</td>
<td></td>
</tr>
<tr>
<td>PhGA</td>
<td>4.59±1.95</td>
<td>3.41±2.6</td>
<td>0.007*</td>
<td></td>
</tr>
<tr>
<td>HAQ</td>
<td>7.28±4.75</td>
<td>6.19±4.05</td>
<td>0.262</td>
<td></td>
</tr>
<tr>
<td>VAS</td>
<td>6.06±1.83</td>
<td>5.38±2.21</td>
<td>0.167</td>
<td></td>
</tr>
<tr>
<td>DAS 28</td>
<td>5.57±0.93</td>
<td>5.05±1.04</td>
<td>0.016</td>
<td></td>
</tr>
<tr>
<td>Steroid cumulative dose in mg</td>
<td>8,299.23±10,824.16</td>
<td>5,252.09±10,599.17</td>
<td>0.084</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td>10 (31.2%)</td>
<td>22 (30.1%)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; SJC, Swollen joint count; TJC, tender joint count; DGA, doctors’ global assessment; HAQ, health assessment questionnaire; VAS, visual analogue scale; DAS 28, disease activity score including 28 joints. *Denotes statistical significance (p<0.05).

**Table III** - Comparison between Group 1 (underweight and normal) and Group 2 (overweight and obese) regarding their laboratory and radiological data.

<table>
<thead>
<tr>
<th></th>
<th>Underweight and normal Group 1</th>
<th>Overweight and obese Group 2</th>
<th>P</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR (mm/hour)</td>
<td>55.28±26.66</td>
<td>46.40±20.14</td>
<td>0.25</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients with</td>
<td>Total number Group 1 (32)</td>
<td>%</td>
<td>Total number Group 2 (73)</td>
<td>%</td>
</tr>
<tr>
<td>Positive RF</td>
<td>29</td>
<td>90.6</td>
<td>62</td>
<td>84.9</td>
</tr>
<tr>
<td>Erosions (in X-ray)</td>
<td>28</td>
<td>87.5</td>
<td>44</td>
<td>60.2</td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate; RF, rheumatoid factor.

**DISCUSSION**

The relation between BMI and RA is controversial. Fassio and colleagues (17) stated that mean BMI was statistically lower in RA patients (P<0.05). However, Albrecht et al. (18), stated, that compared to the general population, a higher prevalence of obesity was observed in all RA cohorts. Body mass index (BMI) can be considered as a simple anthropometric measure that
is associated with less joint damage in the form of decreased frequency of erosions (p=0.006). Similar results were found by many other authors (7, 19-21). This may be accepted when we know that adipocytes were found to be tightly packed in the synovial tissue of obese patients. This lowers the occurrence of crosslink markers in the synovial tissue of obese RA patients and in their urine, reflects inhibited collagen degradation and supports the clinical finding of decreased radiographic joint damage (22). However, the exact physiologic mechanisms underlying the beneficial effects of high body mass or body fat are still widely unknown (23).

In this study, the swollen joints count was higher in the low BMI group (group I) and the difference between the two groups was statistically significant (p=0.006). Similar results were found by other investigators (24, 25). However, other studies (19, 21) found no association between BMI and SJC.

The significant negative correlation between BMI and the disease duration in our results (p=0.029) and in another study (26) may also imply that longstanding RA, especially when active and associated with joint destruction, is associated with low BMI.

We also found that disease activity was higher in group 1 (those with lower BMI) (p=0.016). Similar results were reported by other investigators (27), who stated that lower DAS28 was associated with an increased BMI. Moreover, it was reported that low body mass index is a risk factor for poor long term outcomes in RA (28).

On the other hand, other authors found that high BMI was associated with increased disease activity in RA (29, 18, 30), and that overweight at diagnosis significantly decreases the chance of achieving good disease control during the early phase of RA (31). However, a major difference between our study and the previous two studies is that in these studies the authors studied early RA patients with disease duration ≤12 months, but in our study the patients had established RA with disease duration >12 months, allowing the impact of obesity on the disease process to be apparent.

Others, too, reported that both very low and very high BMI and body fat associate independently with increased disease activity and physical dysfunction (32), and that ethnicity and the different environmental factors may affect the relation between BMI and RA (26).

Although HAQ was higher in group I as compared to group II, the difference between the two groups was not statistically significant. This may be because a BMI >30 kg/m² itself is associated with a decreased physical functioning in healthy obese people (33).

In our opinion, the conflicting reports about RA and BMI may be explained by objective differences in different studies [studying impact of RA on BMI or the reverse, studying the role of BMI in RA pathogenesis or the protective effect of BMI in RA, the type of RA patients included in the study (early or late)]. Thus, the relationship between BMI and clinical activity in RA needs to be approached with further studies with higher methodological quality to obtain solid results concerning any such relationship.

## CONCLUSIONS

Low BMI in longstanding RA patients may indicate more active and erosive disease and it may be considered as a poor prognostic factor in longstanding RA.

**Limitations**

The small number of patients included in this study, and the absence of biological treatment in our patients, represent the most important limitations in our study. Moreover, we think that the use of ACPA and CRP in further studies may be stronger predictors for bone damage rather than ESR or RF.

**Contributions:** all authors approved entirely the submitted material and contributed actively to the study.

**Conflicts of interest:** none.
REFERENCES


