Pulmonary function, aerobic capacity and related variables in patients with ankylosing spondylitis

Ayla ÇAĞLIYAN TÜRK1, Sertaç ARSLAN2, Yusuf KARAVELIOĞLU3, Macit KALCIK4, Sumru ÖZEL5, Ahmet MUSMUL4, Füsun ŞAHİN6

1Department of Physical Medicine and Rehabilitation, Hitit University, Faculty of Medicine, Çorum, Turkey
2Department of Chest Diseases, Hitit University, Faculty of Medicine, Çorum, Turkey
3Department of Cardiology, Hitit University Faculty of Medicine, Çorum, Turkey
4Department of Medical Services and Techniques, Vocational School of Health Services Osmangazi University, Eskişehir, Turkey
5Department of Physical Medicine and Rehabilitation, Pamukkale University Faculty of Medicine, Denizli, Turkey

ABSTRACT

Objectives: To evaluate the cardiopulmonary functions and exercise performance of patients with Ankylosing Spondylitis (AS) and to investigate the relationship between these parameters and disease activity, spine mobility and quality of life.

Patients and methods: Forty-five patients with AS (Group 1) and 30 control subjects (Group 2) were included in the study. Disease activity was assessed with the Bath AS Disease Activity Index (BASDAI) and spinal mobility measures with the Bath AS Metrology Index (BASMI). The AS Quality of Life (ASQoL) Questionnaire and the Maastricht AS Enthesitis Score (MASES) were used. The pulmonary function test (PFT) and Cardiopulmonary Exercise Testing (CPET) were performed.

Results: The mean age was 43.09±12.07 in Group 1 and 42.80±9.96 in Group 2, with no significant difference between them. The peak expiratory flow (PEF) value in PFT was significantly lower in Group 1 (p<0.05). In Group 1, the duration of CPET was significantly shorter, and maximum work load and MET (Metabolic Equivalent) were significantly lower than in Group 2 (p<0.001). VO2max in peak responses, work and heart rate were significantly lower in Group 1. VO2max was negatively correlated with age, MASES and ASQoL (p<0.05).

Conclusion: There was no significant difference in PFT parameters between the groups. On the other hand, CPET parameters were found to be significantly lower in the AS group. While CPET parameters are affected by spinal mobility, declining aerobic capacity affects quality of life.

Keywords: Ankylosing spondylitis, cardiopulmonary exercise testing, pulmonary function test, quality of life.

Ankylosing Spondylitis (AS) is a chronic inflammatory rheumatic condition primarily affecting the axial skeleton. It is the main subtype of spondylarthritis (SpA). Uveitis, osteoporosis, intestinal disease and heart, lung, skin and kidney involvement may be observed in patients with concomitant extra-articular conditions. Aortic regurgitation, cardiac conduction disorders, heart problems, pulmonary fibrosis of the upper lobes and other lung problems have been described. Spinal motion restriction and deformity, functional impairment, severe handicap and decreased quality of life may be observed with disease progression.

It is reported that cardiovascular and pulmonary risk factors are high in this population. The
severity of cardiac involvement may range from asymptomatic to valve defects, severe heart failure and arrhythmia. Increased cardiac morbidity risk, including coronary artery disease, has been reported in patients with AS. Decreased aerobic capacity can be found in relation to cardiovascular disease. Respiratory abnormalities in AS are typically restrictive. Apical pulmonary fibrosis is also associated with AS, but the prevalence is low. However, a decrease in chest expansion may also result in a restriction of vital capacity, and aerobic capacity is reduced compared to the general population. In addition to pulmonary and cardiac dysfunction, other factors that may contribute to aerobic capacity impairment include decreased physical activity, peripheral arthritis, fatigue and muscle weakness. However, previous studies of aerobic capacity in patients with AS are limited in number and contradictory. The relative contribution of all these factors (cardiac, pulmonary, musculoskeletal disorders, inflammation, fatigue) to decreased aerobic capacity has not been quantitatively examined. Improved knowledge in this area will be clinically important both to understand the pathophysiological basis of exercise restriction and to develop effective training/rehabilitation strategies for patients in this setting.

Cardiopulmonary exercise testing (CPET) is a non-invasive procedure that provides diagnostic and prognostic information to assess an individual’s capacity during dynamic exercise. CPET-based exercise under controlled metabolic conditions is based on the investigation of the respiratory system, cardiovascular system and cellular response.

It allows an integrated assessment not only for pulmonary and cardiovascular systems, but also for the response to exercise, including the musculoskeletal system.

In this study, we aimed to evaluate cardiopulmonary functions and exercise performance of AS patients and to investigate the relationship between these parameters and disease activity, spine mobility and quality of life.

**PATIENTS AND METHODS**

The study was planned as cross-sectional. Local ethics committee approval was obtained. A written approval form was completed with all participants. Forty-five patients with AS (Group 1) who met the Modified New York Criteria and 30 age-matched control subjects (Group 2) were included in the study. The control group consisted of patients’ relatives who accompanied them to the hospital and agreed to participate in the study. The exclusion criteria included concurrent cardiac or respiratory disease, use of beta-blockers, arthritis/enthesopathy or contracture in the lower extremity that prevented exercise on the bike and arthroplasty or major surgery in the knee or hip joints. Patients’ age, height, weight, smoking history and past medical history were recorded. Patients’ pain levels were assessed as night and day with a 10 cm Visual Analogue Scale (VAS).

Disease activity was evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Functional status was assessed with the Bath Ankylosing Spondylitis Functional Index (BASFI). Mobility measurements were made with the Bath Ankylosing Spondylitis Metrology Index (BASMI). The following parameters were evaluated for mobility: cervical rotation (CR), lumbar lateral flexion (LLF), modified lumbar Schober (MLS), occiput-to-wall distance (ODW), intermalleolar distance (IMM) and chest expansion. Quality of life was evaluated by the Ankylosing Spondylitis Quality of Life (ASQoL) Questionnaire. The Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) was used for the assessment of enthesitis.

Laboratory tests: For the assessment of disease activity, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP, normal range 0-5 mg/L) levels were measured, and the complete blood count results were evaluated.

Pulmonary Function Test (PFT): Spirometry tests were performed by a trained and experienced spirometry technician in accordance with the American Thoracic Society (ATS) guidelines using the Zan 100 (nSpire Health Inc., Germany) spirometry device. Forced Vital Capacity (FVC), Forced Expiratory volume in one second (FEV1), FEV1/FVC and Peak Expiratory Flow (PEF) ratios were examined.

CPET: According to the guidelines, it was determined whether there was a condition preventing patients from participating in CPET. For this purpose, the medical history, physical
examination, resting electrocardiogram (ECG) and laboratory tests of all participants were evaluated by a cardiologist. In all participants without contraindications, maximum fatigue was defined as the target. The respiratory exchange ratio (RER) was aimed to reach a value of 1.1, and values above 1.05 were also accepted. RER reflects the ratio of carbon dioxide production to oxygen consumption (VCO₂/VO₂). The gas exchange measurement was conducted through breath-by-breath analysis using the Metalyzer 3B (Metasoft Studio 4.8, Cortex Biophysik GmbH, Leipzig, Germany) which continuously and simultaneously determines respiratory oxygen uptake (VO₂), carbon dioxide production (VCO₂) and ventilatory measures. The instantaneous values were determined by the average of the values of every final 10 seconds. All exercise tests were performed by a computer-controlled cycle ergometer (Ergoline Bicycle Ergometer Ergoselect 200, Germany) under supervision by an experienced technician and nurse from 10:30 AM to 1:00 PM in an air-conditioned laboratory with the temperature set at 18°C-22°C. During the test, a continuous recording was performed by a 12-lead ECG (Meta control 3000 connects the CORTEX MetaLyzer). The blood pressure was monitored non-invasively every two minutes by an automated sphygmomanometer with the appropriate cuff size from the right arm before and during the test and periods.

As the test protocol, the ramp protocol on a bicycle ergometer was adopted. Periods of three minutes rest and then three minutes of unloaded cycling, followed by an increase of 10W every minute ramp protocol starting at 25 W, was utilised. It was ensured that the pedaling frequency of the participants was over 60 per minute. According to the guidelines, people were encouraged to continue until they could no longer pedal, except in cases where the test had to be terminated. After the test was completed, the resting phase was started at the end of three minutes of unloaded pedaling. Heart rate, blood pressure, oxygen uptake, metabolic equivalent, work, oxygen pulse and RER were assessed at peak cardiovascular response and at ventilatory threshold.

**Statistical analysis**

Continuous quantitative variables were expressed as n, mean and standard deviation. Qualitative or score variables were expressed as

<table>
<thead>
<tr>
<th>Table 1. Comparison of clinical and laboratory parameters of patients with Ankylosing Spondylitis and control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient group with AS (n=45)</strong></td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Age (year)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Visual analog scale night-time</td>
</tr>
<tr>
<td>Visual analog scale daytime</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Disease Activity Index</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Functional Index</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Metrology Index</td>
</tr>
<tr>
<td>CE (cm)</td>
</tr>
<tr>
<td>ASQoL</td>
</tr>
<tr>
<td>Sedimentation (mm/hr)</td>
</tr>
<tr>
<td>C-reactive protein</td>
</tr>
</tbody>
</table>

SD: Standard deviation.
n, median, 25th and 75th percentiles. Continuous variables consisted of independent measurements and normal distribution was analyzed with Independent Samples T Test. The data without normal distribution was analyzed with Mann-Whitney U Test. Pearson Correlation or Spearman Correlation tests were used to determine the relationship and direction between the variables according to the normality test results. Chi-square tests were applied to variables in the categorical structure. Probability values of p<0.05 were considered significant. All data analyses were performed using the SPSS 21 package program.

RESULTS

The study included 45 patients with AS (12 female, 33 male) and 30 healthy controls (7 female, 23 male). The female/male ratio was similar in both groups (p>0.05). The duration of illness was 13.76±12.04 years in the group with AS. The age, body mass index (BMI), smoking history, VAS, BASDAI, BASFI, BASMI, chest expansion, ASQoL scores, ESR, CRP values and comparisons of the groups are presented in Table 1. In patients with AS, BASMI, ESR and CRP values were significantly higher, while chest expansion was significantly lower than in the control group (Table 1).

In addition, the complete blood count results were compared, and it was determined that only the hemoglobin value was significantly lower in patients with AS than in the control group (group with AS 14.3±1.91, control group 14.84±1.72, p>0.04). A comparison of the PFT values of the control group with AS patients is presented in Table 2. Only the PEF value in the PFT assessment was significantly lower in the group with AS (p<0.05) (Table 2). While a restrictive respiratory pattern was determined in 10 patients in the group with AS and an obstructive respiratory pattern in two patients in the control group, a restrictive respiratory pattern was found in only three patients in the control group (p>0.05).

Comparisons of the CPET values of the group with AS and the control group are presented in Table 3. In the AS group, the duration of CPET was significantly shorter than the control group, while maximum work and maximum MET were significantly lower (p<0.001). VO2max (ml/kg/min) in peak responses, work and heart rate were significantly lower in the AS group, while there was no difference between the resting state parameters of both groups (p<0.05).

The study for the correlation of the demographic and clinical parameters (age, BASDAI, BASFI, ODW and ASQoL) with PFT and CPET parameters in patients with AS is presented in Table 4.

There was a negative correlation between FVC and FEV1 and age, BASMI and ODW (p<0.001). There was a positive correlation between FVC and FEV1 and chest expansion (p<0.001). The duration of CPET and maximum work had a negative correlation with age and BASMI (p<0.001), and it had a positive correlation with chest expansion (p<0.001). VO2max (ml/kg/min) was negatively associated with age (p<0.001), MASES (p<0.001) and quality of life (p<0.05). VO2peak, work (peak) and heart rate (peak) were again negatively correlated with age and BASMI but positively with chest expansion (p<0.05). The VO2peak was also associated negatively with BASFI (p<0.05). Peak MET was negatively correlated with age and MASES (p<0.05), while there was no correlation between RER and clinical variables. VO2 was correlated with all clinical values except

| Table 2. Comparison of PFT values between control group and patients with AS |
|-----------------------------|-----------------------------|-----------------------------|
| Patient group with AS (n=45) | Control group (n=30)       |
| Mean±SD                      | Mean±SD                      |
| Forced vital capacity        | 3.4±0.8                      | 3.7±0.7                      | 0.131*          |
| Forced expiratory volume 1   | 3.0±0.7                      | 3.2±0.6                      | 0.104**         |
| Forced expiratory volume 1/Forced vital capacity (%) | 109.0±6.9                      | 110.5±5.8                      | 0.248**         |
| Peak expiratory flow (/sec)  | 5.9±1.6                      | 6.8±1.7                      | 0.020*          |

SD: Standard deviation; * Independent Samples t test; ** Mann-Whitney Rank Sum test.
Aerobic Capacity in Patients With Ankylosing Spondylitis

Age and quality of life (p<0.05). Whereas ESR was negatively correlated with maximum load and FEV1 (p<0.05), there was no correlation of CRP with CPET and PFT parameters.

**DISCUSSION**

In our study, pulmonary function tests of the patients with AS were similar to that of in control subjects. The aerobic capacities of the patients with AS were significantly reduced compared to controls, but there was no difference between resting CPET measurements. CPET duration, peak work, and peak MET from the aerobic test parameters were decreased with age and BASMI scores. These parameters were positively correlated with chest expansion.

Several studies investigating the aerobic capacities of patients with AS have indicated conflicting results when compared to healthy individuals. A study by Elliott et al. was the first to present that the maximum oxygen uptake (VO2max) and the estimated VO2max in patients with AS was lower than the measured VO2max of the control group. The study sample consisted of six patients with AS and six healthy subjects matched for age and body size. In another pilot study in which 12 patients with AS were assessed,
there was no significant reduction in exercise tolerance,\textsuperscript{27} although there was a broad range of maximum work load and VO\textsubscript{2} peak. In our study, the aerobic capacity was determined to be reduced compared to controls.

The low cardiorespiratory capacity observed in the group with AS is consistent with other studies comparing AS cohorts relative to control groups. The magnitude of the difference varies between 7\% and 24\% in the studies. This variance may be due to different patient characteristics, test protocols and VO\textsubscript{2}peak estimation methods.\textsuperscript{7,8,28,29} The small increases in absolute VO\textsubscript{2}peak are associated with a lower mortality than in cardiovascular disease.\textsuperscript{9}

Cardiovascular fitness decline in patients with AS is associated with mobility, muscle strength, physical function and impaired quality of life. However, fitness is not associated with disease activity.\textsuperscript{30} In addition to these data, CPET was also associated with age and enthesic score, but it was not associated with disease activity in our study.

Another cause of decreased aerobic capacity in patients with AS may be cardiovascular pathologies. According to the results of previous studies, conduction disorders and valvular heart disease are the most important cardiovascular findings in AS.\textsuperscript{31} Recent studies have reported

\begin{table}
\caption{Correlation of demographic and clinical parameters with PFT and CPET parameters in patients with AS}
\begin{tabular}{lcccccc}
\hline
 & Age (year) & BASDAI & BASFI & BASMI & ASQoL & CE & MASES \\
\hline
FVC & & & & & & & \\
\textit{r} & -0.517 & -0.086 & -0.299 & -0.643 & -0.212 & 0.732 & -0.297 \\
\textit{p} & 0.000* & 0.587 & 0.054 & 0.000* & 0.179 & 0.000* & 0.057 \\
FEV\textsubscript{1} & & & & & & & \\
\textit{r} & -0.543 & -0.104 & -0.282 & -0.622 & -0.194 & 0.712 & -0.296 \\
\textit{p} & 0.000* & 0.514 & 0.071 & 0.000* & 0.219 & 0.000* & 0.057 \\
CPET duration & & & & & & & \\
\textit{r} & -0.433 & -0.111 & -0.286 & -0.364 & -0.239 & 0.496 & -0.216 \\
\textit{p} & 0.003* & 0.485 & 0.066 & 0.018* & 0.127 & 0.001* & 0.170 \\
VO\textsubscript{2max} (mL/kg/min) & & & & & & & \\
\textit{r} & -0.441 & -0.021 & -0.287 & -0.187 & -0.337 & 0.271 & -0.512 \\
\textit{p} & 0.002** & 0.893 & 0.065 & 0.236 & 0.029* & 0.082 & 0.001 \\
Work (Max) & & & & & & & \\
\textit{r} & -0.385 & 0.017 & -0.243 & -0.312 & -0.206 & 0.467 & -0.262 \\
\textit{p} & 0.009* & 0.913 & 0.120 & 0.044* & 0.191 & 0.002* & 0.093 \\
VO\textsubscript{2} (peak) & & & & & & & \\
\textit{r} & -0.334 & -0.103 & -0.317 & -0.310 & -0.257 & 0.394 & -0.250 \\
\textit{p} & 0.025* & 0.514 & 0.041* & 0.046* & 0.100 & 0.010* & 0.110 \\
MET (peak) & & & & & & & \\
\textit{r} & -0.431 & 0.073 & -0.132 & -0.154 & -0.282 & 0.276 & -0.369 \\
\textit{p} & 0.003* & 0.645 & 0.406 & 0.329 & 0.070 & 0.077 & 0.016* \\
Work (peak) & & & & & & & \\
\textit{r} & -0.385 & 0.017 & -0.243 & -0.312 & -0.206 & 0.440 & -0.249 \\
\textit{p} & 0.009* & 0.913 & 0.120 & 0.044* & 0.191 & 0.004** & 0.112 \\
Heart rate (peak) & & & & & & & \\
\textit{r} & -0.550 & 0.015 & 0.007 & -0.314 & -0.048 & 0.320 & -0.018 \\
\textit{p} & 0.000** & 0.927 & 0.963 & 0.043* & 0.761 & 0.039* & 0.908 \\
RER (peak) & & & & & & & \\
\textit{r} & -0.122 & -0.054 & 0.086 & 0.078 & -0.172 & 0.139 & -0.114 \\
\textit{p} & 0.426 & 0.732 & 0.586 & 0.622 & 0.277 & 0.380 & 0.471 \\
VO\textsubscript{2} (vt) & & & & & & & \\
\textit{r} & -0.219 & -0.354 & -0.452 & -0.446 & -0.169 & 0.415 & -0.308 \\
\textit{p} & 0.180 & 0.032* & 0.005** & 0.006** & 0.317 & 0.011* & 0.063 \\
\hline
\end{tabular}
\begin{tablenotes}
\item BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; ASQoL: Ankylosing spondylitis quality of life; CE: Chest expansion; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score.
\end{tablenotes}
\end{table}
the impairment of endothelial function and coronary microvascular function in patients with AS. Potential mechanisms for cardiovascular complications include a chronic inflammatory condition with increased levels of circulating cytokines and acute phase reactants. Although heart and valvular pathologies were not evaluated in our study, exercise tolerance was not associated with disease activity.

Exercise tolerance testing is the simultaneous assessment of the ability of vascular and respiratory systems to perform their functions. This is because there is a requirement for an integrated cardiopulmonary response when exercising. It has been stated that fatigue of the inspiratory muscles may contribute to reduced aerobic capacity in patients with AS because there is significant muscular fatigue, especially in the diaphragm and intercostal muscles.

Fisher et al. reported on 33 patients with AS, investigating the correlation between chest expansion, pulmonary function and exercise capacity. They mentioned a significant correlation between chest expansion and vital capacity. Exercise tolerance was significantly associated with vital capacity but not with chest expansion. Vital capacity and exercise tolerance were not correlated with the duration of disease, thoracic kyphosis or ESR. In this study, it was concluded that the limitation of chest expansion in patients with AS could lead to a decrease in vital capacity, but it was not a significant predictive factor determining exercise tolerance. In our study, chest expansion was associated with both PFT and aerobic capacity.

Hsieh et al. compared the aerobic capacity, pulmonary function and disease-related variables in 42 patients with AS and 42 control subjects. They reported that both aerobic capacity and PFT were lower in patients with AS. More specifically, the VO2 peak values of the patients with AS were 13% lower than the normal subjects. Whereas a significant correlation of the aerobic capacity was found with the vital capacity, chest expansion, Schober test, cervical range of motion, age and BASFI in patients with AS, there was no correlation between aerobic and pulmonary vital capacity with the duration of disease and disease activity. This was similar to our study and others. There was no significant statistical difference between the two groups in terms of heart rate, O2 pulse, blood pressure and RER during peak cardiovascular response. This was also similar to our study.

Carter et al. assessed the CPET and aerobic capacities of 20 patients with AS and 20 healthy control patients matched for age and gender. They indicated that the patients with AS showed lower VO2peak values than the healthy controls (25.2±1.4 vs. 33.1±1.6 mL/kg/min), reporting a 24% reduction in aerobic capacity. In addition, they suggested that the ventilator threshold had decreased significantly and that there was no significant difference between the groups in terms of the blood pressure response during exercise. They found that patients with AS had a lower mean working capacity (123 watt-148 watt) compared to controls. In this study, the respiratory and peripheral muscle functions of the participants were also assessed and the peripheral muscle function was demonstrated to be the most important determinant of aerobic capacity. In our study, the patients with AS had lower ventilator thresholds and VO2peak values. The aerobic capacity was significantly lower in patients with AS compared to controls (116.29 watt-154.07 watt), and there was no significant difference between the blood pressure responses of the groups during exercise. The aerobic capacity was reduced by 17.6%.

Carter et al. reported that there were no gas exchange abnormalities at resting phase or during exercise, despite impaired aerobic capacity compared to controls, in patients with AS without cardiac or pulmonary parenchymal disease. Similarly, no RER change was observed in our patient group.

In a study conducted with male patients and controls, it was reported that, although the exercise tolerance was similar, the PFT was lower than the controls. However, patients with AS have been reported to have a higher rate of symptoms, such as exertion and dyspnoea, during exercise. Also, it was indicated that chest expansion was correlated with PFT but not with exercise tolerance. In our study, chest expansion was associated with both respiratory and aerobic capacity parameters. Ozdem et al., found that the respiratory and aerobic capacity parameters correlated with chest expansion. Also, the clinical
parameters not correlated to BASDAI and BASFI presented very to similar results to our study.\textsuperscript{35}

The restrictive respiratory pattern was present in 22.2\% of our patients with AS. Our spirometry test results are consistent with previous studies in the literature in which the restrictive pattern was reported between 18\% and 52\%\textsuperscript{28,36}. Especially in terms of heart rate values in cardiorespiratory exercise testing, heart rate in patients with AS was significantly different compared to controls both at rest and during exercise.\textsuperscript{9} In our study, heart rate was significantly different in both rest and exercise. In addition, MET values were lower than in controls.

The following are the limitations of this study: the cross-sectional design precludes the determination of the causality between variables, the sample selection used may have resulted in selection bias and participants who apply to the clinic of Physical Medicine and Rehabilitation may not be representative of all AS patients.

In conclusion, there was no significant difference in PFT parameters in patients with AS, and CPET parameters were found to be significantly lower in the group with AS than in the control group. This is probably due to the fact that CPET is more sensitive than PFT parameters in predicting lung, muscle and cardiac functions in patients with AS. Since 22.2\% of the patients had a restrictive pattern of respiratory dysfunction, and respiratory dysfunction affects exercise tolerance, supporting patients with appropriate exercise programs is very important. This is because it is known that cardiorespiratory fitness affects the functional status and quality of life positively, independently of disease activity.

Declaration of conflicting interests
The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding
The authors received no financial support for the research and/or authorship of this article.

REFERENCES


McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Research 2011; 63(11):240–52


