ABSTRACT

BACKGROUND/PURPOSE: There has been limited validation of soluble biomarker measures of disease activity in patients with axial spondyloarthropathy (SpA). C-reactive protein (CRP) is most commonly used in clinical practice but sensitivity in ankylosing spondylitis (AS) is only 40-50%. The Ankylosing Spondylitis Disease Activity score (ASDAS) has been proposed as a treat-to-target outcome measure for effective suppression of disease activity in patients with SpA. BASDAI has also been used but does not incorporate objective measures of disease activity. We have performed an exploratory study of the association between a multi-biomarker disease activity (MBDA) score, which measures 12 serum biomarkers and has been validated in RA, and clinically-based measures of disease activity in patients with axial SpA.

METHODS

Disease activity measures based on erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ASDAS, and BASDAI were analyzed for 40 patients with SpA who met modified New York criteria from a systematic, prospective follow-up cohort. The MBDA score was measured in serum samples and is based on the following 12 biomarkers: vascular cell adhesion molecule 1, epidermal growth factor, vascular endothelial growth factor A, interleukin 6, TNF receptor 1, matrix metalloproteinases 1 and 3, bone glycoprotein 39, VCAM-1, leptin, resistin, serum amyloid A, and CRP. These biomarkers were measured by electrochemiluminescence-based multiplexed immunoassays on the Meso Scale Discovery Multi-Array platform. The measured levels for each of the 12 biomarkers were weighted and combined using a formula validated in RA to derive the MBDA score (Vectra® DA score), which ranges from 1 to 100. Correlation between disease activity measures used Pearson correlation coefficient. Group differences were assessed using unpaired t-tests. We also determined what degree biomarker scores reflected low and high disease activity cut-offs for the ASDAS (>1.3, 2.5) and the BASDAI (>4, 6). RESULTS

Patients were of mean (SD) age, 43 (11) years; number (%) males, 26 (65); mean (SD) disease duration, 15 (14) years; number (%) B27+, 30 (75); mean (SD) ESR, 24 (22) mm/hr; mean (SD) CRP, 10 (9) mg/l; mean (SD) BASDAI, 4.2 (2.5); mean (SD) ASDAS-ESR, 2.9 (1.4); mean (SD) ASDAS-CRP, 2.7 (1.2). The MBDA score correlated significantly with the ASDAS-ESR (r=0.63), ASDAS-CRP (r=0.68) and BASDAI (r=0.50). The modified MBDA score calculated without CRP correlated significantly with the 12-biomarker MBDA scores, which includes CRP (r=0.98), ASDAS-ESR (r=0.88), ASDAS-CRP (r=0.63) and BASDAI (r=0.26). Significant differences were observed in MBDA scores between patients with ASDAS-CRP >3.5 versus those with ASDAS-CRP ≤3.5 (37 vs. 25, p<0.002) and patients with BASDAI 24 versus BASDAI ≤4 (41 vs. 33, p<0.01). Several of the biomarkers, including CRP, correlated strongly with the clinical measures. For ASDAS-CRP, serum concentrations of CRP, SAA, IL-6, TNF-R1, and VCAM-1 were significantly elevated at >0.5 (r=0.51-0.71). CONCLUSIONS

The MBDA score was associated with available measures of clinical disease activity in patients with axial SpA and correlated most strongly with the ASDAS.

RESULTS

Matrix of correlation coefficients (Pearson's r) for individual MBDA biomarkers, the MBDA composite score, and the MBDA composite without CRP versus clinical composite measures of disease activity in 40 patients with axial SpA (AS).

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>CRP</th>
<th>SAA</th>
<th>IL-6</th>
<th>YKL-40</th>
<th>TNF-RI</th>
<th>VEGF</th>
<th>MMP1</th>
<th>Resistin</th>
<th>MMP3</th>
<th>VCAM-1</th>
<th>EGF</th>
<th>Leptin</th>
<th>MBDA</th>
<th>BASDAI</th>
<th>ASDAS-ESR</th>
<th>ASDAS-CRP</th>
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</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.66</td>
<td>0.59</td>
<td>0.57</td>
<td>0.45</td>
<td>0.44</td>
<td>0.43</td>
<td>0.39</td>
<td>0.35</td>
<td>0.30</td>
<td>0.21</td>
<td>0.28</td>
<td>0.18</td>
<td>0.06</td>
<td>0.63</td>
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<td></td>
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<tr>
<td>SAA</td>
<td>0.64</td>
<td>0.77</td>
<td>0.55</td>
<td>0.51</td>
<td>0.39</td>
<td>0.12</td>
<td>0.40</td>
<td>0.15</td>
<td>0.32</td>
<td>0.36</td>
<td>0.14</td>
<td>0.08</td>
<td>0.68</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-6</td>
<td>0.36</td>
<td>0.35</td>
<td>0.41</td>
<td>0.38</td>
<td>0.32</td>
<td>0.12</td>
<td>0.11</td>
<td>0.20</td>
<td>0.11</td>
<td>0.26</td>
<td>0.36</td>
<td>0.05</td>
<td>0.39</td>
<td>0.38</td>
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</tr>
</tbody>
</table>

CONCLUSION

The MBDA test is significantly associated with clinical measures of disease activity in patients with axial SpA. Several individual biomarkers (SAA, IL-6, YKL-40) demonstrated strong correlations with ASDAS-CRP. Although the MBDA test is not optimized or validated for use in axial SpA, these results demonstrate the potential for developing a multi-biomarker test for measuring disease activity in patients with axial SpA.

REFERENCES