

# A comparative study of heart rate variability and physical fitness in women with moderate and severe fibromyalgia

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The aim of this study was to compare the physical fitness and cardiac autonomic activity among women with moderate and severe fibromyalgia (FM) and healthy women. This study included 35 women with FM (age:  $46.2 \pm 8.9$  years) and 17 healthy women (age:  $44.3 \pm 9.9$  years). Participants with FM were divided into moderate FM ( $n = 15$ ) and severe FM ( $n = 20$ ) according to the total score obtained in FM impact questionnaire. The heart rate variability was monitored using a portable cardiac monitor with participants resting in supine position during 10 min. Thereafter, the participants performed the chair sit and reach test, the chair stand test, and the 6-min walk test to measure the lower-body flexibility, lower-body muscle strength, and cardiorespiratory fitness, respectively. The lower-body muscle strength and cardiorespiratory

fitness were both reduced in moderate and severe FM compared to healthy women ( $P < 0.01$ ), with greater reduction in severe FM when compared to moderate FM ( $P < 0.05$ ). In addition, the parasympathetic indexes of heart rate variability were all similarly decreased in both moderate and severe FM, when compared to healthy women ( $P < 0.05$ ). The cardiac parasympathetic activity is similarly decreased in women with both moderate and severe FM in comparison to healthy women, despite a greater physical deconditioning in severe FM.

**Keywords:** Chronic widespread pain, Cardiac autonomic dysfunction, Physical deconditioning

## INTRODUCTION


Fibromyalgia (FM) is a disorder characterized by diffuse musculoskeletal pain, which can be accompanied by several other symptoms such as fatigue, sleep disturbances, headache, anxiety and depressive episodes (Schmidt-Wilcke and Clauw, 2011). The estimated prevalence of FM reported in different regions worldwide varies between 0.4% to 9.3%, depending on the diagnostic criteria or questionnaire used (Sarzi-Puttini et al., 2020), and it is more prevalent among middle-aged women (between 30 and 50 years old) (Queiroz, 2013).

A wide range of mechanisms triggering the amplification of the sensory input within the central nervous system (i.e., central sensitization) is well accepted as the most important key point underlying the pathophysiology of FM (Bellato et al., 2012; Sarzi-Puttini et al., 2020). However, a body of evidence suggests that a dys-

function in the autonomic nervous system may also play a role in the etiology and pathogenesis of FM (Lerma et al., 2011; Martinez-Lavin, 2007; Schamne et al., 2021). The abnormalities in the autonomic nervous system among this population has been demonstrated using the analysis of the heart rate variability (HRV) with FM patients under resting condition (Meeus et al., 2013). The cardiac autonomic dysfunction (i.e., reduced HRV) in FM is characterized by an increased sympathetic activity (Cohen et al., 2000; Furlan et al., 2005) and reduced parasympathetic activity (Figuroa et al., 2008; Furlan et al., 2005; Kang et al., 2016; Kulshreshtha et al., 2012; Lerma et al., 2011; Rost et al., 2021), when compared to healthy individuals. The sympathetic hyperactivity and parasympathetic hypoactivity are both moderately associated with a reduced perceived physical function in patients with FM (Cohen et al., 2000).

Although the dysautonomia seems to be directly related to FM

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pathogenesis (Lerma et al., 2011; Martinez-Lavin, 2007; Schamne et al., 2021), the sedentary lifestyle of FM patients promotes a physical deconditioning, which aggravates the dysautonomia (Kulshreshtha and Deepak, 2013; Meeus et al., 2013). It is noteworthy that reduced physical activity and increased bouts of sedentary time are negatively associated with resting cardiac parasympathetic tone (Buchheit et al., 2005; Niemela et al., 2019; Tebar et al., 2020). Interestingly, as the FM severity increases the level of physical activity reduces (Segura-Jiménez et al., 2015; Segura-Jiménez et al., 2020), consequently reducing multiple components of physical fitness (Aparicio et al., 2013; Góes et al., 2012; Soriano-Maldonado et al., 2015). For example, lower-body flexibility, muscle strength, and cardiorespiratory fitness are compromised in patients with severe FM, when compared to patients with moderate FM (Ángel et al., 2012; Aparicio et al., 2013). However, it is unknown whether the patients with severe FM and impaired physical fitness have the cardiac autonomic dysfunction aggravated in comparison to patients with moderate FM.

Thus, the aim of this study was to verify the physical fitness levels and the indexes of cardiac autonomic activity among women with moderate and severe FM and healthy women. We hypothesized that patients with severe FM have lower physical fitness with concomitant exacerbated cardiac autonomic dysfunction when compared to both moderate FM and healthy women.

## MATERIALS AND METHODS

### Study design and participants

A statistical power analysis was performed using G\*power 3.1 software (Kiel University, Kiel, Germany) to estimate the necessary sample size. The chair stand test was used to calculate the sample size as it is considered the functional test that best discriminates the physical fitness between women with FM from those without FM, as well as between women with moderate and severe FM (Aparicio et al., 2013). Considering an effect size of 0.50 regarding the impact of the severity level of FM (absence of FM and moderate and severe FM) on the number of repetitions during the chair stand test (Ángel et al., 2012), the total number of participants required to achieve a power of 0.80 and an alpha level of 0.05 was estimated to be 42 (i.e., 14 participants per group). Thus, 35 women with a clinical diagnosis of FM ( $46.2 \pm 8.9$  years old) and 17 healthy women ( $44.3 \pm 9.9$  years old) matched by age and body mass index took part in this study. Participants were recruited through strategies such as internet postings, advertisements, and flyers in public area, including a local hospital during the year of 2019. The inclusion

criteria for the FM patients were as follows: (a) age from 18 to 59 years and (b) diagnosis of FM by the patient's rheumatologist following the American College of Rheumatology criteria (Wolfe et al., 1990; Wolfe et al., 2010). The exclusion criteria adopted for both patients and healthy women groups were as follows: (a) any cardiovascular abnormalities, (b) tobacco usage, (c) presence of any cardiovascular chronic disease, (d) use of chronotropic and antihypertensive drugs, and (e) participation in regular exercise programs in the past 6 months prior to the study. The FM patients were taking immunomodulatory (9%), antiepileptic (9%), muscle relaxant (11%), antihistamine (11%), anti-inflammatory (26%), anxiolytic (34%), antidepressant (43%), and analgesic (57%) drugs during the study period. Participants signed an informed consent statement before beginning the study, which was approved by the Ethics committee in human research of State University of Ponta Grossa (number protocol approved 2.896.943). This study was conducted in accordance with the recommendations from the Declaration of Helsinki.

### Procedures

Initially, women with FM were asked to complete the Revised Fibromyalgia Impact Questionnaire (FIQR) to assess FM severity (Paiva et al., 2013). The FIQR questionnaire contains 21 questions separated into three subscales: (a) 9 questions about functional impact, (b) 2 questions about overall impact, and (c) 10 questions about the symptoms (Bennet et al., 2009). The FM patients were divided into three groups based on three different score ranges, where 0 to <39 was classified as mild, 39 to <59 was classified as moderate, and 59 to 100 was classified as severe impairment (Bennet et al., 2009). As only three patients were classified with "mild" severity, they were excluded from the study. Thus, only the patients classified as moderate ( $n = 15$ ) and severe FM ( $n = 20$ ) and healthy women ( $n = 17$ ) were included in the subsequent analysis.

After the initial procedures, anthropometric and body composition, and cardiovascular parameters measurements were collected. The height was determined using a Cardiomed stadiometer (WCS model; Cardiomed, Curitiba, Paraná, Brazil) with an accuracy of 0.1 cm, and body mass by a digital scale (UM-080 model; Tanita, Tokyo, Japan) with a precision of 0.1 kg. The waist circumference was measured using a nonstretching tape as the perimeter of the abdomen at the midpoint between the lowest rib and the iliac crest (Ross et al., 2020). The fat and lean mass were determined using a tetrapolar bioimpedance (BF906 model; Maltron, Essex, UK), following pretest instructions provided by the manufacturer. The systolic and diastolic blood pressure were measured 3 times (with

a 3-min interval between measurements) by an automated blood pressure cuff (HEM-7113 INT model; Omron Healthcare, Hoofddorp, The Netherlands), and the average of these three measurements considered as the resting blood pressure.

Then, the R-R intervals (RRi) were continuously recorded during 10 min using a cardiofrequencimeter (V800 model; Polar Electro Oy, Kempele, Finland), with participants resting under a supine position in a quiet room with the temperature controlled at 23°C. Thereafter, participants underwent a battery of tests to assess different components of physical fitness. The participants were instructed to not ingest alcohol or caffeinated beverages, and to not perform vigorous physical activity during the 24 hr before the tests.

### Physical fitness assessment

The main components of physical fitness studied were the lower-body flexibility, lower-body muscle strength, and cardiorespiratory fitness. The chair sit and reach test was used to measure the lower-body flexibility. In this test, the participant was seated on the edge of a chair (43-cm height) with one leg extended and the other leg flexed at 45°. With both the arms extended and the hands positioned on top of each other, they were instructed to bend slowly their hip sliding the hands down the extended leg in an attempt to touch (or pass) the toes. The number of centimeters short of reaching the toe (minus score) or reaching beyond it (plus score) was recorded. Two trials on each leg were measured and the average of best values for each leg was considered as the lower-body flexibility (Carbonell-Baeza et al., 2015). The chair stand test was used to measure the lower-body muscle strength. The participants began the test seated on a chair (43-cm height) with the arms crossed at the chest level. They were instructed to rise to a full stand position with back straight and feet flat on the floor and then return to seated position as many times possible within 30 sec. The number of times that the participants repeated completely the sequence described above were counted and assumed as the lower-body muscle strength (Carbonell-Baeza et al., 2015). Finally, all the participants performed the 6-min walk test to assess the cardiorespiratory fitness. In this test, the maximum distance that they walked during 6 min along a rectangular course (28 m) was determined (Carbonell-Baeza et al., 2015).

### Heart rate variability

The last 5 min of the 10-min resting RRi records was considered to analyze HRV using both linear and nonlinear methods. For the linear methods, the time-domain indexes calculated were the standard deviation of consecutive RRi (SDNN) and the root mean

square of the successive differences between adjacent RRi (RMSSD), both indexes indicate parasympathetic modulation (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). In addition, the frequency domain indexes were obtained from fast Fourier transform. The high-frequency (HF, 0.15–0.50 Hz) and low-frequency (LF, 0.04–0.15 Hz) components were calculated and expressed in absolute units with logarithm transformation ( $\text{ms}^2$ ) and normalized units (n.u.). The LF/HF ratio was also calculated. The LF is predominantly sympathetic-mediated while the HF is a vagal-related index, and the LF/HF represents the sympathovagal balance (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). For HRV analysis using nonlinear methods, the Poincaré plot analysis was performed, and the following indexes were obtained: the standard deviation of the instantaneous beat-to-beat RRi variability (SD1), the standard deviation of the continuous long-term RRi variability (SD2), and their ratio (SD1/SD2). The SD1 represents the parasympathetic modulation on sinus node, while the SD2 is influenced by both parasympathetic and sympathetic components. The SD1/SD2 represents the balance between sympathetic and parasympathetic activities, like LF/HF (Hoshi et al., 2013). All the HRV indexes were obtained using Kubios HRV Standard software (ver. 3.3.1; University of Eastern Finland, Kuopio, Finland).

### Statistical analysis

The Gaussian distribution was checked using Shapiro–Wilk test. The disease duration and the total FIQR score were compared between moderate and severe FM using Mann–Whitney test. All the anthropometric variables, resting blood pressure, body composition, the number of repetitions performed on chair stand test and the distance reached in chair sit and reach test were all compared among severe FM, moderate FM, and healthy women using analysis of variance (ANOVA) one-way followed by Fisher LSD *post hoc* test (when necessary) for multiple comparisons. On the other hand, the total distance walked on 6-min walk test (nonnormally distributed) was compared among the three groups using Kruskal–Wallis with Mann–Whitney *post hoc* test used for subsequent pairwise comparisons. The majority of HRV indexes were compared between moderate and severe FM and healthy women using ANOVA one-way with Fisher LSD *post hoc* test, except the LF/HF and the SD1/SD2 (both nonnormally distributed) which were analyzed by Kruskal–Wallis followed by Mann–Whitney *post hoc* test. Moreover, Pearson correlations between the physical fitness variables (i.e., chair sit and

**Table 1.** Anthropometric, clinical, and physical fitness characteristics among women with moderate and severe fibromyalgia and healthy women

Characteristic	Healthy women (n=17)	Moderate FM (n=15)	Severe FM (n=20)	P-value
Age (yr)	44.3±9.9	43.6±9.5	49.7±6.6	0.076
FIQR total score (0–100)	-	51.2±5.6	75.2±10.2 <sup>#</sup>	0.0001
Disease duration (yr)	-	8.50±6.07	8.57±6.68	0.999
Height (cm)	1.57±0.06	1.61±0.06	1.59±0.06	0.249
Weight (kg)	65.7±9.5	71.3±13.7	65.7±9.5	0.168
Body mass index (kg/m <sup>2</sup> )	26.4±3.7	28.1±4.9	26.5±3.7	0.634
Waist circumference (cm)	90.5±10.9	89.4±11.7	87.8±9.2	0.528
Total body fat mass (kg)	24.9±6.2	29.1±7.9	28.7±9.9	0.282
Total body lean mass (kg)	41.3±3.7	43.4±5.7	42.9±4.5	0.408
Body fat percentage (%)	36.4±6.3	38.9±6.1	38.5±7.4	0.418
Systolic blood pressure (mmHg)	117.7±10.7	117.3±8.5	116.5±11.9	0.941
Diastolic blood pressure (mmHg)	72.6±9.4	75.1±10.1	75.1±9.7	0.698
Heart rate (beats/min)	73.0±10.0	75.0±11.0	76.0±10.0	0.750
Chair sit and reach test (cm)	-3.6±12.1	-6.9±9.4	-10.5±9.5	0.138
Chair stand test (reps)	15.2±1.9	11.4±3.5 <sup>*</sup>	9.1±3.1 <sup>*#</sup>	0.0001
6-Min walk test (m), median (IQR)	538 (68)	496 (101) <sup>*</sup>	448 (62) <sup>*#</sup>	0.0001

Values are the mean ± standard deviation unless otherwise indicated.

FM, fibromyalgia; FIQR, Revised Fibromyalgia Impact Questionnaire; IQR, interquartile range.

<sup>\*</sup>Significantly lower compared to healthy women ( $P < 0.05$ ). <sup>#</sup>Significantly different compared to moderate FM ( $P < 0.05$ ).

reach, chair stand test, and 6-min walk test) and the parasympathetic-related indexes of HRV (i.e., RMSSD, natural logarithm of high-frequency power [lnHF], and SD1) were calculated for the entire group of FM patients (n = 35). The statistical analysis was carried out using IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA). The significance was accepted when  $P \leq 0.05$ .

## RESULTS

### Participants' characteristics and physical fitness

The main characteristics of participants are described in Table 1. The one-way ANOVA test did not detect statistical difference among women with moderate and severe FM and healthy women in anthropometric and body composition characteristics, and cardiovascular parameters ( $P > 0.05$ ). Regarding the performance on physical fitness tests, it was not observed significant difference among women with moderate and severe FM and healthy women for the chair sit and reach test ( $P = 0.138$ ). However, the number of repetitions performed on chair stand test was significantly lower in women with severe ( $P = 0.0001$ ) and moderate FM ( $P = 0.001$ ) when compared to healthy women. In addition, women with moderate FM also performed a lower number of repetitions in the chair stand test compared to severe FM ( $P = 0.019$ ). The distance walked in 6-min walk test was significantly shorter in patients with severe ( $P = 0.0001$ ) and moderate FM ( $P = 0.009$ ) when com-

pared to healthy women. Moreover, women with moderate FM walked a significantly lower distance when compared to severe FM ( $P = 0.039$ ).

### Heart rate variability

The HRV results are shown in Table 2. For the HRV indexes in the time domain, it was not observed significant difference among the moderate and severe FM and healthy women for mean RRi and SDNN ( $P > 0.05$ ). However, RMSSD were significantly lower in both moderate FM ( $P = 0.050$ ) and severe FM ( $P = 0.020$ ) when compared to healthy women. In the frequency domain analysis, the lnLF, LF, and HF expressed in normalized units, and the LF/HF were not significant different among the moderate and severe FM and healthy women (all  $P > 0.05$ ). On the other hand, the lnHF was significantly lower in both moderate FM ( $P = 0.037$ ) and severe FM ( $P = 0.011$ ) when compared to healthy women. Similarly, in the Poincaré plot analysis, the SD1 was significantly lower in both moderate FM ( $P = 0.047$ ) and severe FM ( $P = 0.017$ ) when compared to healthy women, while the SD2 and the ratio SD1/SD2 were both not significantly different among the three groups ( $P > 0.05$ ).

The correlations between physical fitness variables and HRV indexes of parasympathetic activity are shown in Table 3. The lower-body flexibility and cardiorespiratory fitness were not significantly correlated with the RMSSD, lnHF and SD1 ( $P > 0.05$ ).

**Table 2.** Indexes of heart rate variability among women with moderate and severe fibromyalgia and healthy women

Variable	Healthy women (n=17)	Moderate FM (n=15)	Severe FM (n=20)	P-value
Time domain				
RRi (ms)	834.5±114.1	818.7±123.5	807.4±114.1	0.784
SDNN (ms)	32.3±12.9	25.6±10.2	23.8±9.3	0.057
RMSSD (ms)	30.1±12.8	21.9±11.1*	21.1±10.3*	0.044
Frequency domain				
lnLF (ms <sup>2</sup> )	6.1±0.8	5.7±0.8	5.4±1.1	0.085
lnHF (ms <sup>2</sup> )	5.8±0.9	5.1±1.1*	4.9±1.1*	0.037
LF (n.u.)	65.3±12.1	60.7±19.1	57.9±13.1	0.406
HF (n.u.)	42.1±13.2	34.7±12.1	39.3±19.1	0.408
LF/HF, median (IQR)	1.6 (1.1)	2.1 (1.4)	1.9 (2.6)	0.587
Poincaré plot				
SD1 (ms)	21.3±9.1	15.6±7.8*	14.8±6.9*	0.038
SD2 (ms)	40.2±16.6	32.5±12.4	29.9±11.9	0.080
SD1/SD2, median (IQR)	1.9 (0.7)	2.2 (0.6)	1.9 (1.1)	0.526

Values are the mean± standard deviation unless otherwise indicated. RRi, R-R intervals; SDNN, standard deviation of consecutive RRi; RMSSD, root mean square of the successive differences between adjacent RRi; LF, low-frequency power; HF, high-frequency power; lnLF, natural logarithm of low-frequency power; lnHF, natural logarithm of high-frequency power; n.u., normalized units; IQR, interquartile range; SD1, standard deviation of the instantaneous beat-to-beat RRi variability; SD2, standard deviation of the continuous long-term RRi variability. \*Significantly lower compared to healthy women ( $P<0.05$ ).

However, the lower-body muscle strength was positively associated with lnHF ( $r=0.36$ ,  $P=0.032$ ).

## DISCUSSION

In the present study, we aimed to compare the physical fitness and the cardiac autonomic activity among women with moderate and severe FM and healthy women. The main findings of this study suggest that FM patients have a reduced lower-body muscle strength and cardiorespiratory fitness, with a greater impairment for both components of physical fitness in severe FM. In addition, HRV indexes indicating cardiac parasympathetic activity were blunted in both moderate and severe FM compared to healthy women, but were not aggravated in severe FM in comparison to moderate FM.

The women with FM showed reduced cardiorespiratory fitness and lower-body muscle strength compared to healthy women in this study, with a greater reduction for both components of physical fitness in severe FM when compared to moderate FM. The greater physical deconditioning in patients with higher FM severity levels is in accordance with previous findings (Aparicio et al., 2013; Ángel et al., 2012). It is well known that FM patients are less

**Table 3.** Correlation between physical fitness variables and heart rate variability indexes of parasympathetic activity in fibromyalgia patients (n=35)

Variable	Chair sit and reach		6-Min walk test		Chair stand test	
	r	P-value	r	P-value	r	P-value
RMSSD	0.07	0.68	0.10	0.54	0.28	0.09
lnHF	0.09	0.58	0.32	0.06	0.36*	0.032
SD1	0.08	0.65	0.12	0.48	0.29	0.08

lnHF, natural logarithm of high-frequency power; RMSSD, root mean square of the successive differences between adjacent RRi; SD1, standard deviation of the instantaneous beat-to-beat RRi variability; RRi, R-R intervals.

\*Significant correlation ( $P=0.032$ ).

physically active than age- and sex-matched healthy controls (McLoughlin et al., 2011; Segura-Jiménez et al., 2015). Notwithstanding, the sedentary lifestyle of FM patients trend to be more pronounced as the level of FM increases (Segura-Jiménez et al., 2015; Segura-Jiménez et al., 2017). For this reason, the reduced cardiorespiratory fitness and lower-body muscle strength in women with severe FM observed in this study might be a consequence of such decrease level of physical activity. The physical deconditioning in FM results in a greater difficult to perform daily routine activities, such as walking and lifting (Góes et al., 2012). The functional capacity in FM is similar to that observed in elderly people, and may contribute to decrease the quality of life among this population (Santos E Campos et al., 2020). Moreover, the level of FM severity has been negatively associated with overall physical fitness (Carbonell-Baeza et al., 2013; Soriano-Maldonado et al., 2015), which reinforces the importance of regular physical exercise practice as a nonpharmacological tool for the management of FM symptoms.

The lower-body flexibility was similar among the moderate FM, severe FM, and healthy women in the present study. This result did not corroborate with previous findings demonstrating a reduction in lower-body flexibility in FM patients, with greater impairment in severe FM (Ángel et al., 2012; Aparicio et al., 2013). It should be mentioned that the cutoff points used to discriminate the FM severity levels according to total score obtained in the FM impact questionnaire were 39 to 58 points for moderate FM and 59 to 100 points for severe FM in this study. On the other hand, the previously mentioned studies used scores  $<70$  for moderate FM and  $\geq 70$  for severe FM (Ángel et al., 2012; Aparicio et al., 2013). In addition, the sit and reach test was performed in a chair, with measures taken separately for right and left lower limbs in the present study (Carbonell-Baeza et al., 2015). In an aforementioned study, a Wells bench was used to assess the lower-body flexibility for both the right and left lower limbs at the same time (Ángel et al., 2012). Thus, the methodological differences regard-

ing the cut off points of FM impact questionnaire to classify the disease severity and the test used to assess the lower-body flexibility may explain these conflicting results.

As the three groups studied (i.e., healthy women, moderate and severe FM) were different in terms of physical fitness, particularly for lower-body muscle strength and cardiorespiratory fitness, we were therefore able to explore the impact of physical fitness on HRV in women with moderate and severe FM. In this study, women with FM had reduced resting parasympathetic tone (lower RMSSD, lnHF, and SD1) when compared to healthy women. This finding is consistent with several other studies that also found lower resting parasympathetic activity in patients with FM (Figueroa et al., 2008; Furlan et al., 2005; Kang et al., 2016; Kulshreshtha et al., 2012; Lerma et al., 2011; Rost et al., 2021). The main new finding of the present study extends these previous documented abnormalities by providing evidence that parasympathetic hypoactivity was observed in both moderate and severe FM groups, with similar cardiac parasympathetic tone between the two FM severity levels studied. In addition, only the number of repetitions performed on the chair stand test was positively associated with the lnHF. Taken together, these findings indicate that the cardiac parasympathetic tone in women with severe FM is not aggravated, despite lower levels of physical fitness in comparison to moderate FM.

The reason for similar cardiac parasympathetic hypoactivity in moderate and severe FM is unknown. Indeed, a physically inactive lifestyle is associated with impaired cardiovascular autonomic modulation in healthy individuals (Hughson and Shoemaker, 2015; Zaffalon-Júnior et al., 2018), particularly for parasympathetic tone (Buchheit et al., 2005; Niemela et al., 2019; Tebar et al., 2020). However, the RMSSD for moderate and severe FM in this study (~21 ms in average) was close to that reported in other studies with middle-aged FM women (~19 to 21 ms in average) (Kang et al., 2016; Kulshreshtha et al., 2012; Rost et al., 2021). Interestingly, being sedentary was not considered as inclusion criteria in the aforementioned studies. As the cardiac autonomic abnormalities might be linked to FM pathogenesis (Lerma et al., 2011; Martinez-Lavin, 2007; Schamne et al., 2021), it is possible that great physical deconditioning as a consequence of critical reduced physical activity level in severe FM may not decrease much more the cardiac vagal tone, which is already decreased due to the FM pathogenesis. Such idea must be confirmed in future studies. Nevertheless, it should be pointed out that resting cardiac autonomic impairments have been associated with a greater risk of cardiovascular events and mortality (Thayer et al., 2010; Tsuji et al., 1996). Some studies have documented improvements in cardiac autonomic

function after a few weeks of physical exercise intervention in patients with FM (Figueroa et al., 2008; Villafaina et al., 2020). Although the physical exercise interventions seem to be promising to improve cardiac autonomic function, the effects of chronic intervention with regular exercise programs in FM patients have been little studied and deserve further investigation.

Some limitations in this study must be mentioned. Firstly, the inclusion of a group with mild FM severity could help to better understand the physical fitness and HRV, as well as the relationship between these two variables in FM patients with all severity levels. Secondly, there were no control for medications intake before the physical fitness tests in this study. It should be taken into account, however, that increased muscle pain as a consequence of avoiding medications intake on pretest may lead to fear of movement (De Gier et al., 2003) and reduced physical performance (Góes et al., 2012). In addition, the cardiorespiratory fitness and lower-body muscle strength persisted lower in FM patients even under the effect of wide range of medications such as analgesics, anti-inflammatories, and muscle relaxants, all of which decrease the clinical manifestations of FM (Sarzi-Puttini et al., 2020; Schmidt-Wilcke and Clauw, 2011). In this sense, the lack of control for medications intake before the tests might have not impacted our results. Finally, the level of physical activity was not objectively measured in this study. It is noteworthy that the participants were all sedentary with no participation in regular physical exercise practice in the last 6 months prior to the beginning of this study. However, a more accurate determination of the level of physical activity would help to discuss the physical deconditioning and its impact on HRV in FM. Despite these potential limitations, the present study improved the current knowledge about physical fitness and cardiac autonomic function in women with different levels of FM severity.

In conclusion, this study demonstrated that the cardiac parasympathetic activity is similarly decreased in women with both moderate and severe FM in comparison to healthy women, despite a greater physical deconditioning in severe FM. Notwithstanding, strategies aiming to improve the physical fitness and cardiac autonomic function, such as the regular physical exercise practice, should be considered of great importance for FM patients regardless the level of disease severity.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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