

Respiratory muscle performance as a possible determinant of exercise capacity in patients with ankylosing spondylitis

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Reduction of exercise capacity in patients with ankylosing spondylitis is associated with skeletal muscle performance. The contribution of respiratory muscle performance is questionable. This pilot study was designed to investigate the relationship between respiratory muscle performance and exercise capacity in ankylosing spondylitis. Subjects were 12 patients with ankylosing spondylitis. Measurements of maximal respiratory pressures and inspiratory muscle endurance were performed and correlated with maximal exercise capacity. Lung function and chest wall expansion were reduced on average. Maximal inspiratory and expiratory pressures were reduced to $82 \pm 20\%$ of predicted values and $75 \pm 22\%$ of predicted values respectively. On average there was no reduction in inspiratory muscle endurance which remained at $103 \pm 36\%$ of predicted values. No overall reduction was found in maximal exercise capacity, either expressed as maximal workload or as peak oxygen uptake; however, a wide range was found. Maximal workload and peak oxygen uptake correlated significantly with maximal respiratory pressures and respiratory muscle endurance. The best regression model for explaining the total variation of maximal workload and peak oxygen uptake selected maximal inspiratory pressures as the independent variable ($r^2 = 59.6\%$, $p = 0.003$ and $r^2 = 62.5\%$, $p = 0.05$ respectively.) These data suggest respiratory pressure and respiratory muscle endurance, in particular maximal inspiratory pressure, may be determinants of exercise capacity in patients with ankylosing spondylitis. [van der Esch M, van 't Hul AJ, Heijmans M and Dekker J (2004): Respiratory muscle performance as a possible determinant of exercise capacity in patients with ankylosing spondylitis. *Australian Journal of Physiotherapy* 50: 41–45]

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Introduction

Ankylosing spondylitis is a chronic inflammatory joint disease, characterised by fusion of the axial skeleton. Many patients with ankylosing spondylitis complain about reduced exercise capacity and are referred to a physiotherapist. The aim of the treatment is to increase the exercise capacity by use of different interventions, based on different hypotheses. These hypotheses come from several explanations proposed for the reduction in exercise capacity, such as pulmonary function impairment, chest wall restriction, poor respiratory muscle performance, peripheral muscle weakness and deconditioning (Baum and Wolinsky 1994, Boushea and Sundstrom 1989, Carter et al 1999, Casserly et al 1997, Chua et al 1995, Elliott et al 1985, Feltelius et al 1986, Fischer et al 1990, Köseoglu et al 1998, Rosenow et al 1977, Seckin et al 2000). Generally, in these studies no significant correlation between chest wall expansion, pulmonary function, and exercise capacity was found, and the results were somewhat conflicting. Carter et al (1999) concluded that the strength of peripheral muscles (for instance the quadriceps) was the most important determinant, suggesting that deconditioning was the main factor in reduced exercise capacity. Peripheral muscles accounted for 53% of the total variance in exercise capacity ($p = 0.001$). When other variables were added to a regression model only lean body mass significantly improved the explained variance to 78.3%. Respiratory muscle performance was not found to be related to exercise capacity. Surprisingly, Carter et al (1999) reported a higher value of maximum inspiratory pressure

(PI_{max}) in the ankylosing spondylitis group compared to the control, which means that the ankylosing spondylitis patients had greater muscle strength on inspiration than the control group. This result is counter-intuitive and discordant with the conclusions from a study in patients with rheumatoid arthritis (Gorini et al 1990). In that study respiratory muscle performance was recognized as a determinant for exercise capacity. In general, weakness of the inspiratory muscles causes these muscles to be susceptible to fatigue (Bellemare and Grassino 1982, Grassino et al 1979). Vanderschuere et al (1989) also found a reduction in inspiratory and expiratory pressure as a result of reduced muscle performance, but the relationship to exercise capacity was not studied. Thus, the role of respiratory muscle performance as a determinant of exercise capacity in ankylosing spondylitis remains to be clarified.

The objective of the present pilot study was to determine the association between respiratory muscle performance and exercise capacity in ankylosing spondylitis patients. It was hypothesized that respiratory muscle performance is reduced and that respiratory muscle performance is associated with reduced exercise capacity in these patients.

Method

Study population Fifteen male patients with a definite diagnosis of ankylosing spondylitis, as defined by the ACR Criteria for the Classification of Spondylarthropathy (Dougados et al 1991), were randomly selected from a larger population of 60

ankylosing spondylitis patients treated in a specialized, outpatient clinic for rheumatic diseases in Amsterdam. These 60 patients participated in a weekly 1-hour therapy session group of physical training (to improve mobility of the spine and peripheral joints and to strengthen the muscles of trunk and legs), followed by one hour of sporting activities. Every fourth patient was selected from a list. They were selected according to the following criteria: the absence of a (known) co-existent cardiac or respiratory disease (like asthma, chronic bronchitis, or emphysema), and the absence of such severe arthritis or other conditions as would make it impossible to exercise on a bicycle. All patients were in a steady phase of their disease, according to their record and by history taken. Ten patients used a prostaglandin synthesis inhibitor every day; three used non-steroidal anti-inflammatory drugs, or no medication. None of the patients was currently a smoker; one patient had stopped smoking a year before, but the smoking history of the others was unknown. Twelve of the fifteen selected patients with definite ankylosing spondylitis participated in the present study. One patient refused to participate and one could not be contacted. During the first assessment one was excluded from the study because of the presence of a contraindication for a maximal exercise test (hypertension), which was not recognised during the inclusion period.

Local research ethics committee approval was granted for this pilot study and written informed consent was obtained from each patient.

Design All patients were assessed on three separate days at the same time of day. During the first assessment, maximal respiratory pressures and inspiratory muscle endurance were determined. On the second assessment all these tests were repeated. On the third assessment pulmonary function tests and an incremental maximal exercise test on a cycle ergometer were performed.

Patient characteristics Age, weight, height, body mass index, and chest expansion were measured. The measurement of height in patients with ankylosing spondylitis might be hampered because of the flexion position of the spine. Therefore height was calculated from arm span measurements (Hepper et al 1965). Chest expansion was measured with a tape measure placed circumferentially around the ribcage at the level of the fourth intercostal space (Moll and Wright 1972).

Pulmonary function was determined using standard pulmonary function tests^a according to European Respiratory Society recommendations. Assessment included vital capacity (VC), forced expiratory volume in one second (FEV₁), Tiffeneau index (FEV₁/VC), total lung capacity (TLC; body plethysmography), functional residual volume (FRC), residual volume (RV), and transfer factor for carbon monoxide (Tl_{co}; single-breath method). Measurements were related to the reference values of Quanjer et al (1993); this enabled us to express the measurements as a percentage of the predicted value (%pred). Calculation of predicted values was based on the predicted height from arm span measurements. Maximal voluntary ventilation was assessed by measuring the maximal voluntary ventilation over a 12-second interval.

Maximal respiratory pressures were determined using standard procedures according to the method of Black and Hyatt (1969) and were expressed as percentage of their reference values. The reference group of Black and Hyatt is a group of healthy people of varied age, sex, and height. In the Black and Hyatt method measurements are repeated until three technically satisfactory maximal values are obtained, differing by less than 5%. The

Table 1. Subject characteristics and results of respiratory tests.

Characteristic	Mean ± SD	
Age (y)	46.4 ± 9.2	
Weight (kg)	75.0 ± 10.1	
Height (m)	1.76 ± .70	
BMI (kg/m ²)	24.3 ± 3.2	
Chest expansion (cm)	3.3 ± 2.3	
Test	Mean ± SD	(%pred)
FEV ₁ (l)	2.95 ± 0.62	80 ± 14
VC (l)	3.56 ± 0.61	79 ± 11
RV (l)	2.1 ± 0.38	102 ± 17
FRC (l)	3.28 ± 0.43	96 ± 11
TLC (l)	5.75 ± 0.64	84 ± 9
Tl _{co} (mmol/kPa/min)	1.38 ± 0.23	91 ± 13

BMI, body mass index. FEV₁, forced expiratory volume in one second. VC, vital capacity. RV, residual volume. FRC, functional residual capacity. TLC, total lung capacity. Tl_{co}, diffusing capacity for carbon monoxide corrected for alveolar volume.

highest values were used. Maximal inspiratory pressures (PI_{max}) were measured from (near) residual volume and expiratory pressures from total lung capacity. During the measurements subjects wore a nose clip. Between each attempt, subjects were allowed to rest for one minute. Pressure curves were visually displayed on a monitor during each attempt.

Measurements can be expressed as absolute pressures (PI_{max} and PE_{max}) and as percentages of the reference value (PI_{max} %pred and PE_{max} %pred). Since no data are available in the literature about the test-retest reliability of the measurement of PI_{max} and PE_{max} in patients with ankylosing spondylitis, assessments were carried out twice. Statistically significant intraclass correlation coefficients were found for test and retest of PI_{max} and PE_{max} (r = 0.95, p = 0.001). In analysis the results of the second measurement of both respiratory pressure tests were used. These results did not differ on average from the first measurements.

Inspiratory muscle endurance PI_{end} was assessed by a 2-minute maximal incremental inspiratory threshold loading protocol, similar to the method introduced by Martyn et al (1987). Subjects were instructed to breathe through a two-way Hans-Rudolph valve^b. A modified 'threshold'^c could be connected to the inspiratory port, consisting of a spring construction which allowed precise adjustments of the inspiratory load. With this system flow-independent inspiratory loads can be applied reliably in the range of 7–110 cm H₂O (Fairbairn et al 1986, Gosselink et al 1996). In order to determine end-tidal CO₂, a sample for the capnograph^d was taken between the mouth and the two-way Hans-Rudolph valve. The test started with a 5-minute period of unloaded breathing. During the last minute, end-tidal CO₂ was registered. Then the threshold was applied to the inspiratory port of the system and the subjects started breathing through the apparatus with an initial load of 25% of PI_{max}. The load was increased by 5% of PI_{max} every two minutes until participants gave up. Subjects were encouraged to maintain ventilation for as long as possible. During loaded breathing, subjects were not allowed to decrease minute ventilation below resting values (i.e. they were not allowed to increase end-tidal CO₂). Only the loads that could be tolerated for the complete two minutes were used in the statistical analysis. Reference values of Johnson et al (1996 and 1997) were used in the analysing

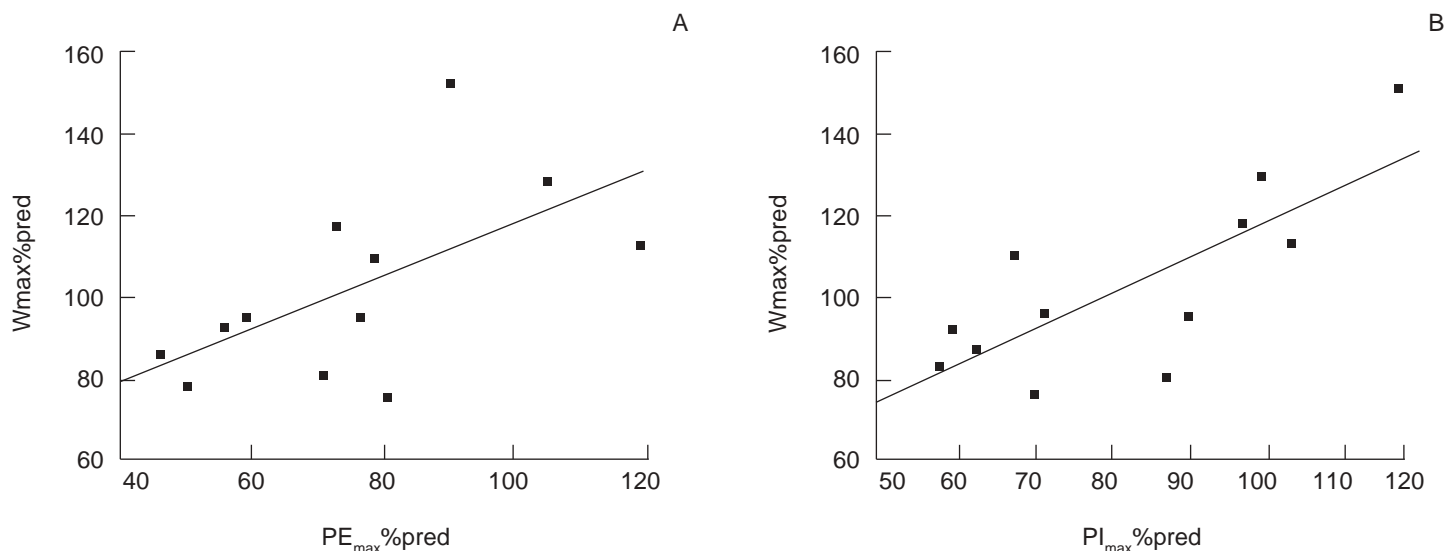


Figure 1. Relationship between respiratory pressures and exercise capacity. A, Maximum expiratory pressure (PE_{\max} %pred) vs maximum workload (W_{\max} %pred). B, Maximum inspiratory pressure (PI_{\max} %pred) vs maximum workload.

procedure. PI_{end} can be expressed as the maximum tolerable load (pressure in cmH_2O) and as percentage of the reference value (PI_{end} %pred). Since no data are available in the literature about the test-retest reliability of the measurements of PI_{end} by the use of this type of test protocol in patients with ankylosing spondylitis, assessments were carried out twice. A significant intra-class correlation coefficient was found between test and retest of PI_{end} ($r = 0.96$, $p = 0.001$). Because tidal expiration is normally passive (i.e. not performed by muscles), PE_{end} was not of interest in this study, and as a consequence no expiratory muscle endurance test was used. In analysis the results of the second measurement were used. The results between the first and second measurement did not differ on average.

Maximal voluntary ventilation MVV ratio was determined prior to the maximal exercise capacity test. During this test the maximal minute ventilation (VE_{\max}) was measured. The relation between the VE_{\max} and MVV gives insight into the extent of the breathing reserve. In healthy subjects, this ratio does not normally exceed 70% at maximal exercise (Wasserman et al 1994).

Maximal exercise capacity A maximal exercise test was performed by each patient on an electrically braked cycle ergometer^e. After three minutes of rest, patients were instructed to exercise for as long as possible. The load of the ergometer was increased each minute by 10% of the individual predicted maximal exercise capacity according to the reference values of Jones et al (1989). During the test, heart rate was monitored continuously using an ECG^f. Ventilation and metabolic measurements were made continuously, breath-by-breath, by a mass flow sensor and medical gas analyser^g. Values were averaged over 20-second time intervals. Maximal exercise capacity is expressed as maximal workload (W_{\max}); maximal workload is expressed as percentage of the predicted value (W_{\max} %pred); peak oxygen uptake ($VO_{2\text{peak}}$) and peak oxygen uptake expressed as percentage of the predicted value ($VO_{2\text{peak}}$ %pred).

Analysis In order to investigate the relationship between the

dependent variables W_{\max} and $VO_{2\text{peak}}$ and the independent variables PI_{\max} , PE_{\max} and PI_{end} , Pearson correlation coefficients were calculated. In addition, multiple linear regression analyses were conducted. In calculating the correlation coefficient and in the regression analysis, the percentage of the reference values (%pred) of the respiratory pressures was used. For all tests, SPSS Advanced Statistics 7.5 for Windows^h was applied. A significance level of 0.05 was used.

Results

Demographic and pulmonary function test data are presented in Table 1.

Mean maximal inspiratory pressure (82 ± 20 %pred) and mean maximal expiratory pressure (75 ± 22 %pred) were less than predicted values. In six patients PI_{\max} was less than the reference value of 80% of predicted values, and PE_{\max} was lower than the reference value in seven patients. Inspiratory muscle endurance (PI_{end}) was not reduced on average (mean = 103 ± 36 %pred).

Although in general no reduction was found in maximal exercise capacity either expressed as W_{\max} or as $VO_{2\text{max}}$, a wide range of exercise capacities was found (75 to 152 %pred). Three of the twelve patients stopped exercise because of reported dyspnoea. All others stopped exercise because of leg fatigue.

The VE_{\max}/MVV ratio (mean of 80 ± 23 %pred) was higher than 70% in seven patients. In four patients it was 100% or higher.

The relationship between maximum respiratory pressures and exercise capacity is depicted in Figure 1. Significant positive correlations were found between maximal inspiratory pressure (PI_{\max} %pred) and both measures of exercise capacity (W_{\max} %pred $r = 0.77$, $p = 0.003$; $VO_{2\text{peak}}$ %pred $r = 0.79$, $p = 0.002$). Maximal expiratory pressure (PE_{\max} %pred) correlated significantly (W_{\max} %pred $r = 0.60$, $p = 0.04$; $VO_{2\text{peak}}$ %pred $r = 0.60$, $p = 0.04$) as did maximal inspiratory pressure (PI_{\max} %pred; W_{\max} %pred $r = 0.65$, $p = 0.05$; $VO_{2\text{peak}}$ %pred $r = 0.67$, $p = 0.03$).

To further analyse the relationship between exercise capacity and respiratory muscle performance, three step-wise multiple regression analyses were conducted: one each with PI_{max} , PE_{max} and PI_{end} as the independent variables, and each with both W_{max} and VO_{2peak} as dependent variables. The addition of any other variable, like lung function and chest wall expansion, did not improve the explained total variation of W_{max} and VO_{2peak} by PI_{max} , PE_{max} and PI_{end} . The best model explaining the total variation of W_{max} is as follows: $W_{max} = 27.81 + 0.90 PI_{max}$ ($p = 0.003$, $r^2 = 59.6\%$, $n = 12$). This means that 60% of the total variation of W_{max} is explained by PI_{max} pred. For VO_{2peak} the best model is: $VO_{2peak} = 44.12 + 0.71 PI_{max}$ ($p = 0.002$, $r^2 = 62.5\%$, $n=12$).

Discussion

The aim of this study was to evaluate in patients with ankylosing spondylitis the relationship between respiratory muscle performance and maximal exercise capacity. Respiratory muscle performance was expressed as maximal respiratory pressures (PI_{max} , PE_{max}) and inspiratory muscle endurance (PI_{end}). As was hypothesised, maximal respiratory pressures were found to be reduced and were strongly associated with maximal exercise capacity. Maximal inspiratory pressure was the strongest predictor for exercise capacity, explaining 59% of the variation of W_{max} and 63% of the variation of VO_{2peak} .

The findings of mild reductions in vital capacity and total lung capacity are in agreement with previous studies (Baum and Wolinsky 1994, Boushea and Sundstrom 1989, Carter et al 1999, Casserly et al 1997, Elliott et al 1985, Feltelius et al 1986, Fischer et al 1990, Köseoglu et al 1998, Rosenow et al 1977, Seckin et al 2000). The chest wall expansion at the level of the 4th rib was on average mildly reduced. However four patients had an expansion of just 1 cm, which means virtually no ribcage movement at all at that level.

Respiratory muscle performance The reduction in maximal respiratory pressures is in agreement with the results described by Vanderschueren et al (1989). They speculated that the reduction in maximal respiratory pressures might be the result of intercostal muscle atrophy due to the reduction in chest wall expansion. Our results are not in agreement with the study of Carter et al (1999), who did not find a significant difference in measures of respiratory muscle strength, although they did report that respiratory muscle endurance measurements were significantly reduced in subjects with ankylosing spondylitis compared to controls. They also reported an increased inspiratory pressure compared to the control group. Differences between our results and those of Carter et al could be explained by the different measurements or protocols. Carter et al (1999) compared respiratory muscle performance in people with ankylosing spondylitis with healthy controls, and in our study we used only reference values. These differences could be responsible for the discrepancy. A limitation of our study is that the function of the diaphragm was not measured. This muscle has an important role in generating inspiratory muscle force. The other parts of the ribcage were also not measured and it is possible that the mobility of the lower ribs might have influenced inspiratory muscle force.

Exercise capacity In the present study, a wide range in maximal exercise capacity of subjects, expressed as $W_{max}\%$ pred, was found. However, overall there was no reduction (mean $104 \pm 23\%$ pred). This is in contrast to the studies performed by Elliott et al (1985) and Fisher et al (1990) who found a reduced maximal exercise capacity in all participating ankylosing spondylitis patients. Since it is known that regular exercise or an active life

style (Seckin et al 2000) may enhance exercise capacity in patients with ankylosing spondylitis (Fischer et al 1990), especially when exercises are performed in a group (Hidding et al 1993), the overall well-preserved exercise capacity in our study could be the result of the exercise regime in which all of our patients were involved.

Inspiratory and expiratory pressure were both significantly related to exercise capacity. Of all the independent variables analysed in this study, maximal inspiratory pressure correlated most strongly with maximal exercise capacity. It must be emphasized however, that the present study was designed to investigate a statistical relationship between respiratory muscle performance and exercise capacity in patients with ankylosing spondylitis and not to study causality. Analysis of the physiological responses at maximal exercise may give some clues with respect to causality between maximal respiratory muscle performance and maximal exercise capacity. In seven patients the VE_{max}/MVV ratio was higher than 70%pred which indicates an abnormally high load on the muscles of the ventilatory pump during (maximal) exercise, especially when chest wall compliance is reduced, as is the case in many patients with ankylosing spondylitis (Noord 1991). This finding is in agreement with Carter et al (1999) who found a higher intensity of breathing effort perceived among 20 patients with ankylosing spondylitis for equivalent levels of work rate and oxygen uptake compared with 20 age- and gender-matched healthy controls. An (abnormally) high load-capacity ratio of the inspiratory muscles makes these muscles susceptible to fatigue (Bellemare and Grassino 1982) and may contribute to exercise limitation. Indeed, in eight patients in the present study, end-tidal CO_2 measured during the exercise test did not decrease at maximal exercise compared to the value at rest. This suggests failure of the ventilatory pump to adapt adequately to increased metabolic demands of maximal exercise. Definite conclusions in this respect require additional measurements, for instance by the use of esophageal pressure measurement or EMG recordings of the respiratory muscles during exercise.

Conclusion

An association was found between maximal respiratory pressures, inspiratory muscle endurance and maximal exercise capacity in patients with ankylosing spondylitis. Future research should provide further insight into the mechanisms of the relationship between respiratory muscle performance and exercise limitation of patients with ankylosing spondylitis. The results of the present pilot study suggest that training of the respiratory muscles and specifically of PI_{max} should be a part of a physiotherapy program for patients with ankylosing spondylitis.

Footnotes ¹Vmax 229, Sensormedics, Bilthoven, The Netherlands ²Kansas City, MO, USA ³Health Scan Products, Inc., Cedar Grove, NJ, USA ⁴Normocap 200; Datex, Finland ⁵Rehcor, Lode, Groningen, The Netherlands ⁶Datascoop, Utrecht, The Netherlands ⁷Vmax 229, Sensormedics, Bilthoven, The Netherlands ⁸SPSS Inc., 233 S. Wacker Dr., Chicago, IL 60606, USA

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