ORIGINAL ARTICLE

Reduction of respiratory muscle strength in subjects with rheumatoid arthritis

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ABSTRACT

Objective: To evaluate the respiratory muscle strength in patients with rheumatoid arthritis (RA) compared to healthy subjects and to correlate it with the level of disease activity (DAS- 28) and body mass index (BMI). **Method:** A cross-sectional study evaluated 18 women (57.94 ± 10.36 years); eight had RA (RA group) and ten were healthy subjects (control group), matched by age. All patients underwent the following evaluations: registration form (identification and clinical data), physical examination (weight, height, and BMI), DAS-28, dosage of C-reactive protein (CRP), and measurement of MIP and MEP with a manometer. **Results:** There were significant differences between the RA and control groups in relation to the MIP (-46.25 ± 17.67 *vs.* cmH_2O -81.00 ± 19.69 cm H_2O) and MEP (58.75 cmH_2O ± 17.26 *vs.* 78.00 ± 6.32 cmH_2O). Also there was difference between RA group and predicted age values in relation to the MIP (-46.25 ± 17.67 *vs.* -81.06 ± 4.11 cmH_2O) and MEP (58.75 cmH_2O ± 17.26 *vs.* 78.92 ± 5.33 cmH_2O). Moreover, a significant correlation was observed between MEP and BMI. There was no significant correlation between MIP - CRP, DAS- 28 and BMI, and between MEP - DAS and CRP. **Conclusion:** This data reinforces the systemic nature of RA and points out the need for a comprehensive assessment of the patient, not just focusing on the articular component, but also checking the strength of the respiratory muscles of these individuals to determine more specific therapeutic strategies of treatment.

Keywords: Arthritis, Rheumatoid, Muscle Strength, Respiratory Muscles

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that manifests predominantly with symmetrical peripheral polyarthritis, possibly resulting in joint destruction.[1,2] The evolution of the disease presents different aspects over time, from light and intermittent episodes to the progressive development of functional disabilities and deformities.[3] In addition, clinical observations have shown a prevalence of injuries disseminated to other regions of the body, pointing to the systemic nature of the disease and its increasing severity.[1,4,5]

In this context, pulmonary impairment has been frequently seen in RA patients.[6] In most cases, the pulmonary impairment begins after the joint symptoms,[7] being referred to as a significant morbidity factor, as well as the third main cause of mortality in this pathology.[8] However, respiratory symptoms could be masked by the restriction to ambulation and mobility stemming from the osteoarticular involvement.[9] The clinical course of the pulmonary disease in RA presents a heterogeneous aspect, with some asymptomatic patients and others with severe cases of respiratory dysfunction resulting from light exertions.[10] Studies made by Gorini et al.[11] and Çimen et al.[12] in 2001 reported that, even in the absence of significant pulmonary lesions, there is impairment of respiratory muscle strength in RA.

The factors that can lead to loss of respiratory muscle strength range from pleuro-pulmonary impairment to lesser cardiorespiratory fitness imposed by physical inactivity in the active periods of the disease that can persist even in periods of remission.[12,13] For Gorini et al.,[11] the respiratory muscle strength can be altered due to impairment of the costosternal and costovertebral joints, malnutrition, and pain, which would lead to a global functional limitation in RA, with deficits in respiratory muscle performance. The pathogenesis of the rheumatoid pulmonary disease has been also associated with greater activity of the disease.[14,15] Additionally, there are consistent results in the literature that the greater the activity of the disease, the higher will be the BMI classification.[16] In this way, sedentarism and obesity are interrelated in RA, due to the functional limitation imposed by the disease resulting in less physical activity, which may, in turn, contribute to obesity and to a lower cardiorespiratory aptitude.[17]

Confirming pulmonary involvement is done through imaging exams and a pulmonary function test (PFT). The most sensitive method for determining pulmonary lesions is the High Resolution Computerized Tomography of the thorax. The PFT done via spirometry evaluates the pulmonary function predicting the progression of pulmonary disease in RA.[9,18] However, the cost of these exams hinders its common use in the evaluation of pulmonary involvement of these patients.[15] This is why authors such as Pappas et al.[19] defend that, for a more assiduous clinical investigation, the observation of respiratory signals and symptoms (coughing, dyspnea, phlegm, and wheezing) as predictors of pulmonary involvement should occur. Supplementing the previous analysis, the evaluation of respiratory muscle strength in individuals with RA through manovacuometry could be a useful approach, for besides being a low cost and easy to apply test, it provides additional information to determine therapeutic strategies.[15] However, there are few studies about respiratory muscle strength in individuals with RA.[11,12,15,20]

OBJECTIVE

This study seeks to evaluate the respiratory muscle strength of patients with Rheumatoid Arthritis (RA) in comparison with healthy individuals and make correlations with the disease activity score (DAS-28) and body mass index (BMI).

METHOD

This was a cross-sectional, descriptive, and correlational study, based on an intentional non-probabilistic sampling composed of 18 women with mean age of 57.94 years, where eight women had a clinical diagnosis of RA (RA Group) and ten were considered healthy (Control Group), paired by age (± 2 years).

The RA patients were forwarded by rheumatologists from the metropolitan area of Florianópolis, state of Santa Catarina, or from the Physiotherapy Clinic at the Health and Sports Science Center, Santa Catarina State University (CEFID/UDESC). The healthy participants were recruited in the community.

The present study was approved by the Human Research Ethics Committee of the Santa Catarina State University (CEPSH/UDESC), under the number 11742613.6.0000.0118. The participants formally agreed to the study procedures by signing a Free and Informed Consent Form.

Other inclusion criteria were considered for the RA Group patients, in addition to their RA diagnoses, in accordance with the classification rules of the American College of Rheumatology,[21] such as disease in activity (DAS28 > 2.6)[22] and age greater than 18 years. Healthy women were included in the Control Group who were aged over 18 years.

The exclusion criteria for both groups were previous or current history of tobacco smoking, occupational respiratory exposure, accentuated thoracic deformities, history of fractures in costal arches, diagnosed neurological or pulmonary pathologies, and gestation.

Each participant's data was collected in one sitting, always in the morning, at the Multisectorial Analyses Laboratory (*Laboratório de Análises Multissetorial - MULTILAB*), located at the Santa Catarina State University (UDESC). All the tests and measurements were made by the same researcher. The volunteers were informed of the objectives and procedures of the study and signed a Free and Informed Consent Form. For the evaluation of clinical aspects and respiratory muscle strength, the following evaluations were made:

Registration Form

Information on the clinical data of the RA patients was collected, in addition to their age and time with the diagnosis of the disease.

Physical Examination

The participants were submitted to a simplified anthropometric evaluation, where their body mass (kg) and height (m) were verified on a digital scale with a stadiometer (Toledo®, São Paulo, SP, Brazil). Based on these data, their BMI was calculated through the formula [BMI = weight (kg)/height^2 (m)].[23]

Disease activity score

The disease activity score in individuals with RA was verified through the Disease Activity Score (DAS-28).[22] It is an evaluation that comprises the bilateral palpation of 28 joints (shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, and knees), with the purpose of verifying the number of painful and swollen joints. In addition, a grade on the patient's perception of the RA global activity in the last seven days

was obtained, by means of a visual analogue scale (0-100 scale). Adding to the parameters mentioned previously, the dosage value of the C-reactive protein (CRP) was used in the final calculation of the DAS-28. For that, the calculator from the official site www.das-score.nl was used. The score from the DAS-28 varies from 0 to 10 and the greater the value, the greater the disease activity level. The classification is made in the following manner: ≤ 3.2 is considered low activity for the disease; 3.2 < DAS-28 ≤ 5.1 is considered moderate activity for the disease; > 5.1 is considered high activity for the disease. For this study, the patients with DAS-28 value higher than 2.6 were considered as having active RA.

C-reactive protein

The determination of the CRP concentration was made after collecting approximately 5mL of venous blood from the patient. The analysis was made using turbidimetric methods with a kit specific for the measuring of CRP - CRP turbilatex (Biotécnica®, Belo Horizonte, MG, Brazil). The reactions were read using a spectrophotometer model BTLyser 100 (Biotécnica®, Belo Horizonte, MG, Brazil) at a wavelength of 540 nm. The values were expressed in mg/L and any values greater than 6mg/L were considered normal.

Respiratory muscle strength

The respiratory muscle strength was obtained by the Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) measuring techniques, according to the standards of the American Thoracic Society and the European Respiratory Society (ATS/ERS).[24] This device was equipped with a rigid mouthpiece containing an orifice 2 mm diameter to minimize the effects of the mouth musculature responsible for the increase of intraoral pressure, which in its turn, may interfere with the results.[25]

The values observed for MIP and MEP are dependent on the pulmonary volume from which the measurement is taken (residual volume (RV)), the total pulmonary capacity (TPC) or the functional residual capacity (FRC).[24,26]

The maximal respiratory pressures from the FRC were measured by Almeida et al.[27] where it was observed that this measurement underestimates the MIP values in relation to the measurements made from the RV and MEP in relation to the TPC and justified by the fact that when the muscle fibers were at their greatest length, they were capable of generating greater contraction force. The study mentioned above corroborates Souza,[26] who reports that the values obtained do not depend only on the respiratory muscles' strength, but also on the pulmonary volume in which those measurements were made.

Thus, based on the data found in the literature, for the present study, we chose the measuring technique from RV and from the TPC, considering that measuring by the FRC would underestimate the MIP and MEP values obtained.

The maximal respiratory pressure measurements were made with the participants seated with their trunks at an angle of 90° in relation to the hip, feet supported on the floor, and nostrils occluded with a nasal clip during all the maneuvers. In order to determine the MIP, each participant was oriented to exhale into the mouthpiece until the Residual Volume (RV) and, then, to make their maximal inhalation effort, sustained for a second or two, against one occluded nostril. For the MEP, the participants were instructed to inspire into the mouthpiece until the Total Pulmonary Capacity (TPC) and, then, to make their maximal expiratory effort, sustained for one or two seconds, against one occluded nostril.[26] At least three acceptable maneuvers were made, with intervals of one minute.

As reproducible results, the highest values of MIP and MEP obtained were considered, as long as they did not exceed the second highest value by 10%.[26,28] The MIP and MEP measured in the present study were compared to the values predicted by age, according to the Neder et al.[28] equations described below:

MIP - Women: y = -0.49 (age) + 110.4
MEP - Women: y = -0.61 (age) + 115.6

Statistical analysis

As for the characterization of the study's subjects, a descriptive statistic was made using mean and standard deviation values for the quantitative variables.

The Shapiro-Wilk test was used to test the normality of the variables. After that, an Analysis of Variance (Anova One-way) was made, followed by the Tukey's Post-hoc test to identify differences between the groups due to the MIP and MEP. Also, the Pearson correlation test between the MIP and MEP variables and the DAS-28, CRP and BMI variables was made.

The statistical analysis was made using the Software Statistical Package for the Social Sciences, version 20.0 (SPSS®, Chicago, IL, USA). The level of significance adopted was 5% ($p < 0.05$).

RESULTS

The mean age of both groups was 57.94 ± 10.36 years. In the RA Group, the mean time with the disease diagnosed was 13.37 ± 7.44 years. As for body mass, the mean was 74.32 ± 12.60 kg, and 1.57 ± 0.06 m for height. As to their BMI, the mean was 30.03 ± 3.82 kg/m^2, classifying the group as Grade 1 Overweight. The CRP variable presented mean values of 6.25 ± 10.49 mg/L, and the DAS-28 presented a mean of 4.99 ± 1.02, characterizing the group as having a moderate level of disease activity. In the Control Group the mean was 66.26 ± 7.49 kg for body mass and 1.60 ± 0.08 m for height. The BMI showed a mean of 25.73 ± 3.19 kg/m^2, classifying the group as Pre-obese. These data are shown in Table 1.

In the evaluation of respiratory muscle strength, the mean of MIP values confirmed in the RA and Control groups was -46.25 ± 17.67 cmH_2O and -81.00 ± 19.69 cmH_2O, respectively. For the MEP, the RA Group mean was 58.75 ± 17.26 cmH_2O and for the Control Group it was 78.00 ± 6.32 cmH_2O. The calculation of the MIP and MEP values predicted for the age, made by the equations proposed by Neder et al.[28] (MIP: y = -0.49 (age) + 110.4 and MEP: y = -0.61 (age) + 115.6) provided the following results: predicted MIP of - 81.06 ± 4.11 cmH_2O and predicted MEP of 78.92 ± 5.33 cmH_2O. The comparison of MIP and MEP values between the RA and the Control groups, as well as with the values predicted for these variables showed statistically significant differences in the MIP and MEP variables between the RA Group and the Control Group ($p \leq 0.01$-Anova One-way, followed by Tukey's test). These data are shown in Table 2.

The correlation between the respiratory variables and DAS-28, CRP, and BMI are shown in Table 3. A significant correlation was found only between the MEP and the BMI ($p = 0.03$) variables. The other correlations between the MIP, CRP, DAS-28, and BMI variables, and between the MEP - DAS, and CRP were not significant.

Table 1. Clinical Characteristics of the RA and Control Groups

Clinical and Physical Data	RA Group (8) Mean ± SD	Control Group (10) Mean ± SD
Age (years)	57.94±10.36	
Time with Diagnosis (years)	13.37 ± 7.44	-
Body Mass (kg)	74.32 ± 12.60	66.26 ± 7.49
Height (m)	1.57 ± 0.06	1.60 ± 0.08
BMI (kg/m^2)	30.03 ± 3.82	25.73 ± 3.19
CRP (mg/L)	6.25 ± 10.49	-
DAS-28	4.99 ± 1.02	-

RA: rheumatoid arthritis; BMI: body mass index; CRP: C-reactive protein; DAS-28: disease activity score

Table 2. Mean values of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) found and predicted in the participants of the study

	MIP (cmH_2O) Mean ± SD	MEP (cmH_2O) Mean ± SD
RA Group	-46.25 ± 17.67*	58.75 ± 17.26*
Control Group	-81.00 ± 19.69	78.00 ± 6.32
Predicted (RA Group)	-81.06 ± 4.11	78.92 ± 5.33

MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; RA: rheumatoid arthritis. * $p < 0.05$, Anova One-Way followed by Tukey's Post-hoc Test, in the comparison between RA and Control Groups and RA Group and predicted values

Table 3. Correlation between respiratory variables and DAS-28 disease activity index, CRP, and BMI of the RA Group

	DAS-28	CRP	BMI
MIP	r = 0.268	r = 0.275	r = -0.310
	$p = 0.26$	$p = 0.25$	$p = 0.10$
MEP	r = 0.446	r = -0.022	r = -0.443
	$p = 0.13$	$p = 0.48$	$p = 0.03$*

MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; BMI: body mass index; CRP: C-reactive protein; DAS-28: disease activity index. * Pearson's Coefficient of correlation with statistically significant difference ($p < 0.05$)

DISCUSSION

The present study observed that the RA Group individuals presented MIP and MEP values significantly lower than those found in the Control Group individuals, as well as those values predicted by the equations proposed by Neder et al.[27] These results are similar to the study by Gorini et al.[11] who reported MIP values significantly lower in 15 individuals with RA in comparison with the Control Group individuals, paired by age and gender. Borges[15] also pointed out a worse respiratory function, lower MIP, and strong tendency to lower MEP in 50 individuals with RA in relation to 50 individuals from the Control group, corresponding in age and gender. Accentuated disability in respiratory muscle strength was also found in 31 individuals with juvenile RA, measured by significantly lower MIP and MEP in comparison with the Control group, paired by age and gender.[20]

In a study by Çimen et al.[12] to investigate the pulmonary function, respiratory muscle strength, and the aerobic capacity of 25 RA patients they found that RA patients had a normal pulmonary function test, however they showed significantly reduced MIP, MEP, and aerobic capacity when compared to the 21 individuals of the control group. Ekdahl & Broman[13] also reported lower values for aerobic capacity, isometric muscle strength, and muscle isokinetic resistance of the lower limbs in 67 RA individuals in comparison with the Control group, paired by age and gender. In the same way, Ekblon et al.[29] demonstrated that, in 31 RA female patients, the cardiorespiratory ability and muscle strength of the lower limbs were approximately 25% and 33-52% lower, respectively, in comparison with healthy individuals of the same age bracket. In a study made by Beals et al.,[30] it was verified that RA patients had less physical ability, grip and isotonic muscle strength, and aerobic capacity in relation to the Control group individuals.

For Borges,[15] the loss in pulmonary function and the reduced MIP and MEP values in RA individuals can be related to the DAS-28 scores. The individuals of the present study were classified as having a moderate level of disease activity. These data are in agreement with the study by Sany et al.[31] where of the 1,109 people examined, the average of RA individuals was also found to have moderate disease activity. However, there was no correlation between the MIP and MEP with the DAS-28 verified in the present study. This result coincides with that of Pappas et al.,[19] who did not observe any worsening of pulmonary function related with the DAS-28 in the evaluation of 159 RA patients. Çimen et al.[12] also confirmed no relation in the MIP and MEP results with the disease activity indices evaluated through the Ritchie articular index, erythrocyte sedimentation rate (ESR), and CRP. In the same way, Fuld et al.,[32] in a longitudinal study, found no correlation between compromised pulmonary function and the ESR, CRP, Rheumatoid Factor (RF), and the Ritchie articular index.

Nevertheless, the present study found a significant correlation between the MEP and the BMI. As for body composition, the average BMI results classified the Control group and the RA Group individuals of the present study, respectively, as Pre-obese and Grade 1 Overweight. Similar results were found by Silva et al.,[33] who evaluated 83 females with RA, establishing a BMI average that defined them as overweight or with some degree of obesity. For Costa et al.[34] this increase in the body mass index can lead to respiratory work overload and, consequently, to inefficient respiratory muscle performance. According to Mancini & Carra,[35] as the BMI increases, changes can occur in the pulmonary dynamics such as capacity and reduction of pulmonary volume in those individuals.

Previous studies state that RA can reduce the level of physical activity, contractions, and muscle atrophies, leading to bad physical conditioning.[36] A decrease in either thoracic or columnar mobility due to the physical inactivity imposed by the disease was suggested to be a major factor in the development of pulmonary function abnormalities.[37] Reduction of aerobic capacity could also be related to the fatigue of respiratory muscles, thus creating less thoracic expansibility with consequent reduction in the values of volume and pulmonary flows.[38]

Muscle weakness can therefore result in deficient pulmonary function, in combination with a growing decline in the functional

capacity of the patient. This condition can promote a cycle of pain, stiffness, and reduction of physical activity leading to generalized muscle weakness, expressed by abnormalities in pulmonary function and aggravation of the patient's disability.[39] Muscle weakness also results in joint stiffness and reduction of daily life activities and quality of life for individuals with RA.[40]

CONCLUSION

The present study achieved its objective, showing that patients with RA presented a significant reduction of MIP and MEP values, reinforcing the systemic character of the disease and clarifying the need for global evaluation and therapeutic strategies that are more specific and appropriate for the treatment of patients with RA.

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