THE OUTCOME OF ANKYLOSING SPONDYLITIS: A STUDY OF 100 PATIENTS

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SUMMARY

The outcome was studied in 100 patients with adult-onset primary ankylosing spondylitis (AS). After a mean disease duration of 16 yr, 51.5% of the patients were employed in full-time work. Cessation of work occurred at a mean disease duration of 15.6 yr, and was significantly associated with female sex, low levels of education, acute anterior uveitis, ‘bamboo spine’ and the co-existence of non-rheumatic diseases. Functional outcome was studied by analysing activities of daily living, and revealed similar findings in males and females. Most of the loss of function occurred during the first 10 yr of disease, and correlated significantly with the occurrence of peripheral arthritis, spinal X-ray changes of AS and development of ‘bamboo spine’. After >20 yr of disease, >80% of the patients still complained of daily pain and stiffness, and >60% reported daily use of drugs.

KEY WORDS: Ankylosing spondylitis, Outcome, Employment.

ANKYLOSING spondylitis (AS) predominantly affects young men and women, of whom >90% carry the HLA antigen B27 [1–3]. The disease is characterized clinically by pain and stiffness of the back, and radiologically by arthritic changes in the sacroiliac joints and frequently also in the spine. Not infrequently, the spinal disease is accompanied by arthritis of the peripheral joints and acute anterior uveitis (AAU) [4, 5]. Occasionally, serious disease complications, such as renal amyloidosis, cardiac conduction disturbances and cardiac valve dysfunctions, intervene [6–8].

AS is traditionally regarded as a chronic progressive disease leading to a variable degree of restricted mobility of the spine with consequent loss of functional capacity [9–12]. In the present study, the outcome of AS and its impact on various functional and social factors were studied in 100 patients attending two different hospitals in Norway.

MATERIALS AND METHODS

Patients

One hundred consecutive patients hospitalized or seen by the out-patient clinic during the period 1992–1994 were studied. Fifty-four patients were selected from the Department of Rheumatology of the Central Hospital of Aust Agder in south Norway, which is the only referral centre for rheumatology in this region. Forty-six patients came from the Department of Rheumatology of the Regional Hospital of Trondheim, which is both a secondary and tertiary referral centre for rheumatology. There are no private practising rheumatologists in these areas.

Methods

All patients met the New York criteria for AS [13]. Patients with psoriasis, inflammatory bowel disorders and juvenile-onset AS were excluded.

All patients were asked to fill out a mailed questionnaire which contained questions about employment and marital status, degree of pain and stiffness (verbal rating scale), use of drugs (verbal rating) and level of education. In addition, a Goldberg questionnaire (30 questions with 0–90 points) [14] was filled out. Finally, a questionnaire with 17 questions regarding activities of daily living (ADL) was mailed to the patients. The whole questionnaire was mailed to 121 patients, of whom 100 cases returned it and thus were included in the present investigation. Further information was collected from the hospital records. The rate of unemployment in the general population by 1 January 1992 was ~3%.

Clinical features

The diagnoses of peripheral arthritis and AAU were accepted only if verified by a rheumatologist or an ophthalmologist, respectively.

Statistics

Fisher’s exact test, χ² test and Student’s t-test were used for the determination of statistical significance and a P value of 0.05 was accepted as statistically significant.

RESULTS

Demographics

There were 100 patients, 67 men and 33 women (ratio 2:1). The average age at onset, age, disease duration and prevalence of HLA B27 of the patients are presented in Table I.

The average duration from onset of symptoms to diagnosis was 8.6 yr among cases diagnosed in the
characteristics of 100 patients with adult-onset ankylosing spondylitis

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>100</td>
<td>33</td>
<td>67</td>
</tr>
<tr>
<td>Average age (yr)</td>
<td>41.8</td>
<td>43.1</td>
<td>41.1</td>
</tr>
<tr>
<td>Average duration (yr)</td>
<td>16.5</td>
<td>16.8</td>
<td>16.3</td>
</tr>
<tr>
<td>Average age at onset (yr)</td>
<td>25.3</td>
<td>26.2</td>
<td>24.8</td>
</tr>
<tr>
<td>Prevalence of HLA B27 (%)</td>
<td>95.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>39.8</td>
<td>42.8</td>
<td>38.5</td>
</tr>
<tr>
<td>Acute anterior uveitis</td>
<td>33.3</td>
<td>29.0</td>
<td>35.5</td>
</tr>
<tr>
<td>Renal amyloidosis</td>
<td>1.0</td>
<td>0.0</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Radiological manifestations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis of the sacroiliac joints</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Available in 100 patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis only</td>
<td>68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bony bridges</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obliterated</td>
<td>26</td>
<td></td>
<td></td>
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<tr>
<td>Spinal changes typical of AS</td>
<td>58.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Available in 81 patients)</td>
<td></td>
<td></td>
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<tr>
<td>Syndesmophytes only</td>
<td>34.3</td>
<td></td>
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</tr>
<tr>
<td>Signs of ankylosis</td>
<td>5.7</td>
<td></td>
<td></td>
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<tr>
<td>‘Bamboo spine’</td>
<td>18.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical changes typical of AS</td>
<td>56.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Available in 32 patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormalities due to AS</td>
<td>56.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs of ankylosis</td>
<td>21.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis only</td>
<td>18.8</td>
<td></td>
<td></td>
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<tr>
<td>Atlantoaxial dislocation</td>
<td>15.6</td>
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</table>

Clinical manifestations

Peripheral arthritis, including hips (five patients) and shoulders (two patients), was documented in 39.8% of the cases. In two cases, information about the occurrence of arthritis was missing. Three patients underwent implantation of a hip prosthesis.

Information regarding the possible occurrence of AAU was available in 93 cases. Of these, AAU was recorded in 33.3%. Renal amyloidosis was observed in one patient. Neurological disease complications and cervical fractures were not seen.

Regular cardiological examinations consisting of echocardiography and 24 h ECG registrations performed every third year had been performed in 41 of the 54 patients selected from Arendal. Thirteen patients were not included due to a temporary lack of technical equipment. Among the 41 patients, six had aortic insufficiency (AI) (14.6%). Only one out of 26 males (3.8%) suffered from AI, which contrasted with five out of 15 female cases (33.3%) (P < 0.05). One female patient required surgical valve replacement. All five female patients with AI had peripheral arthritis compared to two out of 10 patients without AI (P < 0.01). Patients with AI had a lower mean ADL score than females without AI (P < 0.05). Mean disease duration among patients affected by AI was 18.8 yr compared to a disease duration of 12.0 yr in unaffected cases. Cardiac conduction disturbances were not found among the 41 patients regularly examined by a cardiologist.

Radiological manifestations

Arthritis of the sacroiliac joints was present in all cases. The distribution, frequency and severity of the radiological manifestations are presented in Table I.

Patients with radiological abnormalities of the cervical spine had AAU significantly more often (68.8%) than cases without such radiological features (25%) (P < 0.01). Patients with cervical changes also more frequently exhibited radiological abnormalities in the thoracic and lumbar spine (80%) than patients without cervical involvement (36.9%) (P < 0.02).

Functional outcome

The index concerning ADL had a maximum score of 51 points, a score which would indicate no problems in pursuing such activities. Altogether, 98 patients returned the ADL questionnaire. For the whole group of AS patients, an average of 39.7 points was calculated which gave a 22.2% reduction in ADL. During the first 10 yr of disease, a reduction of 18.4% was calculated for the whole group of AS patients. Patients employed in full-time work scored higher (41.1 points) compared to unemployed cases (34.7 points) (P < 0.01).

There was a significant association between ADL reduction and frequency of employment, peripheral

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
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<tbody>
<tr>
<td>ADL reduction (%)</td>
<td>0–10</td>
<td>10.1–25</td>
<td>&gt;25</td>
</tr>
<tr>
<td>Number of patients</td>
<td>18</td>
<td>44</td>
<td>37</td>
</tr>
<tr>
<td>Females/males</td>
<td>1.17</td>
<td>1.72</td>
<td>1.22</td>
</tr>
<tr>
<td>Average age (yr)</td>
<td>40.7</td>
<td>41.6</td>
<td>42.3</td>
</tr>
<tr>
<td>Duration of AS (yr)</td>
<td>13.1</td>
<td>15.7</td>
<td>19.3</td>
</tr>
<tr>
<td>Employed (%)</td>
<td>80.0</td>
<td>61.4</td>
<td>31.4</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard (%)</td>
<td>12.5</td>
<td>27.2</td>
<td>40.0</td>
</tr>
<tr>
<td>High (%)</td>
<td>87.5</td>
<td>72.8</td>
<td>60.0</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral arthritis (%)</td>
<td>41.2</td>
<td>25.0</td>
<td>59.5</td>
</tr>
<tr>
<td>Hip prosthesis (%)</td>
<td>2.0</td>
<td>2.3</td>
<td>13.5</td>
</tr>
<tr>
<td>Acute anterior uveitis (%)</td>
<td>23.5</td>
<td>30.0</td>
<td>47.1</td>
</tr>
<tr>
<td>Other diseases (%)</td>
<td>22.2</td>
<td>29.5</td>
<td>45.9</td>
</tr>
<tr>
<td>Radiological</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Spinal (%)</td>
<td>21.4</td>
<td>54.8</td>
<td>64.0</td>
</tr>
<tr>
<td>‘Bamboo spine’ (%)</td>
<td>0.0</td>
<td>16.7</td>
<td>32.0</td>
</tr>
</tbody>
</table>

Statistically significant differences (P < 0.05):
*Group I vs Group III males, Group II vs Group III males, all cases.
*Group III vs Group II males, all cases.
*Group III vs Group I and II, all patients.
*Group I vs Group II males, all patients. Group I vs Group III males, all patients. Group II vs Group III females, all patients.
*Group I vs Group II males, females, all patients. Group I vs Group III males, females, all patients.
arthritis, spinal X-ray abnormalities typical of AS and development of ‘bamboo spine’ (Table II). There was no correlation between reduction of ADL and diagnostic delay, marital status and cervical spine involvement (data not shown).

Employment

Information about the status of present employment could be obtained in 99 patients, and the data are shown in Table III. Altogether, 51.5% of the cases were in full-time work. There were significantly more men working full time (66.7%) than females (21.2%) \((P < 0.0001)\). However, there were significantly more women working half-time (24.2%) than men (4.5%) \((P < 0.02)\). The frequency of unemployment was significantly higher in females (42.4%) than in men (19.7%) \((P < 0.01)\).

The average age at retirement from work was 39.4 yr (42.9 yr in men and 31.1 yr in females). The average disease duration at cessation of work was significantly \((P < 0.02)\) longer (15.6 yr) in men compared to females (6.4 yr). The mean disease duration at cessation of work for all patients was 10.8 yr. The cause of work cessation was AS in 96.2% of the cases. Of the 26 retired patients, 20 (76.9%) received social welfare support.

There were significantly more cases with higher education among those employed than among those unemployed (Table IV). The frequencies of AAU, ‘bamboo spine’ and non-rheumatic diseases were also significantly higher among those employed compared to those continuing to work. The occurrence of peripheral arthritis, hip prosthesis and radiographic involvement of the spine was also higher among unemployed patients, but the differences did not reach statistical significance.

Goldberg Health Questionnaire (GHQ)

A 29-question index was used, and the average of GHQ was 22.5 points, with no difference between males and females (22.2 and 23.3 points, respectively). Unemployed patients scored higher (39.3 points) than employed cases (20.0 points), but the difference did not reach statistical significance.

<table>
<thead>
<tr>
<th>TABLE III</th>
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<tbody>
<tr>
<td>The frequency of employment, early retirement and unemployment among 99 patients with ankylosing spondylitis</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Status</th>
<th>Men</th>
<th>females</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed 100%</td>
<td>44</td>
<td>66.7%</td>
<td>51</td>
</tr>
<tr>
<td>Employed 50%</td>
<td>3</td>
<td>4.5%</td>
<td>11</td>
</tr>
<tr>
<td>Retired</td>
<td>2</td>
<td>3.0%</td>
<td>3</td>
</tr>
<tr>
<td>Unemployed</td>
<td>13</td>
<td>19.7%</td>
<td>27</td>
</tr>
<tr>
<td>Work not obtained</td>
<td>3</td>
<td>4.5%</td>
<td>6</td>
</tr>
<tr>
<td>School/student</td>
<td>1</td>
<td>1.5%</td>
<td>1</td>
</tr>
</tbody>
</table>

*\(P < 0.05)\.

<table>
<thead>
<tr>
<th>TABLE IV</th>
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<tbody>
<tr>
<td>Certain characteristics among employed and unemployed patients with ankylosing spondylitis</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Demographics</th>
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<tbody>
<tr>
<td>Present age (yr)</td>
</tr>
<tr>
<td>Present disease duration (yr)</td>
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</table>

<table>
<thead>
<tr>
<th>Social</th>
</tr>
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<tbody>
<tr>
<td>Standard education (%)</td>
</tr>
<tr>
<td>Higher education (%)</td>
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<table>
<thead>
<tr>
<th>Clinical</th>
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<tbody>
<tr>
<td>Peripheral arthritis (%)</td>
</tr>
<tr>
<td>Hip prosthesis (%)</td>
</tr>
<tr>
<td>Spinal X-ray changes (%)</td>
</tr>
<tr>
<td>‘Bamboo spine’ (%)</td>
</tr>
<tr>
<td>Acute anterior uveitis (%)</td>
</tr>
<tr>
<td>Presence of other diseases (%)</td>
</tr>
</tbody>
</table>

Pain, stiffness and use of disease-related drugs

Daily pain and stiffness due to AS were reported by 71.1 and 81.4% of the patients, respectively. Among patients with a disease duration exceeding 20 yr, 85.2% reported daily pain and 88.9% complained of daily stiffness. Disease-related drugs, mostly non-steroidal anti-inflammatory drugs, were consumed every day by 57.7% of the patients. The use of such drugs was equally distributed among the various disease duration groups.

DISCUSSION

As pointed out by previous workers [15], disease outcome includes a number of different dimensions, of which death, disability, discomfort and cost appear most important. In the present retrospective study, it was possible to analyse only a few of these dimensions and subdimensions. Moreover, the present study was not designed to make use of recently suggested health assessment indexes for AS [16, 17]. Instead, certain well-defined aspects of outcome, such as functional outcome and unemployment, were dealt with in detail.

In order to restrict our study to a well-defined group of AS, 100 patients suffering from adult-onset primary AS excluding cases with spondyloarthropathy associated with inflammatory bowel disease and psoriasis were selected. As the number of female patients was high (33%) compared to most reports on AS [18], data were analysed separately for men and women to avoid possible selection bias. Furthermore, there were generally no major discrepancies between the present
patients and those of previous studies of hospitalized AS cases regarding clinical or radiological manifestations [11, 19–32].

Aortic valve insufficiency is reported in 1–10% of patients with AS, and is due to subvalvular fibrosis [33]. The prevalence of AI increases with age, disease duration and presence of peripheral arthritis [34]. In the present study, females with AI had a lower ADL score and more often peripheral arthritis than females without such cardiac manifestations. Although the disease duration was somewhat longer (18.8 yr) among females with AI than among those without AI (12.0 yr), the presence of AI in females with AS may indicate a less favourable outcome.

The study focused primarily on various aspects of outcome of AS. Of great interest are the possible effects of early therapy and diagnosis upon outcome. Unfortunately, we did not have the ability to examine the consequences of therapy and early diagnosis on the degree of pain and stiffness, but a beneficial effect of physical therapy on function and disability has been shown by previous workers [35, 36]. Regarding early diagnosis, the present study confirmed previous observations [37] that the time from onset of symptoms to diagnosis has been significantly reduced during the last few decades. However, the present study failed to establish evidence suggesting that early diagnosis in itself reduces the risk of subsequent work cessation or improves functional outcome.

In the present study, an ADL score was used to measure loss of function. Males were not more severely affected than females, a finding which confirmed previous observations [18, 26, 38]. Important factors impairing function, as measured by ADL status, were peripheral joint involvement, occurrence of spinal X-ray changes and development of ‘bamboo spine’. Thus, previous observations [23, 39] of a positive correlation between certain objective signs of disease severity and loss of function was observed. Consequently, the aim of future therapy of AS should be to prevent or reduce the development of arthritic abnormalities.

To some extent, the present study confirms previous suggestions that the first 10 yr of disease are of particular importance regarding subsequent disease development [19, 40]. Among our cases, most of the reduction in ADL appeared during the first 10 yr of disease. However, a gradual decrease in ADL was noted for both sexes after 20 yr of disease. These findings indicate that careful follow-up of patients with AS during the first 10 yr of disease is important, but that the need for rheumatological expertise remains throughout the entire disease course of AS.

Employment is another important outcome variable in AS [41–47]. Among the present patients, there was a clear correlation between loss of function, as measured by ADL, and occupation. Patients who were working had a better ADL status than those unemployed. Whether this means that reduced function results in unemployment, or that employment in itself leads to preservation of function and better management of the burdens of everyday living, is difficult to decide.

There were significantly less females working than men, and the former left their occupation after a shorter mean disease duration than men (Table I). Such differences may also exist among non-AS individuals, but the present findings suggest female sex as a risk factor for work cessation in AS. Consequently, our findings did not lend support to previous suggestions of a more favourable outcome in females as compared to males.

A further analysis of factors responsible for unemployment in AS showed that a higher level of education increased the likelihood of continuing occupational activity. We did not have the opportunity to study the influence of type of occupation on the rate of unemployment in AS. Other workers [27, 41, 47] have shown, however, that rather few patients with AS continue to work in occupations requiring hard manual labour. One may speculate whether a higher level of education might allow for a less physical occupation and therefore leads to a longer working life. Nevertheless, not only the administration of drugs and physical therapy need consideration in the early phases of AS, but also the adjustment of working conditions and education should be subjected to serious concern.

We also found that the development of an ankylosed spine, the occurrence of AAU and the co-existence of other non-rheumatic diseases were related to unemployment. These results are in agreement with the findings of McGuigan et al. [24] who found that restriction of movement in the lumbar spine impaired work capability in individuals with AS. Unfortunately, the number of patients with available cervical spine X-rays and surgical hip replacements was rather small in the present study, and thus restricted extensive prognostic considerations. It was found, however, that cervical spine involvement was significantly associated with the development of both AAU and radiological manifestations elsewhere in the spine. To some extent, these findings support the notion that affection of the cervical spine significantly impairs function in AS [42].

It was found that after >20 yr of disease, >80 and 85% of our patients still complained of daily pain and stiffness, respectively. Thus, AS does not seem to ‘burn out’ [43], but remains symptomatic throughout the entire disease course, at least in AS patients attending hospital. Cases diagnosed and treated by general practitioners or selected through population surveys [11, 12] may experience a significantly better outcome than those admitted to hospital departments. Future studies of the outcome of AS should thus be aimed at prospective investigations of the total population of AS patients.

This study clearly shows that AS, in spite of impressive scientific progress regarding aetiology and genetics, still represents a challenge to the practising rheumatologist. Both the administration of drugs and physical therapy and adjustment of working
conditions should be subjected to serious concern. A

careful clinical and radiological evaluation of the

patient during the first 10 yr of disease may provide

valuable information regarding the final outcome.

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The natural disease course of ankylosing spondylitis.


41. Lehtinen K. Working ability of 76 patients with