Substituting sedentary time with physical activity in fibromyalgia: association with quality of life and impact of the disease. The al-Ándalus project

Authors:

Blanca Gavilán-Carrera, BSc[1], Víctor Segura-Jiménez, PhD[2,1], Rania A. Mekary, PhD,[3,4,5], Milkana Borges-Cosic, BSc[1], Pedro Acosta-Manzano, BSc[1], Fernando Estévez-López, PhD[1,6,7], Inmaculada C. Álvarez-Gallardo, PhD[2,1], Rinie Geenen, PhD[7], Manuel Delgado-Fernández, PhD[1]

Affiliations:

[1] Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain.

[2] Department of Physical Education, Faculty of Education Sciences, University of Cádiz, Cádiz, Spain.

[3]Harvard T.H. Chan School of Public Health, Boston, MA, USA

[4]Department of Pharmaceutical Business and Administrative Sciences, MCPHS University, Boston, MA

[5]Computational Neuroscience Outcomes Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

[6]Institute of Nursing and Health Research, School of Health Sciences, Ulster University, Northern Ireland, United Kingdom

[7]Department of Psychology, Faculty of Social and Behavioural Sciences, Utrecht University, Utrecht, The Netherlands.

Corresponding author

Blanca Gavilán-Carrera, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain. Carretera de Alfacar, s/n (Granada), Spain. Telephone number: +34 958 244 375

Email: bgavilan@ugr.es

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Significance and Innovations

- Substituting 30 minutes of sedentary behaviour with physical activity of any intensity was positively associated with different dimensions of quality of life and impact of the disease in women with fibromyalgia
- Substituting sedentary time with light physical activity had a positive association with *better* dimensions of quality of life and impact of fibromyalgia, while moderate-to-vigorous physical activity was related to *stronger* theoretical changes in the outcomes.

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ABSTRACT

Objective: There is an awareness of the detrimental health effects of sedentary time (ST) in fibromyalgia. However, data are limited on how replacing ST with physical activity (PA) of different intensity may be related to health in this condition. This study aimed to examine the association with quality of life and disease impact upon substituting ST with light physical activity (LPA) or moderate-to-vigorous physical activity (MVPA).

Methods: This study comprised 407 women with fibromyalgia aged 51.4 ± 7.6 years. The time spent in ST and PA was measured with triaxial accelerometry. Quality of life and impact of the disease were assessed using the 36-item *Short-Form Health Survey* (SF-36) and the *Revised Fibromyalgia Impact Questionnaire* (FIQR), respectively. The associations between substituting ST with an equivalent time of LPA or MVPA and the outcomes were examined using isotemporal substitution analyses.

Results: Substituting 30 min of ST with LPA in the isotemporal model was associated with better bodily pain (B=0.55), vitality (B=0.74), and social functioning (B=1.45) of SF-36, and better scores at all of the domains (function, overall impact, symptoms, and total impact) of FIQR (B ranging from -0.95 to -0.27; all p<0.05). When ST was replaced with MVPA, better physical role (B=2.30) and social functioning (B=4.11) of the SF-36 and function of FIQR (B=-0.73) were observed (all p<0.05).

Conclusions: In regression models, allocating time of sedentary behavior to either LPA or MVPA was associated with better quality of life and lower disease impact in women with fibromyalgia.

Key words: accelerometry; GT3X+; isotemporal substitution; mental health; physical health; severity;

INTRODUCTION

Fibromyalgia is a chronic condition with persistent and widespread pain as key symptom (1). Other symptoms are frequent, including but not limited to fatigue, non-restorative sleep or cognitive difficulties (1). The disease impact of fibromyalgia includes physical disability, psychological distress, symptoms, and reduced work status (2). Moreover, patients with fibromyalgia usually have a reduced general quality of life (3), which is the individual perception of health in different spheres of life (physical, mental and social). Because fibromyalgia has no cure, treatments focus on disease management and improvement of quality of life. Thus, it is relevant to identify modifiable factors that might be related to these fibromyalgia-specific (impact of the disease) and general (quality of life) health outcomes.

Compelling evidence supports the efficacy of physical exercise interventions in the management of fibromyalgia (4). However, although the worth of physical exercise interventions in fibromyalgia is endorsed (4), guideline articles generally do not answer the question whether low, moderate or high intensity physical exercise should be recommended. Moreover, patient acceptability, treatment adherence, premature termination, and especially the high dropout rates are serious concerns for exercise-based interventions in fibromyalgia (5). Perhaps moderate or even low-intensity physical exercise programs are more appropriate to achieve long-term results than high-intensity programs in this group that is so easily sensitized towards pain and other symptoms (6). Greater insight into the relationship between physical activity (PA) levels and patient-reported outcome measures may indicate the potential usefulness of stimulating low and moderate-to-vigorous intensity activity levels.

Whereas most effect studies pertain to systematic physical exercise interventions in groups, the most frequent intervention in rheumatic diseases is probably education and advice about daily PA given during a consultation or through a brochure or the internet (7). A positive relationship between total self-reported PA and quality of life in fibromyalgia has been described (8,9). Lifestyle interventions (10,11) and observational studies (12–14) have described the positive influence of light intensity PA (LPA) in the physical function domain of quality of life (10,11) and fibromyalgia symptoms (10,12–14). Furthermore, increasing moderate-to-vigorous PA (MVPA) promoted better physical function and well-being (15), and greater levels of vigorous PA have been associated with less pain, fatigue, and overall impact of the disease (14). Despite these benefits, a high percentage of patients do not achieve the recommended 150 min of MVPA per week (16,17), and tend to be highly sedentary (16). While the relationship between PA and symptoms or physical domains of quality of life has been largely addressed on prior research (10–15), evidence regarding the potential influence of reducing sedentary time (ST), which might be a more attainable goal for some patients, is scarce. To get insight into the benefits of pursuing this goal, it should be examined how decreasing ST through an increase of time in different intensity levels of PA is specifically related to quality of life and impact of the disease in fibromyalgia.

ST has shown to exert a deleterious effect on health in the general population (18). In fibromyalgia ST has been associated with worse pain regulation (12), pain, fatigue and impact of the disease (14). Although the inverse relationship between ST and quality of life has been described in other conditions (19,20), the precise association between them in fibromyalgia is unknown. It would be relevant to know the benefits of substituting ST with PA. Given that total daily time is finite (24 hours), decreasing time in one specific behavior requires increasing time in another. The isotemporal substitution modelling (21)

allows to study the effect of time substitution while controlling for the confounding effect of other activities. Therefore, given that ST, LPA, and MVPA have shown to be associated with fibromyalgia symptoms (12–15), it is possible to determine how replacing time spent in one specific behavior (e.g. ST) with an equal amount of time in another behavior (e.g. LPA) might be related to different health outcomes in this population. Prior applications of isotemporal substitution models have demonstrated positive effects on quality of life and health outcomes of replacing ST with an equal amount of PA of different intensities in adults (22–25) and elderly (19,26,27). These findings, however, do not necessarily generalize to patients with fibromyalgia.

Therefore, the aim of this study was to analyze how substituting ST with LPA or MVPA was associated with quality of life and impact of the disease in women with fibromyalgia.

METHODS

Patients from southern Spain (Andalusia) were recruited through fibromyalgia associations via email, letter and social media. After providing detailed information about the aims and study procedures, participants signed an informed consent (n=646). Inclusion criteria for the current study comprised a previous diagnosis by a rheumatologist and meeting the official 1990 American College of Rheumatology (ACR) fibromyalgia criteria (28). Participants were excluded if they had either acute or terminal illness, severe cognitive impairment or were >65 years old (to avoid the influence of prevalent other conditions such as osteoarthritis). The study was approved by the Ethics Committee of the "*Hospital Virgen de las* Nieves", Granada (Spain).

The assessment protocol was carried out on 2 alternate days. On day one, fibromyalgia diagnosis according to ACR criteria (28) (widespread pain for more than 3 months, and pain with 4 kg/cm^2 of pressure reported for 11 or more of 18 tender points) was confirmed.

Body composition was also evaluated and participants filled out self-reported sociodemographic and clinical data questionnaires. The 36-item *Short-Form Health Survey* (SF-36) and the *Revised Fibromyalgia Impact Questionnaire* (FIQR) (along with other questionnaires) were given to patients to be completed at home. On the second day, questionnaires were collected and checked by the researcher team. Subsequently, participants received instructions on how to complete the sleep diary and the accelerometers were provided.

Quality of life: the quality of life was assessed using the SF-36. This questionnaire has been validated for Spanish populations (29) and has demonstrated a good reliability among chronic pain patients (30). The SF-36 is composed of 36 items that assess eight dimensions of health (i.e., physical functioning, physical role, bodily pain, general health, social functioning, emotional role, mental health, and vitality) and two component summary scores (i.e., physical and mental health). The score in each dimension is standardized and it ranges from 0 (worst health status) to 100 (best health status).

Impact of the disease: The FIQR (31) represents a disease-specific tool to assess overall fibromyalgia severity through a wide range of symptoms, comorbidities, and complaints related to this chronic condition. It is a self-administered questionnaire with 21 individual questions (rating scale of 0 to 10), divided into three linked sets of domains: function, overall impact, and symptoms severity. The FIQR total score ranges from 0 to 100, with a higher score indicating greater impact of the syndrome on one person's life.

Physical activity intensity levels and sedentary time: Patients wore a triaxial accelerometer GT3X+ (Actigraph, Pensacola, Florida, USA) around the hip, secured with an elastic belt for nine whole days (24 h) except for water-based activities. Using the default mode filter option, data were collected at a rate of 30 Hz and at an epoch length

of 60 seconds (32). Given that patients received the accelerometer at different times throughout the first day and because time is needed to extinguish reactivity to the awareness of being monitored, we excluded this familiarization day from the analysis. The last day (device return) was excluded from the analysis as well. A total of 7 continuous days with a minimum of 10 valid hours/day were required to be included in the analysis. Data download, reduction, cleaning, and analyses were conducted using the manufacturer software (Actilife^{TM} v.6.11.7 desktop).

Accelerometer wearing time was calculated by subtracting sleeping time and non-wear periods. Sleeping time was obtained from the sleep diary, where patients indicated the time they went to bed and time they woke up. According to Choi algorithm (33), non-wear periods considered bouts of 90 continuous minutes (30 minutes small window length and 2 minutes skip tolerance) of 0 counts. PA intensity levels (light, moderate, and vigorous) were calculated based upon recommended PA vector magnitude cut points (32,34): 200-2689, 2690-6166 and ≥6167 cpm, respectively. ST was estimated as the time accumulated below 200 counts per minute (cpm) during periods of wear time (33). Participants presented extremely low values of vigorous PA (0.4 min/day); therefore, vigorous PA was excluded from all the analysis and MVPA was used instead. A 10-minute activity bout was defined as 10 or more consecutive min ≥2690 cpm (up to 2 min below the cut point allowance). The proportion of women meeting the current PA recommendations for adults aged 18-64 years (at least 150 minutes/week of MVPA accumulated in bouts ≥10 minutes) (17) was also calculated. All values were initially expressed in min/day but were converted to units of 30 minutes (1 represents 30 minutes) for a better interpretation of the results. To do this, min/day spent in ST, LPA, MVPA and total wear-time were divided by 30.

Other variables

Tenderness: Following the 1990 ACR criteria for classification of fibromyalgia (21), we assessed eighteen tender points using a standard pressure algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). We obtained the mean pressure of two measurements at each tender point. A tender point was considered as positive when the patient felt pain at pressure ≤ 4 kg/cm^2. The total number of positive tender points was recorded for each patient.

Sociodemographic and clinical data: We collected socio-demographic and clinical data by using a self-reported questionnaire including date of birth, marital status (married/ not married), education level (university/non-university), and occupational status (working/not working). Furthermore, patients reported the consumption of antidepressants (yes/no) during the previous two weeks. Additionally, to assess an exclusion criterion, participants were asked: 'Are you currently diagnosed with an acute or terminal illness?'.

Anthropometry and body composition: Weight (kg) and total body fat percentage were assessed using a portable eight-polar tactile-electrode bioelectrical impedance device (InBody R20, Biospace, Seoul, Korea). The validity and reliability of this instrument has been reported elsewhere (35,36). As recommended by the manufacturer, participants were requested not to have a shower, not to practice intense PA, and not to ingest large amounts of fluid and/or food within the 2 hours before the measurement. Patients were also asked not to wear either clothing (except for underwear) or metal objects during the measurement.

Statistical analyses

Descriptive statistics were used to examine the sociodemographic and clinical characteristics of the sample.

Multiple linear regression models were used for isotemporal substitution models in order to examine the associations of substituting ST with LPA and MVPA with quality of life and impact of the disease in women with fibromyalgia. The description and rationale behind these analyses have been described in detail before (21). Briefly, in this model, the finite nature of time is considered so that performing one activity results in displacing the time spent in another behaviour. These regression models include as independent variables the total time (sum of ST, LPA and MVPA, which is the total accelerometer wear time variable) and all of the individual activities (e.g., LPA and MVPA) except for the activity of interest (e.g., ST). The coefficient from the regression analysis for each of the included variables is an estimation of the mean effect on the outcome of substituting a fixed amount of time (e.g.: 30 min) of the omitted activity with the same amount of each of the included activities (while holding time spent in other activities constant). For instance, an isotemporal substitution model can be expressed as follows:

SF-36 scores = (β_1) LPA + (β_2) MVPA + (β_3) total time + (β_4) covariates

Because ST is omitted from the model, β_1 expresses the change in Quality of Life (SF-36 scores of each dimension) which resulted from reallocating 30 minutes of ST to LPA. The β_2 coefficient would provide the same information in relation to MVPA. Pearson's correlations were used to check for the association of potential confounders (age, marital status, education level, working status, fat percentage, antidepressant consumption) with quality of life and impact of the disease. As a result of significant associations (p<0.05)

with most of the outcomes, the following confounders were entered in all models: age, current occupational status, fat percentage, and use of antidepressants.

Normal probability plots of the standardized residual and scatterplots of residuals were generated to test for normality, linearity, and homoscedasticity. Non-autocorrelation assumption was also met (Durbin-Watson-test; $1.5<d<2.5$ for all regression models). No multicollinearity problems among the predictor variables of the model were found (all variance inflation factor statistics <10.0).

All analyses were performed using the Statistical Package for Social Sciences, version 20.0 (SPSS Statistics for Windows, IBM, Armonk, NY, USA), and the level of significance was set at $p<0.05$.

RESULTS

The flowchart of the participants included in this study is presented in **Figure 1**. The final sample size included in the analyses comprised 407 women with fibromyalgia. **Table 1** provides an overview of the patients' sociodemographic and clinical characteristics according to the achievement of the PA recommendations (at least 150/week per week of MVPA in bouts of at least 10 minutes).

In the isotemporal substitution models for the SF-36 scores (**table 2**), replacing 30 minutes of sedentary behaviour with 30 minutes of LPA was associated with better bodily pain (*B*=0.55; 95% Confidence Interval (CI) 0.03 to 1.07), vitality (*B*=0.74; 95% CI, 0.09 to 1.39), and social functioning (*B*=1,45; 95% CI, 0.61 to 2.30), all $p<0.05$. Replacing 30 minutes of sedentary behaviour with 30 minutes of MVPA was associated with better physical role (*B*=2.30; 95% CI, 0.2 to 4.38) and social functioning (*B*=4.11; 95% CI, 1.78 to 6.44), all $p<0.05$.

When the FIQR was modelled as the outcome variable (**table 3**), replacing 30 minutes of ST with the same amount of LPA was associated with better functioning (*B*=-0.32; 95% CI, -0.55 to -0.09), overall impact (*B*=-0.27; 95% CI, -0.45 to -0.08), symptoms (*B*=-0.37; 95% CI, -0.63 to -0.11), and total impact of the disease (*B*=-0.95; 95% CI, -1.52 to -0.38), all $p<0.01$. Substituting 30 minutes of ST with 30 minutes of MVPA was only associated with better functioning (*B*=-0.73; 95% CI, -1.37 to -0.09), $p=0.025$.

DISCUSSION

Our results showed that the substitution of 30 minutes of ST with LPA resulted in better scores in bodily pain, vitality, social functioning domains of SF-36 and all domains of FIQR (function, symptoms, overall impact, and total impact). When this amount of time was conferred to MVPA instead, patients presented better physical role and social functioning in SF-36 and FIQR function. Our results complement previous research (8,9) by estimating how varying the distribution of ST, LPA and MVPA throughout the waking hours is related to patients' quality of life and impact of the disease.

Overall, the results of the isotemporal substitution models allocating ST to LPA displayed smaller estimated effects but in more dimensions (*B* rating from 0.55 to 1.4 in seven dimensions) of quality of life and impact of the disease in comparison to those allocating ST to MVPA (*B* rating from 0.73 to 4.1 in three dimensions). Although MVPA is recommended for health benefits (17), the intensity of PA that best correlates with quality of life in fibromyalgia is still unknown and presents mixed results in other populations. Replacing ST with MVPA showed greater benefits for quality of life in adults (22), whereas increasing LPA might be more effective in elderly (19,26), except for physical domains that were associated with higher intensities. The results in our participants are more similar to those in the elderly population, probably due to similarities when showing

a reduced fitness level (37). Indeed, LPA is of special relevance among individuals with reduced physical capacity (17) or inactive individuals (38), given that low intensity levels of PA are shown to be stimuli that elicit improvements in health (17,38). In fibromyalgia, small increases in LPA were associated with improved key symptoms (10). As women with fibromyalgia are highly sedentary (16), it is plausible that one of the adequate intensities of PA to achieve benefits falls below the recommendations of moderate-to-vigorous intensity for the general population (17). Increasing daily MVPA might, however, be also of interest for patients with fibromyalgia due to its association with a lower physical impact of the disease as shown in the current and a previous research (15). Therefore, a graded sustainable and thus feasible strategy to achieve health benefits in this condition might be to first replace inactivity with LPA behaviors and to eventually increase PA to moderate-intensity levels.

Increasing time in MVPA was positively related to the physical role in SF-36 and the FIQR function. In fact, this affinity is consistent with the closeness between these domains of both questionnaires (2). Congruent with our findings, a previous study showed improvements in the function domain of the FIQR after an intervention aimed at increasing MVPA among patients with fibromyalgia (15). Physical role of SF-36 includes limitations in the kind and amount of work due to physical problems. Physical barriers to continue working such as physical capacity and symptoms (39) have been associated with MVPA (15,17), which is in agreement with the results of the current study. Patients who increase their level of PA might also be more confident and present greater self-efficacy to engage in movement-related tasks of daily living that require physical effort (40) and perceive less limitations in functional status (8). Hence, promoting behaviors of moderate-to-vigorous intensity as an ultimate goal seems a safe (15) strategy of special interest for benefits in physical domains of quality of life in women with fibromyalgia.

In the present study, when ST was substituted with LPA, a better reported symptomatology (bodily pain, vitality, and lower impact of the symptoms) was observed. Our results are consistent with previous interventions where increasing steps per day resulted in better reported pain interference (11) and intensity (10). Moreover, low levels of PA have been previously linked to better brain responses in pain modulation regions of patients with fibromyalgia (13). The chronic widespread pain in fibromyalgia may be due to or modulated by an altered processing of nociceptive signals in central nervous system, known as central sensitization (41). The pain relief promotion mechanisms of PA are thought to act on central pain facilitation (reduced NMDA receptor phosphorylation (41,42)) and endogenous inhibitory systems (reduced serotonin transporter expression, increased serotonin levels, and increased opioids in pathways including different brain areas (12,13), the periaqueductal grey and rostral ventromedial medulla (42,43)). Although the dose of PA to elicit pain modulatory mechanisms is not clear, to maintain even a low level of physical activity and/or avoid periods of sustained ST has been related to modulation of central nervous system in fibromyalgia (12).

Fatigue, that is strongly linked to pain and its mechanisms (44), has also a great impact on quality of life (44). In agreement with our results in the vitality domain, the level of fatigue has been related to LPA in fibromyalgia (14) and other pain conditions such as arthritis (45). However, a lifestyle intervention increasing self-selected light PA, unlike the suggestion of our findings, did not produce changes in the fatigue severity of patients with fibromyalgia (12). The heterogeneity in tools to assess the multiple facets of fatigue (44) and the use of different accelerometers and thresholds to categorize PA, may represent impediments for direct comparisons to prior studies. Previous research in healthy women has also stressed the importance of meeting the recommended level of MVPA and reducing prolonged sedentary behavior for a better energy and fatigue profile

(46). We also observed a borderline association between increasing MVPA and vitality, but our analyses only showed a significant estimated association derived from reallocating ST to LPA. Accordingly, it has been observed that greater improvements in fatigue of moderate-intensity exercise in healthy population may not extend to sedentary people with persistent fatigue (47), who can benefit from low intensity activities (47). The central nervous system appears to be also involved in the relationship between PA and fatigue (48). More specifically, PA might perhaps have a positive influence on fatigue in fibromyalgia trhough changes in IGF-1 and resistin levels (48), yet further research is needed on this topic.

The estimated benefits of LPA in all domains of the FIQR are also in line with previous PA interventions where a change from sedentary to low active habits reduced the total impact of the disease of patients with fibromyalgia (10). The magnitude of the effect, however, notably differed from our estimations: 10.2 (10) vs 0.95 points reduction in the total score, respectively. Several methodological issues might underlie these differences: 1) The FIQ (previous version of the FIQR) presents different weighting among domains with more importance given to symptoms instead of function as opposed to FIQR (2), 2) the lifestyle intervention not only aimed to increase PA but also coping and adherence strategies, 3) differences in study design. In light of these findings, strategies for health promotion among these patients might also target the replacement of sedentary behaviors with activities of light intensity, which are also the most likely activities that patients would be expected to engage in (13).

The greatest estimated benefits were detected in the social functioning domain as a result of substituting ST either with LPA or MVPA. Congruent with our results, Suorsa et al. (49) observed a lower social contact in the most sedentary fibromyalgia patients. This group of patients usually present social isolation concerns (50) and a high prevalence of

loneliness (51) that might be negatively influenced by the decreased communication that sedentary behaviors entail (52). Conversely, it is likely that the practice of PA provides opportunities for social interactions, especially during accessible activities that are shared experiences such as walking, which may support our findings. Nonetheless, further intervention designs are needed to ascertain the nature of this relationship.

Strengths of our study included a relatively large sample size of women with fibromyalgia representative from southern Spain (Andalusia) and the use of accelerometers to objectively assess PA instead of self-reported measures (53). In addition, we used general (SF-36) and disease-specific (FIQR) instruments, providing a more comprehensive view of the actual reported health status of these patients (54). Furthermore, the robustness of our analyses was also enhanced by considering a reasonable number of potential confounders.

Limitations included the cross-sectional study design; thus, the associations found in a between-subjects analysis cannot be explained via a causal pathway as a within-subject mechanism. Indeed, previous research has shown how quality of life can discriminate different levels of PA (8). Therefore, some of the relationships found work in both directions. Additionally, due to the large quantity of factors related to quality of life and the impact of the disease, it is difficult to ascertain the true association between the variables. Given that only women took part in this study, future studies should investigate whether these associations also occur in men.

In conclusion, this study provided preliminary evidence that replacing 30 minutes of ST with PA of either light or moderate-to-vigorous intensity was positively associated with different domains of quality of life and impact of the disease in fibromyalgia. When ST was substituted with LPA, a better bodily pain, social function, vitality, and impact of the disease in all its domains were observed. When ST was substituted with MVPA, we

detected better scores in physical role, social functioning, and function. This may be a simple message to communicate in clinical practice. However, longitudinal and intervention studies on actual behavioral reallocation effects are needed to further confirm our results.

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