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Víctor Segura Jiménez

UTILIDAD DE CRITERIOS DIAGNÓSTICOS, CONDICIÓN FÍSICA, CUESTIONARIOS DE ACTIVIDAD FÍSICA Y EJERCICIO FÍSICO EN FIBROMIALGIA

USEFULNESS OF DIAGNOSTIC CRITERIA, PHYSICAL FITNESS, PHYSICAL ACTIVITY QUESTIONNAIRES AND PHYSICAL EXERCISE IN FIBROMYALGIA

DEPARTAMENTO DE EDUCACIÓN FÍSICA Y DEPORTIVA
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VÍCTOR SEGURA JIMÉNEZ

2014

A mi familia…

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VÍCTOR SEGURA JIMÉNEZ

Directores de Tesis [Thesis Supervisors]

Ana Carbonell Baeza
PhD
Profesora Contratada Doctor
Universidad de Cádiz

Manuel Delgado Fernández
PhD
Catedrático de Universidad
Universidad de Granada

Miembros del Tribunal [Committee]

Vanesa España Romero
PhD
Profesora Sustituta Interina
Universidad de Cádiz
España

José C Adsuar Sala
PhD
Profesor Ayudante Doctor
Universidad de Extremadura
España

Pablo Tomás Carús
PhD
Profesor Auxiliar
Universidad de Évora
Portugal

Miguel Martín Matillas
PhD
Profesor Contratado Doctor
Universidad de Granada
España

Mª Belén Feriche Fernández-Castanys
PhD
Profesora Titular
Universidad de Granada
España

Granada, 12 de Diciembre de 2014

Prof. Dr. Ana Carbonell Baeza

Profesora Contratada Doctor

Dpto. Didáctica de la Educación Física, Plástica y Musical

Facultad de Ciencias de la Educación

Universidad de Cádiz

ANA CARBONELL BAEZA, PROFESORA CONTRATADA DOCTOR DE LA UNIVERSIDAD DE CÁDIZ

CERTIFICA:

Que la Tesis Doctoral titulada "Utilidad de criterios diagnósticos, condición física, cuestionarios de actividad física y ejercicio físico en fibromialgia" que presenta D. **VÍCTOR SEGURA JIMÉNEZ** al superior juicio del Tribunal que designe la Universidad de Granada, ha sido realizada bajo mi dirección durante los años 2011-2014, siendo expresión de la capacidad técnica e interpretativa de su autor en condiciones tan aventajadas que le hacen merecedor del Título de Doctor, siempre y cuando así lo considere el citado Tribunal.

Fdo. Ana Carbonell Baeza

En Granada, 24 de septiembre de 2014

Prof. Dr. Manuel Delgado Fernández

Catedrático de Universidad

Dpto. Educación Física y Deportiva

Facultad de Ciencias del Deporte

Universidad de Granada

MANUEL DELGADO FERNÁNDEZ, CATEDRÁTICO DE LA UNIVERSIDAD DE GRANADA

CERTIFICA:

Que la Tesis Doctoral titulada "Utilidad de criterios diagnósticos, condición física, cuestionarios de actividad física y ejercicio físico en fibromialgia" que presenta D. **VÍCTOR SEGURA JIMÉNEZ** al superior juicio del Tribunal que designe la Universidad de Granada, ha sido realizada bajo mi dirección durante los años 2011-2014, siendo expresión de la capacidad técnica e interpretativa de su autor en condiciones tan aventajadas que le hacen merecedor del Título de Doctor, siempre y cuando así lo considere el citado Tribunal.

Fdo. Manuel Delgado Fernández

En Granada, 24 de septiembre de 2014

El doctorando D. VÍCTOR SEGURA JIMÉNEZ y los directores de la tesis D. MANUEL DELGADO FERNÁNDEZ y Dña. ANA CARBONELL BAEZA:

Garantizamos, al firmar esta tesis doctoral, que el trabajo ha sido realizado por el doctorando bajo la dirección de los directores de la tesis y hasta donde nuestro conocimiento alcanza, en la realización del trabajo, se han respetado los derechos de otros autores a ser citados, cuando se han utilizado sus resultados o publicaciones.

Director/es de la Tesis

Fdo. Ana Carbonell Baeza

Doctorando

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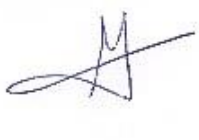

Fdo. Manuel Delgado Fernández

En Granada, 24 de septiembre de 2014

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PROYECTOS DE INVESTIGACIÓN [RESEARCH PROJECTS]

El trabajo desarrollado y los artículos que componen la presente memoria de Tesis Doctoral están basados en los siguientes proyectos de investigación:

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- Efectos de programas de actividad física en la calidad de vida de personas con fibromialgia (EPAFI). Fundación MAPFRE.
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- Perfil del paciente con fibromialgia: características biomédicas, genéticas y psicosociales. Cátedra Real Madrid, Universidad Europea de Madrid. Escuela de Estudios Universitarios Real Madrid.
  Fecha: 30/07/2010 al 29/07/2011.

- Actividad físico-deportiva en poblaciones especiales: actividad física y calidad de vida relacionada con la salud en personas con fibromialgia y Valoración del estado de salud y calidad de vida del grupo de investigación CTS545. Apoyo a la Investigación en Biosalud. Proyecto Campus de Excelencia Internacional 2009, Subprograma de I+D+I y Transferencia (Programa GREIB).
  Fecha: 01/01/2011-21/12/2011.

- Niveles de actividad física, condición física, salud y calidad de vida en población andaluza con fibromialgia: efectos del ejercicio físico y determinantes genéticos.

CTCD-201000019242-TRA. Consejería de Turismo, Comercio y Deporte, Junta de Andalucía.
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- Physical activity in women with fibromyalgia: effects on pain, health and quality of life (Actividad física en mujeres con fibromialgia: efectos sobre el grado de dolor, salud y calidad de vida). DEP2010-15639. Plan Nacional I+D+i 2008-2011, Ministerio de Ciencia e Innovación.
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  Fecha: junio 2009 – mayo 2010

- Beca Colaboración del Ministerio de Educación. Departamento de Educación Física y Deportiva. Facultad de Ciencias del Deporte. Universidad de Granada.
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I. **Segura-Jiménez V**, Álvarez-Gallardo IC, Carbonell-Baeza A, Aparicio VA, Ortega FB, Casimiro AJ, Delgado-Fernández M. Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: the al-Ándalus project. *Semin Arthritis Rheum*. 2014 *in press*. **IF: 3.629**.

II. **Segura-Jiménez V**, Aparicio VA, Alvarez-Gallardo IC, Soriano-Maldonado A, Estévez-López F, Delgado-Fernández M, Carbonell-Baeza A. Validation of the modified 2010 American College of Rheumatology diagnostic criteria for fibromyalgia in a Spanish population. *Rheumatology (Oxford)*. 2014;53(10):1803–11. **IF: 4.435**.

III. Aparicio VA, **Segura-Jiménez V**, Alvarez-Gallardo IC, Soriano-Maldonado A, Castro-Piñero J, Delgado-Fernández M, Carbonell-Baeza A. Fitness Testing in the Fibromyalgia Diagnosis: the al-Ándalus Project. *Med Sci Sports Exerc*. 2014 *in press*. **IF: 4.459**.

IV. **Segura-Jiménez V**, Alvarez-Gallardo IC, Romero-Zurita A, Camiletti-Moirón D, Munguía-Izquierdo D, Carbonell-Baeza A, Ruiz JR. Comparison of physical activity using questionnaires (LTPAI and PAHWI) and accelerometry in fibromyalgia patients: the al-Ándalus project. *Arch Phys Med Rehabil*. 2014;95(10):1903–11. **IF: 2.441**.

V. **Segura-Jiménez V**, Munguía-Izquierdo D, Camiletti-Moirón D, Alvarez-Gallardo IC, Ortega FB, Ruiz JR, Delgado-Fernádez M. Comparison of the International Physical Activity Questionnaire (IPAQ) with a multi-sensor armband accelerometer in women with fibromyalgia: the al-Ándalus project. *Clin Exp Rheumatol*. 2013;31(6 Suppl 79):S94–101. **IF: 2.855**.

VI. **Segura-Jiménez V**, Carbonell-Baeza A, Aparicio VA, Samos B, Femia P, Ruiz JR, Delgado-Fernández M. A warm water pool-based exercise program decreases immediate pain in female fibromyalgia patients: uncontrolled clinical trial*. Int J Sports Med*. 2013;34(7):600–5. **IF: 2.433**.

VII. **Segura-Jiménez V**, Romero-Zurita A, Carbonell-Baeza A, Aparicio VA, Ruiz JR, Delgado-Fernández M. Effectiveness of tai-chi for decreasing acute pain in fibromyalgia patients. *Int J Sports Med*. 2014;35(5):418–23. **IF: 2.268.**

RESUMEN

La fibromialgia es un trastorno dimensional complejo de etiología desconocida que se caracteriza por la presencia de dolor músculo-esquelético y otros síntomas importantes, tales como fatiga, rigidez, trastornos del sueño, problemas cognitivos, depresión, ansiedad, y otras muchas manifestaciones. Esta extensa sintomatología limita la mayor parte de las actividades diarias del paciente, lo que supone un enorme impacto en su calidad de vida.

El objetivo general de esta Tesis Doctoral ha sido analizar el potencial de los nuevos criterios de diagnóstico de la fibromialgia y de los test de condición física como herramienta de ayuda al diagnóstico y seguimiento de la fibromialgia. Así mismo se ha analizado la utilidad de cuestionarios de actividad física para medir los niveles de actividad física de los pacientes con fibromialgia y el efecto de diversos programas de ejercicio físico sobre el dolor agudo en esta población.

Los principales hallazgos de esta Tesis Doctoral sugieren que: *a)* La fibromialgia debe ser entendida como un trastorno dimensional complejo, y no sólo como una condición de dolor crónico generalizado. Además, la fibromialgia parece tener un mayor impacto en la dimensión física que en la dimensión psicológica, aunque ambas se ven afectadas en gran medida. *b)* Los criterios modificados de 2010 del American College of Rheumatology (ACR) son una herramienta válida para el diagnóstico de la fibromialgia en España. Se recomienda la combinación de los criterios de 1990 y los criterios modificados de 2010 del ACR, ya que este enfoque presenta las mejores características de diagnóstico. *c)* Los tests curl de bíceps, 30 segundos de sentarse y levantarse, y fuerza de prensión manual discriminan a las mujeres con fibromialgia de aquellas que no la tienen. *d)* Los instrumentos auto-administrados de registro de la actividad física utilizados en la presente Tesis Doctoral muestran una utilidad discutible para medir la actividad física en pacientes con fibromialgia, ya que difieren consistentemente con los registros de acelerometría. *e)* Un programa de ejercicio en piscina de agua caliente de 3 meses de duración y un programa de Tai-Chi de 6 meses de duración reducen el dolor agudo en mujeres con fibromialgia. Las mejoras son más elevadas en las mujeres de

mayor edad y en aquellas con dolor más intenso. Parece que es necesario un período superior a 3 meses de duración para observar cambios en el dolor a largo plazo.

SUMMARY

Fibromyalgia is a complex dimensional disorder of unknown etiology characterized by the presence of musculoskeletal pain and other important symptoms such as fatigue, stiffness, sleep disorders, cognitive problems, depression, anxiety, and other complaints. This vast symptomatology limits most of daily fibromyalgia patients' activities, which entails an enormous impact on their quality of life.

The overall objective of this thesis has been to analyse the potential of new diagnostic criteria for fibromyalgia and the capacity of fitness testing as a tool for the diagnosis and monitoring of the fibromyalgia. Additionally, to test the potential of physical activity questionnaires to assess physical activity levels of fibromyalgia patients and the effect of various exercise programs on acute pain in this population.

The main findings from this Thesis suggest that: *a)* fibromyalgia must be understood as a complex dimensional disorder beyond chronic widespread pain condition. Furthermore, fibromyalgia seems to have a greater impact on physical than on psychological outcomes, though both are largely affected. *b)* The modified 2010 American College of Rheumatology (ACR) criteria are a valid tool for the diagnosis of fibromyalgia in Spain. The combination of the 1990 ACR and the modified 2010 ACR criteria is recommended, since this approach showed the best diagnostic characteristics. *c)* The arm curl, 30-s chair stand, and handgrip strength tests powerfully discriminate women with fibromyalgia from those without fibromyalgia. *d)* The self-administered physical activity instruments used in this Thesis show questionable usefulness to assess physical activity in fibromyalgia patients, since they differ from accelerometry data. *e)* A 3-month warm water pool-based exercise program and a 6-month Tai-Chi program reduce acute pain in fibromyalgia women. Improvements are higher in older women and in those with more intense pain. It seems that longer than 3-month period is necessary for observing cumulative changes in pain.

LISTA DE ABREVIATURAS [LIST OF ABBREVIATIONS]

ACR	American College of Rheumatology
ANOVA	Analysis of the variance
ANCOVA	Analysis of the covariance
BDI-II	Beck Depression Inventory-II
BIA	Bioelectrical Impedance Analysis
CI	Confidence Intervals
FM	Fibromyalgia
FIQR	Revised Fibromyalgia Impact Questionnaire
ICC	Intraclass Correlation Coefficient
IPAQ	International Physical Activity Questionnaire
LTPAI	Leisure Time Physical Activity Questionnaire
MFI-S	Spanish version of the Multidimensional Fatigue Inventory
MMSE	Mini Mental State Examination
MET	Metabolic Equivalent
NLR	Negative Likelihood Ratio
NPV	Negative Predictive Value
PA	Physical activity
PAHWI	Physical Activity at Home and Work Instrument
PASAT	Paced Auditory Serial Addition Task
PLR	Positive Likelihood Ratio
PPV	Positive Predictive Value
PSD	Polysymptomatic Distress Scale
PVAS	Pain Visual Analogue Scale;
RAVLT	Rey Auditory Verbal Learning Test
ROC	Receiving Operator Characteristics
RPE	Rate of Perceived Exertion
SD	Standard Deviation
SE	Standard Error
SEM	Standard Error of Measurement

SF-36	Short-Form health survey 36
SIQR	Symptom Impact Questionnaire
SS	Symptom Severity score
STAI	State Trait Anxiety Inventory-I
SWA	Sense Wear Pro Armband
TP	Tender Points
TPC	Tender Points Count
VAS	Visual Analogue Scale
WPI	Widespread Pain Index

INTRODUCCIÓN [NTRODUCTION]

1. Characteristics of the disorder

1.1. Definition, etiology and prevalence

Fibromyalgia is a chronic disease characterized by widespread musculoskeletal pain, as well as the presence of multiple locations of tender points[1]. Chronic widespread pain can be defined as pain for at least three months in both sides of the body, both above and below the waist[1,2]. Fibromyalgia has been considered as a disorder of pain regulation of unknown etiology[3], characterized by increased sensitivity to painful stimuli (hyperalgesia) and lowered pain threshold (allodynia)[4]. However, beyond a chronic widespread pain condition, fibromyalgia has recently been defined as a complex dimensional disorder with pain as its main symptom[5], but there are other equally presumable important non-pain symptoms, such as fatigue, stiffness, cognitive problems, depression, anxiety, and other complaints[5,6]. The ample symptomatology limits most of daily fibromyalgia patients' activities, such as walking or carrying objects, which entails an enormous impact on patients' quality of life[7]. Fibromyalgia has become a worryingly health condition in our modern society and its treatment implies time consuming and high economic burdens[8]. A deep study of the fibromyalgia's key symptoms may provide a more fitted and appropriate guidance for treatment decisions and strategies. Furthermore, it is unknown if fibromyalgia affects more severely those components related to physical (e.g. functionality), or psychological (e.g. depression) domains [*PAPER I*].

The causes of fibromyalgia are still unknown[9]. Patients do not only present increased pain sensitivity with mechanical stimuli, but also heat, cold and electrical stimuli[10,11]. Central pain processing mechanism is emerging as a novel explanation to the increased pain sensitivity of these patients, since central nervous system sensory processing shows

abnormalities in this population[4,12,13]. Psychological and social factors might also be involved in triggering the development and continuity of fibromyalgia[14]. Some patients relate the onset of the disease with emotional trauma, chronic stress or physical stressors[15]. Additional contributing factors as infections agents and vaccination have been suggested as possible triggers of fibromyalgia[16]. Although the pathophysiology of fibromyalgia still remains unclear, recent studies indicate that genetics and environmental factors play a key role in the etiology of the disease[17]. A genome-wide linkage study reported that siblings of patients with fibromyalgia have a 13-fold increased risk of developing the condition compared with the general population. In this study, a single region on chromosome 17 was linked to fibromyalgia[18].

General prevalence of fibromyalgia vary from 0.5 to 5% depending on the country[19]. The point prevalence of fibromyalgia in Spain is ~2.4%[20]. It is remarkable that fibromyalgia is more common in women (~4.2%) than in men (~0.2%) and in the rural (~4.1%) than in urban setting (~1.7%)[20]. This represents a Spanish women/men fibromyalgia proportion of approximately 22:1[20], although it has been suggested that the inclusion of the new preliminary fibromyalgia criteria[21,22] might lead to a greater proportion of men diagnosed. Due to the low number of diagnosed fibromyalgia men, research has mainly focused in women, ignoring somewhat the study of fibromyalgia men. This might be the reason why the differential characteristics of fibromyalgia based on gender seem to be divergent. While some studies have suggested that fibromyalgia women are more likely to experience increased severity in certain symptoms than fibromyalgia men[23–25], other studies have shown the opposite[26–30]. In parallel, some studies have revealed that clinical and psychological features of fibromyalgia women and men are similar[31–33].

1.2. Burden

The fibromyalgia patients incur in significant direct and indirect medical care costs[34,35]. Direct costs correspond to health care costs, whereas indirect costs correspond to sick leave and early retirement. In Spain, fibromyalgia patients result in an expense of 614€

and 4,397€ over the average annual cost of the direct and indirect medical care costs, respectively in comparison with a reference group[35]. This implies a total annual extra cost of 5,010€ per patient. Furthermore, both, direct and indirect costs have been significantly correlated to disease severity, the degree of functional disability, the presence of depressive symptoms, the existence of comorbidities, and a younger patient age[36]. Therefore, a delay in the diagnosis of the disease appears to be another factor contributing to the high health care costs of fibromyalgia[36,37]. An up-to-date study has shown that treated patients with fibromyalgia in daily practice improve their clinical symptoms and reduce the cost of the illness. The extra cost of drugs is substantially compensated by less use of other healthcare resources and fewer days off work[37].

1.3. Diagnosis

In 1990 the American College of Rheumatology (ACR) reported the first criteria to differentiate fibromyalgia from other chronic widespread pain syndromes[1]. The 1990 ACR criteria[1] required widespread pain for at least 3 months and the presence of 11 of 18 tender points with ≤ 4kg/cm^2. This ACR classification criteria created a crude definition of fibromyalgia as widespread pain by imposing the presence of 11 tender points[21].

As time passed, objections to the 1990 ACR criteria developed, being the bases that the presence of different tender points cannot be an objective assessment of whole body pain[38]. Furthermore, digital palpation instead of algometry is the most widely used method among examiners[39]. Without an objective instrument, the application of an equal pressure of 4 kg is therefore doubtful[38,39]. Finally, fibromyalgia is defined as a complex multidimensional pain disorder[5,21] with the inclusion of other non-pain symptoms, such as fatigue, stiffness, depression and cognitive problems among other complaints[5,6]. The thoughtlessness of these symptoms is therefore another important weakness of the 1990 ACR criteria[21,38].

In 2010, the ACR proposed a new diagnostic criteria, which simplified clinical diagnosis avoiding the requirement of tender points examination[21]. Because most of the 2010 ACR criteria items were obtained by self-administration, the criteria were modified in 2011 to allow complete self-administration[22]. This modified 2010 ACR criteria eliminated the physicians' subject assessments thus making it a self-administered questionnaire suitable for epidemiological studies[22].

The preliminary diagnostic criteria are composed by two scales: a) The Widespread Pain Index (WPI) is a measure of the number of painful body regions. The patients are asked to indicate in which of 19 body areas they had pain during the week before. The minimum total score of WPI is 0 and the maximum total score is 19. b) The Symptom Severity (SS) score is a measure of symptomatology: patients are asked to indicate the severity of fatigue, trouble thinking or remembering and waking up tired (unrefreshed) over the previous week; and to answer whether (or not) they have had pain or cramps in the lower abdomen, depression or headache during the previous 6 months. The minimum total score of SS is 0 and the maximum total score is 12. This preliminary diagnostic criteria establish 3 conditions: i) WPI ≥ 7, and SS ≥ 5, or WPI between 3-6 and SS ≥ 9. ii) Symptoms have been present at a similar level for at least 3 months. iii) The patients do not have a disorder that would otherwise explain the pain.

With the new 2010 and modified 2010 ACR criteria, fibromyalgia has shifted the fibromyalgia concept from a *peripheral pain-defined condition* to a *systemic symptom-based condition*[38,40]. The criteria can be satisfied by a high level of symptoms if the WPI score is not high enough[22].

The main problem in fibromyalgia criteria is the absence of a gold standard or case definition[21]. This fact represents a problem when assessing the validity of diagnostic criteria. In the absence of this gold standard, an expert consensus was first adopted by Wolfe et al.[1] in the 1990 ACR criteria validation study. Subsequently this approach has been used in both the 2010 original version and modified 2010 ACR validation study[21,22]. Until date, the 2010 ACR criteria and the modified 2010 ACR criteria have been validated

in different languages[21,22,41–44]. It is necessary to test the validity of the modified 2010 ACR criteria in Spanish-speaking population [*PAPER II*].

2. Physical fitness and fibromyalgia

Patients with chronic pain usually reduce their physical activity (PA) levels, resulting in deconditioned fitness status[45,46]. Overall, physical fitness is decreased in people with fibromyalgia compared to age-matched healthy peers[46–48], and is similar to healthy older adults[46,49,50]. This highlights the risk of this disease to premature dysfunctionality. Fibromyalgia patients show reduced aerobic capacity[51] and flexibility levels[52]. Flexibility is substantially important to perform daily tasks, and low levels of overall flexibility lead to a reduction in movement ability and functionality[53]. Moreover, fibromyalgia is associated with balance problems and increased risk of falls[54]. Gait parameters are severely impaired compared with healthy peers[55]. Hence, fibromyalgia patients have an impaired functional capacity[49,51,56] with a high risk of disability and difficulties on doing tasks associated with staying physically independent[49].

Different components of physical fitness are associated with pain and general symptomatology in fibromyalgia. Lower limb strength and cardiorespiratory fitness have shown an inverse association with tender points count[46] and a positive association with pain threshold[46,57]. Upper and lower body flexibility is also associated with pain threshold[46]. Furthermore, the higher the muscle strength the higher the pain threshold[58] and the lower the pain[46,58] and symptomatology reported[57,58].

It has been suggested that fitness testing (specially the handgrip strength and the 6-min walk tests) might be a complementary tool used in the clinical examination when planning treatment for fibromyalgia patients[47]. Since the relationship between physical fitness and fibromyalgia severity and symptomatology has been previously reported[46,59], the usefulness of fitness testing for the assessment and monitoring of fibromyalgia has been recommended[60,61]. The handgrip strength and the 30-second chair stand tests have shown to be useful complementary tools for the diagnosis and monitoring of the

disease[60,61]. In spite of this, no fitness cut-off points for different age groups have been claimed [*PAPER III*].

3. Physical activity and fibromyalgia

Physical inactivity is one of the major public health problems of the 21st century[62] and several longitudinal studies have shown the negative consequences on health through an inactive lifestyle[63–65].

Several symptoms and functional limitations in daily life has been strongly associated with chronic pain, including deficient energy and muscular discomfort, physical mobility limitations, lifting groceries, climbing stairs, and stooping[45]. Moreover, women, but not men, with chronic pain trend to refrain from PA[45]. Fear of pain in the fibromyalgia population limits voluntary PA[66], and make fibromyalgia patients mostly spend their time in sedentary behaviours[66,67].

Self-reported PA in fibromyalgia women is positively associated with the central nervous system processing of pain[68]. In fact, fibromyalgia women who are physically active seem manage their ability to modulate pain better than those who are less active[68]. It has also been suggested that peripheral mechanisms, such as abnormalities in microcirculatory capillaries[69], irregularities in mitochondria[70] and alteration of muscle oxygen utilization[71] might reduce peripheral tissue oxygenation and have an important role in central sensitization. In this context, an increase of tissue oxygenation following exercise could reduce peripheral and central sensitization and, consequently, reduce clinical pain[72].

Fibromyalgia patients can benefit from PA to maintain or improve their health[73]. International organisations support the use of PA-based interventions as a complementary tool in the therapeutic armamentarium against fibromyalgia[74,75]. Fibromyalgia patients with active lifestyle patterns show greater physical function and lower levels of pain than those who trend to be physically inactive[76,77]. This knowledge suggests the existence of a cyclic relation between PA and fibromyalgia symptoms[78].

Despite the proven benefits of PA on their symptomatology, fibromyalgia women are usually less physically active than healthy controls[78]. Fibromyalgia patients decrease their PA levels due to fear of pain[66,79], and this, contrary to what they think, triggers a worsening of symptoms, which in turns is followed by higher levels of inactivity.

Given that PA has shown to report large benefits in the management of fibromyalgia, it is important to have appropriate tools for its measurement. Self-report questionnaires are still the most commonly used methods to assess PA at population level, because they are inexpensive and easy to administer. However, PA is generally difficult to recall, quantify and categorize in healthy adults. This implies that PA information derived from self-reports is potentially subject to response bias[80]. In fact, over-reporting is common in all populations in the use of PA questionnaires[80–82]. The cognitive problems (attention, working memory, long-term verbal memory and spatial memory)[83,84] associated to fibromyalgia and even the nature of fibromyalgia symptoms itself (widespread pain, physical function impairments, reduced PA, tiredness, fatigue, depression, etc.)[6] might distort or alter the fibromyalgia patients' perception about their PA levels. Furthermore, fibromyalgia patients usually have a rate of perceived effort higher than healthy people[85], thus they might tend to misclassify their activities. Taken together, this may negatively affect the accuracy of self-reported PA. It is important, then, to test the usefulness of potential PA questionnaires in fibromyalgia populations [*PAPER IV and PAPER V*].

4. Management of fibromyalgia

Treatment of fibromyalgia is a complex and controversial process, but a wide range of effective pharmacological[86], cognitive behavioural[87] and exercise-based interventions[88] are available. The most common non-pharmacologic treatments are exercise-based interventions[88,89] and psychological-educative programs[87,89].

Physical exercise has proven to be effective in the management of fibromyalgia[73–75]. Moreover, fibromyalgia patients who are more physically active exhibit lower levels of

pain perception[78]. In fact, previous studies have shown improvements on several fibromyalgia-related symptoms after exercise interventions[9]. Exercise therapies are relatively economical, easily accessible and widely used in clinical practice as a strategy for pain management[74,75]. Aerobic exercise[73,90], aquatic exercise[91–94] and multidisciplinary programs[88,95,96] have exhibited benefits the general symptomatology of fibromyalgia patients.

4.1. Land- and water-based exercise in fibromyalgia

Exercise-based therapies for fibromyalgia patients have been traditionally focused on land- or water-based intervention programs [95,97–101].

Hydrotherapy (with or without exercise) has been recommended for the management of fibromyalgia because of the water's buoyancy and warm temperature[91,98,100]. The density of water limits the impact of exercise on the joints compared to the load produced on land-based exercise[91,98]. Furthermore, warm water can lead to vasodilation which in turns may improve muscle ischemia and have an analgesic action[91]. Balneotherapy sessions appear to reduce pain and increase mobility dynamics in women with fibromyalgia[102,103]. In addition, the combination of exercise therapy with the warm water reduces pain in this population[104] with greater benefits than exercise by itself[105] and with longer effects on pain management[97]. Some studies showed that pool exercise improves health status and chronic widespread pain in fibromyalgia patients[92,106]. Indeed, previous studies observed improvements on pain assessed by means of different measures after a pool-based intervention program[91,104,105,107,108]. Therefore, the physical properties of warm water and the benefits of the adapted exercise[74,75] could collectively promote an analgesic effect and thus reduce pain substantially in fibromyalgia women.

Most previous studies measured pain intensity just before and after the treatment[104–106], and did not include measurements of pain rating before and after each session. Given that fibromyalgia patients usually avoid PA when they feel pain, the study of the

effect of single exercise sessions on acute pain is of clinical relevance in fibromyalgia patients [*PAPER VI*].

4.2. Complementary and alternative therapies in fibromyalgia

Together with the physical exercise, the mind-body exercise (which incorporates human biological and psychological aspects into treatment, with the intent of using the mind to affect physical functioning and promote health[90]) and relaxation therapies can increase pain tolerance in fibromyalgia patients[95,109,110]. Recently, there has been an increase in complementary and alternative modalities for managing fibromyalgia (some examples include: Tai-Chi, Biodanza, Yoga, breathing exercises)[9,73]. These new approaches have exhibited great benefits for the fibromyalgia population[109–112].

One of the most spread complementary and alternative modalities is an ancient form of exercise called Tai-Chi. This discipline is performed at low speed and can be classified as a low-impact exercise[113] with aerobic nature[114]. Slow movements, non-maintained muscle contractions and low-moderate intensity exercise characterize the Tai-Chi exercise. Breathing, relaxation and mental concentration are essential while exercising in Tai-Chi discipline[90]. Therefore, Tai-Chi exercises combine aspects of mind-body therapy and physical exercise[90].

Tai-Chi has shown benefits on diverse physical (balance, gait, muscle strength, flexibility, cardiovascular) and psychological (attentiveness, sleep and anxiety) variables in different study populations and varied chronic pain conditions[115]. In fibromyalgia, Tai-Chi interventions have shown improvements on functional capacity, symptomatology, psychological outcomes and pain in fibromyalgia women[111]. Benefits of Tai-chi in several outcomes such as pain, different components of physical fitness, anxiety, depression and the overall impact have been observed in fibromyalgia men[116,117].

Several studies have reported improvements in pain by means of different questionnaires[90,111,118] and algometry[111]. While a positive reduction of pain after a Tai-Chi program in fibromyalgia patients has been described[90,111,118], further research is

needed to support evidence-based practice[90]. The multicomponent combination, physical exercise and mind-body practice of Tai-Chi might have an immediate short-term usefulness and therefore be considered as an option for treating acute pain in fibromyalgia [*PAPER VII*].

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OBJETIVOS

General

El objetivo general de esta Tesis Doctoral ha sido analizar la validez de los nuevos criterios de diagnóstico de la fibromialgia y de los test de condición física como herramienta de ayuda al diagnóstico y seguimiento de la fibromialgia. Así mismo se ha analizado el potencial de cuestionarios de actividad física para medir los niveles de actividad física de los pacientes con fibromialgia y el efecto de diversos programas de ejercicio físico sobre el dolor agudo en esta población.

Específicos:

- ✓ Distinguir los síntomas específicos de la fibromialgia con respecto a otros síntomas que podrían también estar presentes en mujeres sin fibromialgia. Comprobar si la fibromialgia afecta más a las características físicas que a las psicológicas (Artículo I).

- ✓ Validar los criterios preliminares modificados de la ACR de 2010 para el diagnóstico de la fibromialgia en una población Española (Artículo II).

- ✓ Determinar la habilidad de una batería de test de condición física para discriminar la presencia/ausencia de fibromialgia en mujeres (Artículo III).

- ✓ Comparar los niveles de actividad física medidos con diferentes cuestionarios auto-administrados y la actividad física medida con acelerometría en pacientes con fibromialgia; y analizar la fiabilidad test-retest de estos cuestionarios (Artículos IV y V).

- ✓ Explorar los cambios producidos por diferentes programas de intervención con ejercicio físico sobre el dolor agudo (antes vs. después de cada sesión) y el dolor acumulado (después de la intervención completa) en pacientes con fibromialgia (Artículos VI y VII).

AIMS

Overall:

The overall objective of this thesis has been to analyze the potential of new diagnostic criteria for fibromyalgia and the capacity of fitness testing as a tool for the diagnosis and monitoring of the fibromyalgia. Additionally, to test the potential of physical activity questionnaires to assess physical activity levels of fibromyalgia patients and the effect of various exercise programs on acute pain in this population.

Specifics:

- ✓ To distinguish specific factors of the fibromyalgia syndrome from other symptoms which might also exist in non-fibromyalgia women. To test whether fibromyalgia affects more severely physical or psychological outcomes (Paper I).

- ✓ To validate the modified 2010 ACR preliminary criteria for fibromyalgia in a Spanish population (Paper II).

- ✓ To determine the ability of a set of physical fitness tests to discriminate presence/absence of fibromyalgia in women (Paper III).

- ✓ To compare the levels of self-reported PA assessed by means of different questionnaires and PA measured with accelerometry in fibromyalgia patients; and to analyze the test-retest reliability of these questionnaires (Papers IV and V).

- ✓ To explore the changes elicited by different exercise interventions in acute pain (before vs. after session) and cumulative pain (before vs. after intervention) in fibromyalgia patients (Papers VI and VII).

MATERIAL Y MÉTODOS [MATERIAL AND METHODS]

The material and methods section of the current Doctoral Thesis are summarized in the table below, which includes the most relevant methodological information from the scientific papers which compose the PhD dissertation.

Table 1. Summary table of the methodology used in the current thesis.

	Paper	Study design	Participants	Main variables studied	Methods
I.	Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: the al-Ándalus project.	Case-control study.	459 FM women. 214 control women.	Tenderness, FM impact, fatigue, health-related quality of life, cognitive performance, mental health.	Algometry, FIQR, SIQR MFI-S, SF-36, MMSE, BDI-II, STAI, PASAT, RAVLT.
II.	Validation of the modified 2010 American College of Rheumatology diagnostic criteria for fibromyalgia in a Spanish population.	Case-control study.	579 (550 women) FM patients. 294 (240 women) control participants.	Tenderness, pain, symptomatology, FM impact, health-related quality of life, fatigue, depression, cognitive function.	Algometry, WPI, SS, PSD, FIQR, SF-36, MFI-S, BDI-II, MMSE.
III.	Fitness Testing in the Fibromyalgia Diagnosis: the al-Ándalus Project.	Case-control study.	487 FM women. 250 control women.	Physical fitness, tender points, BMI, pain, symptomatology, FM impact.	30-s chair stand, arm curl, hand grip (dynamometry), chair sit and reach, back scratch, 8-feet-up-and-go and 6-min walk tests, algometry, anthropometry, BIA, WPI, SS and FIQR.
IV.	Comparison of physical activity using questionnaires (LTPAI and PAHWI) and accelerometry in	Cross-sectional study.	99 (94 women) FM patients.	PA, BMI.	LTPAI, PAHWI, accelerometry (GT1M), anthropometry, BIA.

	Paper	Study design	Participants	Main variables studied	Methods
	fibromyalgia patients: the al-Ándalus project.				
V.	Comparison of the International Physical Activity Questionnaire (IPAQ) with a multi-sensor armband accelerometer in women with fibromyalgia: the al-Ándalus project.	Cross-sectional study.	183 FM women.	PA, BMI.	IPAQ, accelerometry (SenseWear Pro Armband), anthropometry, BIA.
VI.	A warm water pool-based exercise program decreases immediate pain in female fibromyalgia patients: uncontrolled clinical trial.	Uncontrolled trial.	33 FM women.	Acute pain, BMI.	PVAS, Anthropometry, BIA.
VII.	Effectiveness of tai-chi for decreasing acute pain in fibromyalgia patients.	Uncontrolled trial.	36 (29 women) FM patients.	Acute pain, BMI.	PVAS, Anthropometry, BIA.

BDI-II: Beck Depression Inventory-II, BIA: Bioelectrical Impedance Analysis, FM: fibromyalgia, FIQR: Revised Fibromyalgia Impact Questionnaire, IPAQ: International Physical Activity Questionnaire, LTPAI: Leisure Time Physical Activity Questionnaire, MFI-S: Spanish version of the Multidimensional Fatigue Inventory, MMSE: Mini Mental State Examination, PA: physical activity, PAHWI: Physical Activity at Home and Work Instrument, PASAT: Paced Auditory Serial Addition Task, PSD: Polysymptomatic Distress Scale, PVAS: Pain Visual Analogue Scale, RAVLT: Rey Auditory Verbal Learning Test, SF-36: Short-Form health survey 36, SIQR: Symptom Impact Questionnaire, SS: Symptom Severity score, STAI: State Trait Anxiety Inventory-I, WPI: Widespread Pain Index.

RESULTADOS Y DISCUSIÓN [RESULTS AND DISCUSSION]

The results and discussion are presented in the form that have previously been published/accepted in the scientific journals.

1. FIBROMYALGIA FEATURES

(Paper I)

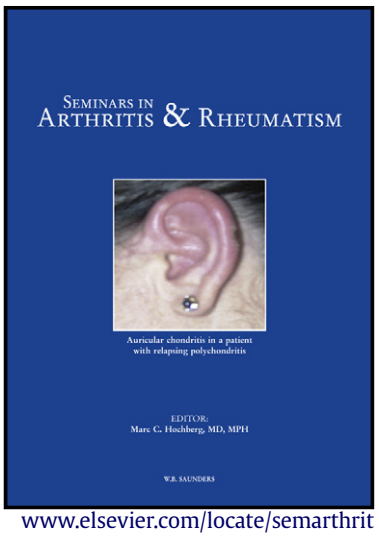
I

Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: the al-Ándalus project.

Segura-Jiménez V, Álvarez-Gallardo IC, Carbonell-Baeza A, Aparicio VA, Ortega FB, Casimiro AJ, Delgado-Fernández M.

Seminars in Arthritis and Rheumatism

In press



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Fibromyalgia Has a Larger Impact on Physical Health Than on Psychological Health, Yet Both are Markedly Affected: The Al-Ándalus Project

Víctor Segura-Jiménez BSc, Inmaculada C. Álvarez-Gallardo BSc, Ana Carbonell-Baeza PhD, Virginia A. Aparicio PhD, Francisco B. Ortega PhD, Antonio J. Casimiro PhD, Manuel Delgado-Fernández PhD.

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Title: Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: the al-Ándalus project.

Short title: Physical and psychological health in fibromyalgia.

Authors: Víctor Segura-Jiménez[1], BSc; Inmaculada C Álvarez-Gallardo[1], BSc; Ana Carbonell-Baeza[2], PhD; Virginia A Aparicio[3], PhD; Francisco B Ortega[1], PhD; Antonio J Casimiro[4], PhD; Manuel Delgado-Fernández[1], PhD.

Affiliation:

[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]Department of Physiology, Faculty of Pharmacy, University of Granada, Granada, Spain.

[4]Department of Didactics for Language and Literature, Social Science and Physical and Sports Education, University of Almería, Almería, Spain.

Corresponding Address: Víctor Segura Jiménez, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada. Carretera de Alfacar, s/n,

18011, Granada, Spain. Telephone number: +34 958244375. Fax number: +34 958244369.

e-mail: *vsegura@ugr.es*

Abstract

Objectives: To characterize a representative sample of fibromyalgia women based on a set of relevant factors known to be related to this disease. To distinguish specific factors of the disease from other symptoms that might also exist in non-fibromyalgia women. To test whether fibromyalgia affects more severely physical or psychological outcomes.

Methods: A total of 459 fibromyalgia women vs. 214 non-fibromyalgia (control) women from southern Spain (Andalusia) took part in this cross-sectional study. Several instruments were used to assess tenderness, impact of fibromyalgia, fatigue, health-related quality of life, mental health and cognitive performance.

Results: Overall, fibromyalgia women showed a worse status in pain, fatigue, health-related quality of life, depression and anxiety than controls ($P<0.01$). In general, the observed associations presented very large effect sizes (Cohen's *d* from ~1 to ~5.5). No differences between fibromyalgia and controls were observed in cognitive and memory performance, except for delayed recall, but the observed effect size was low (~0.25). The effect size observed for the global physical component (~3.3) was larger than that for the global psychological component (~1.3), all $P<0.001$.

Conclusions: Our results reinforce the understanding of fibromyalgia as a polysymptomatic distress condition with pain as its main symptom. Our findings support that fibromyalgia seems to have a greater impact on physical than on psychological outcomes, though both are largely affected.

Keywords: women; tenderness; impact of fibromyalgia; health-related quality of life; mental health; cognitive performance

INTRODUCTION

Fibromyalgia is a chronic musculoskeletal pain condition of unknown aetiology. General prevalence of fibromyalgia vary from 0.5 to 5% depending on the different countries [1–3]. Similarly to the differences observed in the fibromyalgia prevalence among countries [1–3], the specific characteristics and symptoms reported by patients with fibromyalgia might differ depending on the region. In fact, previous studies have shown geographical variations in reported symptoms among patients with chronic widespread musculoskeletal pain [4, 5]. Fibromyalgia patients are a heterogeneous group and the rating, number and impact of different symptoms is expected to vary between different populations.

Fibromyalgia has become a worryingly health condition in our modern society and its treatment implies time consuming and high economic burdens [1]. Beyond a chronic widespread pain condition, fibromyalgia has recently been defined as a complex dimensional disorder with pain as its main symptom [2], but the inclusion of equally presumable important non-pain symptoms, such as fatigue, stiffness, cognitive

problems, depression, anxiety, and a long list of other complaints [2, 6, 7]. This new approach highlights the need to know which of this large variety of symptoms are more characteristic of this disease, which might help in its accurate management.

According to Queiroz et al. [3], epidemiological studies are important to better understand the extent of the problem in specific settings. No previous large population-based studies examining a vast variety of symptoms have been carried out previously in Spanish fibromyalgia patients and an age-matched control group. Furthermore, it is unknown if fibromyalgia affects more severely those components related to physical (e.g. functionality), or psychological domains (e.g. depression). A deep study of the fibromyalgia's key symptoms may provide a more fitted and appropriate guidance for treatment decisions and strategies. Therefore, the present study aimed: 1) To characterize a representative sample of fibromyalgia patients from southern Spain (Andalusia) in a set of relevant factors known to be related to this disease. This will provide useful reference values for clinicians and researchers so that they can better interpret their evaluations according to our population-based sample. 2) Many symptoms have been suggested to be related to fibromyalgia, but it is unknown which of them are more specific of the disease. In the present study we will include a region and age-matched non-fibromyalgia sample in other to distinguish specific factors of the disease from other symptoms that might also exist in non-fibromyalgia women. For this purpose we will use standardized statistic (effect size) to be able to compare different factors and dimensions. 3) A 'global physical component' and a 'global psychological component' will be created to clarify which of them is more affected in fibromyalgia patients compared with controls.

METHODS

Participants

In order to obtain a fibromyalgia sample representative of the Andalusian population, the sample size needed was calculated (n=300). Then, a sex and province proportional recruitment was planned (see **Supplementary Table 1**). Fibromyalgia patients were recruited from different fibromyalgia associations via e-mail, letter or telephone. We also asked those fibromyalgia patients interested in participate, to recruit a pairwise non-fibromyalgia individual (control) with similar age and socio-demographic characteristics in order to carry out appropriate comparisons between groups. We additionally contacted control participants via e-mail and internet advertisements. The study assessments were carried out between November, 2011 and January, 2013. All interested participants (n=960) gave their written informed consent after receiving detailed information about the aims and study procedures. The inclusion criteria for fibromyalgia patients were: i) to be previously diagnosed by a rheumatologist; ii) to meet the 1990 American College of Rheumatology (ACR) fibromyalgia classification criteria [8]; iii) not to have acute or terminal illness, and severe dementia (Mini Mental State Examination (MMSE) < 10) [9]. The inclusion criteria for control participants were: 1) not to meet the 1990 ACR fibromyalgia criteria [8]; 2) not to have acute or terminal illness, and severe dementia (Mini Mental State Examination (MMSE) < 10) [9]. Men were not included in the present study (86 men excluded). Thirty-eight patients were not previously diagnosed. 92 fibromyalgia patients did not meet the 1990 ACR criteria whereas 6 control participants met it. Additionally 1 fibromyalgia patient had severe dementia. To achieve age-matched groups, women <37 and >65 years were not included in the present study (64 participants excluded). The final study sample comprised 459 fibromyalgia vs. 214 control women. The study was reviewed and

approved by the Ethics Committee of the *"Hospital Virgen de las Nieves"* (Granada, Spain).

Procedure

Measurements were performed on two different occasions separated by one day and performed by the same trained researchers group in order to reduce inter-examiners error. The first day the MMSE was applied and self-reported socio-demographic data and Beck Depression Inventory (BDI-II) were filled by participants. Furthermore, assessment of tender points according to the 1990 ACR criteria was performed and weight and height were measured. Subsequently, participants received several questionnaires to be filled at home. At the second appointment, participants returned the filled questionnaires to the research team and the Paced Auditory Serial Addition Task (PASAT) and the Rey Auditory Verbal Learning Test (RAVLT) were interviewed.

Outcome measures

Anthropometric measures

Weight (kg) and height (cm) were measured using a portable eight-polar tactile-electrode impedanciometer (InBody R20, Biospace, Seoul, Korea) and a stadiometer (Seca 22, Hamburg, Germany), respectively. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.

Tenderness

Tenderness. We assessed 18 tender points according to the 1990 ACR criteria for classification of fibromyalgia [8] using a standard pressure algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). Two alternative measurements at each tender site were performed and the mean score was recorded. A pressure threshold ≤ 4 kg/cm^2 was considered a positive tender point. The total count of positive tender points (tender points count) was recorded for each participant. An algometer score was calculated as the sum of the minimum pain-pressure values obtained for each tender point.

Fibromyalgia impact

The Revised Fibromyalgia Impact Questionnaire (FIQR) is a self-administered questionnaire, comprising 21 individual questions with a rating scale of 0 to 10. This questions compose 3 different domains: function, overall impact and symptoms score (ranging 0-30, 0-20 and 0-50, respectively) [10]. The FIQR total score range from 0 to 100, with a higher score indicating greater effect of the condition on the person's life. We used the Symptom Impact Questionnaire with control participants. The SIQR [11] is a slightly modified version of the FIQR used with non-fibromyalgia patients. Number of questions, domains and scoring is the same as the FIQR.

Fatigue

The Spanish version of the Multidimensional Fatigue Inventory (MFI-S) was used to measure fatigue severity. Five subscales compose this questionnaire: general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation [12, 13]. Each subscale includes four items with five-point Likert scales. Scores on each subscale range from 4 to 20, with higher scores indicating greater fatigue.

Health-related quality of life

The *Short-Form Health Survey 36 (SF-36)* is a generic instrument for assessing health-related quality of life [14]. It contains 36 items grouped into 8 dimensions: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role, and mental health. The scores range from 0 to 100 in every dimension, where higher scores indicate better health. The standardized physical component (range 0-100) and the standardized mental component (range 0-100) were also calculated.

Mental health and cognitive performance

The Mini Mental State Examination was used to evaluate cognitive capacity and severity of dementia [15]. The MMSE is a brief cognitive screening test which assesses five areas of cognitive functioning: orientation, immediate memory, attention/concentration, delayed recall and language.

The Beck Depression Inventory-II was used to assess depression severity [16]. It contains 21 items and the range of score is 0 - 63 with higher score indicating greater depression.

The State Trait Anxiety Inventory-I (STAI) was used to assess the level of current anxiety [17]. It is a 20-item self-administered questionnaire; the range of score is 20 - 80, with higher scores indicating a greater state of anxiety.

The Paced Auditory Serial Addition Task [18] was used to measure sustained and divided attention, auditory information processing speed, and stimulus competition filtering skill. It was administered at the slowest presentation rate of 2.4 seconds. The

score is the number of correct responses over 60 trials, with higher scores indicating greater results.

The Rey Auditory Verbal Learning Test [19] is a multiple-trial verbal list learning test. It measures immediate free recall, delayed free recall, delayed recognition, and verbal learning with higher scores indicating a greater learning.

Statistical analysis

The t-test was used to analyse the differences between fibromyalgia and controls in continuous socio-demographic variables. Chi-square was used for socio-demographic categorical variables. To analyse the differences in tenderness, impact of fibromyalgia, fatigue, health-related quality of life, mental health and cognitive performance between fibromyalgia and controls, we carried out an analyses of the covariance (ANCOVA), where significant socio-demographic variables (educational status, current occupational status and BMI) were used as covariates in all the analyses. The effect size statistic was calculated in all the analyses by means of the Cohen's *d* (standardized mean difference) [20]. The effect size was interpreted as small (~0.25), medium (~0.5) or large (~0.8 or greater) [20].

To distinguish which specific factor (physical or psychological) better characterize fibromyalgia compared to controls, a standardized age- and sex-specific normalized index ([value-mean]/standard deviation [SD]) was created for all outcomes. The algometer score, SF-36 (standardized physical and mental components), MMSE total score, PASAT (correct answers) and RAVLT (all items) indexes were inverted (since higher values imply better performance). A 'global physical component' was calculated as the average of the algometer score, tender points count, FIQR (function, overall, pain,

energy, stiffness, tenderness, balance problems and environmental sensitivity), MFI-S (general fatigue, physical fatigue and reduced activity) and SF-36 (standardized physical component). A 'global psychological component' was calculated as the average of the FIQR (sleep quality, depression, memory problems and anxiety), MFI-S (reduced motivation and mental fatigue), SF-36 (standardized mental component), MMSE total score, BDI-II total score, STAI total score, PASAT (all items) and RAVLT (all items). An ANCOVA with educational status, current occupational status and BMI as covariates was used to test the differences in the global physical and psychological components between the study groups.

The Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 20.0, Armonk, New York) was used. Due to the large number of comparisons, the level of significance was set at $P<0.01$.

RESULTS

The socio-demographic variables of the study groups are shown in **Table 1**. BMI differed between fibromyalgia and control women (28.6 vs 26.7 kg/m^2, respectively; $P<0.001$). There were differences in educational status between women groups ($P=0.018$), with a greater percentage of primary school in fibromyalgia compared to controls (47.8 and 39.0%, respectively) and lower percentage of university higher degree in fibromyalgia compared to controls (5.0 and 9.9%, respectively). Current occupational status was statistically different between the fibromyalgia and control groups ($P<0.001$) with lower working full time (15.2 vs. 31.0%) and greater retired (14.1 vs. 2.8%) and sick leave (7.6 vs. 0.9%) percentage of fibromyalgia than controls.

Fibromyalgia and control participants' tenderness is shown in **Supplementary Table 2**. Pain threshold score for all tender points were lower in fibromyalgia compared to controls (all, P<0.001). Very large effect sizes were observed in all tender points. The trapezius and supraspinatus tender points showed the largest effect sizes (Cohen's d > 3.40). The total number of tender points was higher in fibromyalgia compared to controls (P<0.001) with very large effect sizes (Cohen's d = -5.72). A visual representation of the areas with the largest differences (i.e. more discriminant) between fibromyalgia and controls is shown in **Figure 1**.

Symptomatology for fibromyalgia and control participants is shown in **Table 2**. Fibromyalgia women presented significantly higher scores in all the FIQR dimensions compared to their control counterparts (all, P<0.01). The effect sizes were generally very large, except for tenderness (low effect size). The FIQR function domain and FIQR total score showed the largest effect sizes (Cohen's d > 2.40). Fatigue showed higher values in fibromyalgia women when compared to their control counterparts (all, P<0.001). The effect sizes were generally very large. General and physical fatigue showed the largest effect sizes between women groups (Cohen's d = -2.19 and -1.76, respectively).

Health-related quality of life for fibromyalgia and control participants is shown in **Table 3**. All the health-related quality of life dimensions showed worse values in fibromyalgia compared to control women (all, P<0.001). Very large effect sizes were observed in all the dimensions. Quality of life related to physical health (physical function, physical role, bodily pain, general health and vitality) showed overall larger effect sizes than quality of life related to social and mental health (social functioning, emotional role and mental health).

Mental health and cognitive performance for fibromyalgia and control participants is shown in **Table 4**. The MMSE scores were not different between the fibromyalgia and control women. Levels of depression and anxiety were higher in fibromyalgia compared to controls (all, P<0.001). The effect sizes for depression and anxiety were very large. No differences in the performance of the PASAT were shown between fibromyalgia and controls. No differences in cognitive performance were observed between fibromyalgia and controls, except for delayed recall where fibromyalgia women showed lower values than control women (P=0.003) but the effect size was low (Cohen's d = 0.28).

The global physical component and the global psychological component for fibromyalgia and control participants is represented in **Figure 2**. Both components were worse in fibromyalgia compared to the control women (all, P<0.001). The effect size observed for the global physical component (-3.28) was larger than that for the global psychological component (-1.37).

DISCUSSION

As expected, the current study showed large differences in general tenderness, impact of fibromyalgia, fatigue, health-related quality of life, depression and anxiety in fibromyalgia women compared to control women. In addition, the only difference found on cognitive performance were observed in delayed recall and the effect size was low. Overall, the differences presented very large effect sizes. Pain was confirmed as the most important and characteristic symptom distinguishing fibromyalgia from non-fibromyalgia women. Furthermore, fibromyalgia seems to more severely impair physical than psychological domains, although both dimensions are sternly affected.

Fibromyalgia women showed lower educational status than control women. This finding concurs with previous studies affirming that lower levels of education are associated with an increase prevalence of pain [4]. Higher prevalence rates of this condition have been observed in low educated patients [3]. We also observed lower working full time, and higher index of incapacity retirements and sick leaves in the fibromyalgia group compared with the control women group, which is consistent with the literature [21]. This implies an indirect economic repercussion, leading to lower incomes, which have also been related to higher prevalence rate of fibromyalgia [3, 4, 22].

Fibromyalgia patients usually present higher pain pressure thresholds than controls [8]. This underlines the presence of an alteration in the regulation of pain. Tender points were the variables with the largest effect sizes of all variables studied, which reinforces pain as the most predominant and distinctive symptom in fibromyalgia [23]. Previous literature supports that fat tissue thickness, soft tissue surfaces, and/or closeness to bone muscle and nerve tissues might influence pain pressure levels [24–26]. Our findings

concur with previous studies showing lower pain thresholds in some specific points such as occiput, anterior cervical or second rib. Particularly, the anterior cervical was the tender point with higher sensitivity in the fibromyalgia group, which is consistent with previous studies [24–26]. However, this tender point was also observed to be the most sensitive to pressure in controls. Therefore, the anterior cervical cannot be the most valuable tender point for diagnosis. Specifically, our results showed that trapezius and supraspinatus tender points were those which better discriminate between fibromyalgia and non-fibromyalgia women. A previous study confirmed that the supraspinatus had the most powerful discriminative ability of all tender points together with the lateral epicondyle [27].

The large effect size presented in pain by means of algometry was also confirmed by the 'pain dimension' from both the FIQR and SF-36. These questionnaires are commonly used together in the fibromyalgia studies since quality of life is indeed influenced by the impact of fibromyalgia [28]. Interestingly, the largest effect sizes in both questionnaires were observed in the physical function dimension. This highlights the enormous impact of fibromyalgia on the management of daily simple tasks, as bathing, doing the bed or simply walking [28, 29] and consequently on health-related quality of life [28, 30]. The presence of other symptoms such as low energy, high stiffness, balance problems and environmental sensitivity point to an overall increased symptom expression and a heightened physical sensitivity in fibromyalgia patients. Previous studies have shown very large differences in the SF-36 between fibromyalgia patients and controls, showing mean values very similar to those observed in the present study [28, 30, 31]. A recent study [32] showed similar differences in the physical and mental component summary score between fibromyalgia and controls (n=380 fibromyalgia and 1579 controls; Cohen's $d \sim 1.3$), although women and men were analysed together, and the distribution

of gender was different (92.4% and 50.2% of women in the fibromyalgia and control group, respectively). However, in concordance to our findings, it seems that generally physical dimensions of quality of life are more impaired than mental dimensions in fibromyalgia when compared to controls [28, 31], with special emphasis in physical function [31] and role limitations [30, 31].

Fatigue has been shown as the second most reported symptom in fibromyalgia [6, 23]. Our results concurred with general knowledge, corroborating a general and continuous fatigue perception reported by fibromyalgia patients [6, 13, 33, 34]. However, fibromyalgia patients usually experience multiple manifestations of fatigue, and studies suggest studying these diverse types of fatigue [13, 33, 34]. The questionnaire used in the present study [13] let us study different dimensions of fatigue. It is noteworthy that according to our data, physical fatigue seemed to be more specific to this condition in contrast to mental fatigue. The constant pain in muscles and general stiffness in this population is a constant source of exhaustion, which might explain the high levels of physical fatigue. The raised degree of overall fatigue may also be related with distress, work dysfunction and a drop in overall health status in this population [33].

The present study showed large differences between fibromyalgia and control women in both depression and anxiety. Depression and anxiety have directly been related to a worsening of fibromyalgia disease [30, 35]. In fact, depression and anxiety are associated with several psychosocial variables in fibromyalgia, as previous experience, coping and social and marital support [36]. However, a functional magnetic resonance imaging research [37] has suggested that depression and anxiety are not involved in the neural processing of experimental pain and negative affect in fibromyalgia patients, which concurs with recent findings [38]. Although the mechanism of pain and negative affect in fibromyalgia needs deeper investigation, it is clear that depression and anxiety

are very common symptoms in fibromyalgia which are negatively associated to perceived health-related quality of life [30, 35, 37] and even have a substantial influence on the level of disability [28]. Although differences in depression and anxiety between fibromyalgia and controls showed very large effect sizes (Cohen's $d \sim 1.2$), these were lower than other outcomes studied as tender points, bodily pain, physical function, physical role, overall health, general fatigue and physical fatigue.

Cognitive and memory performance are recently a matter of increasing interest in this disease. In fact, memory problems have been included as part of the modified 2010 ACR criteria for fibromyalgia diagnosis [23]. Interestingly, we did not observe cognitive or memory problems in fibromyalgia women compared to controls, except for delayed recall. General knowledge supports some working memory difficulties in fibromyalgia, especially with the presence of a distraction factor [39, 40], which concurs with our finding. Although the RAVLT includes a source of distraction, it could be possible that other cognitive tests with higher sources of distraction might be more appropriate to investigate cognitive deficits in this population. Cognitive dysfunction study still needs further investigation. Previous studies have overall used self-reported measures and low sample sizes [40]. Furthermore, it has been stated that cognitive symptoms in these patients may be exacerbated by the presence of pain, and other reported symptoms [41]. In fact, it has been speculated that fibromyalgia patients might tend to overestimate their perceived memory deficits [42]. A recent study showed some minor differences by means of different neuropsychological tests between fibromyalgia and controls regarding cognitive function [43]. However, fibromyalgia patients self-reported large cognitive impairments when compared to controls, which reinforces the hypothesis of some overestimation in self-report cognitive dysfunction in fibromyalgia.

As a subjective symptom, cognitive dysfunction is difficult to evaluate in an objective manner and future studies should clarify our findings.

With the new preliminary diagnostic criteria for fibromyalgia [7, 23] the understanding of this disease as a multi-symptom-dimension complex condition does not intend to focus solely on pain [44]. Overall the results of the present study support the idea of fibromyalgia as a multi-dimensional condition. Fibromyalgia is a disorder characterized by hyperalgesia and allodynia [8, 23]. This is reflected in an altered perception of musculoskeletal pain, which in turns causes fatigue, disability and poor physical condition. This might explain that fibromyalgia patients showed more severe physical than psychological impairments, according to our results. In this context, diverse physical exercise intervention programs have proved their efficiency reducing fibromyalgia symptomatology [45], being even more effective than pharmacology therapies [46]. Results from the present study reinforce the idea that treatments should focus both on physical and emotional dysfunction, with an especial emphasis in the physical domain, since it shows the largest differences compared to age-matched controls. Furthermore, as some psychological components (e.g. depression and anxiety) influence the level of disability in fibromyalgia [28], their proper treatment might lead to a physical function improvement. Therefore, multidisciplinary interventions [47] combining exercise and cognitive behavioural therapies could achieve the greatest benefits in this context [46].

A limitation of the present study is the cross-sectional design of the study which do not allow causality be ascertained. Since the recruitment of fibromyalgia patients was mainly carried out through fibromyalgia associations (support groups) and an age criteria was used to achieve age-matched groups, the sample from the current study may not necessarily apply to all fibromyalgia patients. Furthermore, the composition of the

global physical and psychological components is not a standardized technique, and although we tried to be as concise as possible, the composition of physical and psychological parameters is a non-objective difficult task. On the other hand, the number of fibromyalgia women included in this study is relatively large and sampling was done in all the provinces of Andalusia and according to proper sample size calculation to achieve an optimal power. Moreover, a vast number of study outcomes were examined in the present study. As pain increases with age [4] due to degenerative processes, the fibromyalgia and control groups of the present study were age-matched to avoid the potential effect of aging in general pain.

CONCLUSIONS

The results of the present study suggest that fibromyalgia must be understood as a complex dimensional disorder beyond chronic widespread pain condition. Despite pain remains as the primary symptom, the overall impact of fibromyalgia, general fatigue, health-related quality of life, depression, and anxiety are also characteristics to this population. Furthermore, the cognitive performance seems not to be as impaired as it had been suggested. Treatment options should focus on both physical and psychological improvements. However, the results of the current study provide consistent and novel findings supporting that fibromyalgia might affect physical outcomes more severely than psychological outcomes. These findings have important implications for diagnosis and treatment in fibromyalgia.

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Competing interests

The authors declare no conflict of interests.

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Table 1. Clinical and socio-demographic characteristics of the study samples.

	Women		
	Fibromyalgia (n=459)	Control (n=214)	P
	Mean (SD)	Mean (SD)	
Age (years)	52.2 (7.1)	51.3 (7.0)	0.122
Body mass index (kg/m^2)	28.6 (5.5)	26.7 (4.2)	<0.001
	n (%)	n (%)	
Marital status			
Married	350 (76.3)	155 (72.8)	
Single	34 (7.4)	21 (9.9)	
Separated	15 (3.3)	13 (6.1)	0.324
Divorced	38 (8.3)	14 (6.6)	
Widow	22 (4.8)	10 (4.7)	
Educational status			
No studies	47 (10.2)	15 (7.0)	
Primary school	220 (47.9)*	83 (38.8)*	
Professional training	72 (15.7)	32 (15.0)	0.015
Secondary school	58 (12.6)	35 (16.4)	
University medium degree	39 (8.5)	28 (13.1)	
University higher degree	23 (5.0)*	21 (9.8)*	
Current occupational status			
Working full time	70 (15.3)*	66 (30.8)*	
Working part time	47 (10.2)	23 (10.7)	
Housewife	145 (31.6)	78 (36.4)	
Student	5 (1.1)	3 (1.4)	<0.001
Retired/pensioner	14 (3.1)	6 (2.8)	
Retired/Incapacity pension	65 (14.2)*	6 (2.8)*	
Sick leave	34 (7.4)*	2 (0.9)*	
Unemployed	79 (17.2)	30 (14.0)	
Time since diagnosis			
≤ 5 years	183 (40.9)		
> 5 years	264 (59.1)		

SD, standard deviation. The asterisk (*) represent those subgroups statistically different.

Table 2. Fibromyalgia and control participants' symptomatology.

	Women		P	Effect size
	Fibromyalgia (n=442)	Control (n=200)		
	Mean (SE)	Mean (SE)		
FIQR				
Function (0-30)	17.1 (0.3)	2.8 (0.4)	<0.001	-2.47
Overall (0-20)	12.3 (0.2)	2.9 (0.4)	<0.001	-1.86
Pain (0-10)	7.4 (0.1)	3.0 (0.2)	<0.001	-2.09
Energy (0-10)	7.1 (0.1)	3.0 (0.2)	<0.001	-1.72
Stiffness (0-10)	6.9 (0.1)	2.4 (0.2)	<0.001	-1.80
Sleep quality (0-10)	8.4 (0.1)	3.4 (0.2)	<0.001	-2.08
Depression (0-10)	5.4 (0.2)	1.8 (0.2)	<0.001	-1.12
Memory problems (0-10)	6.9 (0.1)	3.5 (0.2)	<0.001	-1.25
Anxiety level (0-10)	6.4 (0.1)	2.6 (0.2)	<0.001	-1.23
Tenderness (0-10)	7.0 (0.1)	6.3 (0.2)	<0.001	-0.27
Balance problems (0-10)	5.7 (0.1)	2.1 (0.2)	<0.001	-1.31
Environmental sensitivity (0-10)	7.9 (0.1)	5.0 (0.2)	<0.001	-1.15
FIQR symptoms (0-50)	34.6 (0.4)	16.6 (0.6)	<0.001	-2.32
FIQR total score (0-100)	64.0 (0.7)	22.4 (1.1)	<0.001	-2.67
MFI-S				
General fatigue (4-20)	17.9 (0.2)	10.6 (0.2)	<0.001	-2.19
Physical fatigue (4-20)	16.5 (0.2)	10.5 (0.2)	<0.001	-1.76
Reduced activity (4-20)	12.9 (0.2)	8.0 (0.3)	<0.001	-1.05
Reduced motivation (4-20)	13.2 (0.2)	8.9 (0.3)	<0.001	-1.11
Mental fatigue (4-20)	14.3 (0.1)	11.7 (0.2)	<0.001	-1.02

FIQR, Revised Fibromyalgia Impact Questionnaire. MFI-S, Spanish version of the Multidimensional Fatigue Inventory. SE, standard error. Differences between fibromyalgia and control groups were performed using analyses of the covariance (ANCOVA) with educational status, current occupational status and body mass index entered as covariates. Effect size statistics are expressed as Cohen's *d*.

Table 3. Health-related quality of life of the study groups.

	Women			
	Fibromyalgia (n=441)	Control (n=202)	P	Effect size
	Mean (SE)	Mean (SE)		
SF-36				
Physical function	39.3 (0.9)	77.9 (1.4)	<0.001	1.97
Physical role	34.2 (1.0)	75.7 (1.6)	<0.001	1.89
Bodily pain	21.5 (0.9)	60.4 (1.3)	<0.001	2.15
General health	29.3 (0.8)	60.6 (1.2)	<0.001	1.86
Vitality	22.7 (0.9)	59.6 (1.4)	<0.001	1.94
Social functioning	44.3 (1.2)	78.4 (1.8)	<0.001	1.38
Emotional role	56.6 (1.3)	81.4 (1.9)	<0.001	0.92
Mental health	46.0 (1.0)	67.8 (1.5)	<0.001	1.04
Standardized physical component	29.9 (0.4)	46.9 (0.5)	<0.001	2.27
Standardized mental component	35.9 (0.6)	47.7 (0.9)	<0.001	0.98

SE, standard error. SF-36, Short-Form Health Survey 36. Differences between fibromyalgia and control groups were performed using analyses of the covariance (ANCOVA) with educational status, current occupational status and body mass index entered as covariates. Effect size statistics are expressed as Cohen's *d*.

Table 4. Mental health and cognitive performance of the study samples.

	Women					
	Fibromyalgia (n=459)		Control (n=213)		P	Effect size
	Mean	(SE)	Mean	(SE)		
MMSE	28.0	(0.1)	28.2	(0.1)	0.381	
BDI-II	26.1	(0.5)	11.4	(0.8)	<0.001	-1.35
STAI	34.8	(0.6)	21.1	(0.9)	<0.001	-1.12
PASAT						
Correct answers	32.2	(0.5)	33.0	(0.8)	0.455	
Wrong answers	7.5	(0.3)	8.2	(0.4)	0.184	
Not answered	20.2	(0.5)	18.8	(0.7)	0.126	
RAVLT						
Immediate memory	61.9	(0.6)	63.9	(0.8)	0.062	
Delayed recall	9.4	(0.1)	10.3	(0.2)	0.002	0.28
Verbal learning	47.0	(0.4)	48.4	(0.6)	0.061	
Recognition memory	34.9	(0.3)	35.9	(0.4)	0.047	

BDI-II, Beck Depression Inventory-II. MMSE, Mini Mental State Examination. PASAT, Paced Auditory Serial Addition Task. RAVLT, Rey Auditory Verbal Learning Test. SE, standard deviation. Differences between fibromyalgia and control groups were performed using analyses of the covariance (ANCOVA) with educational status, current occupational status and body mass index entered as covariates. Effect size statistics are expressed as Cohen's *d*.

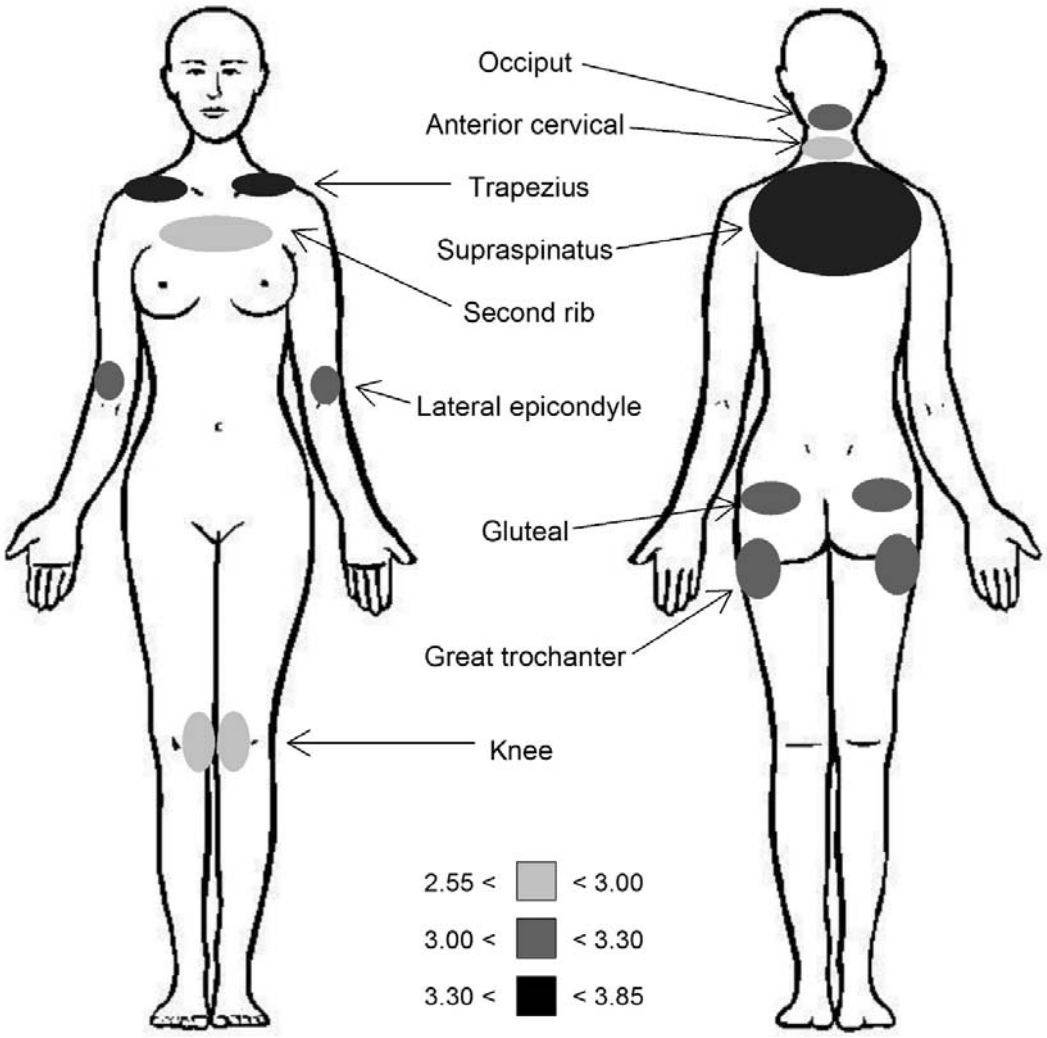

Figure 1. Visual representation of pressure pain thresholds according to tender points' examination. The darker the zones the better discriminative ability between fibromyalgia and non-fibromyalgia women, according to the effect size of the groups' differences (Cohen's *d*). For further information about mean, standard error, P-value and effect size of each specific tender point, tender points count and algometer score, see supplementary material.

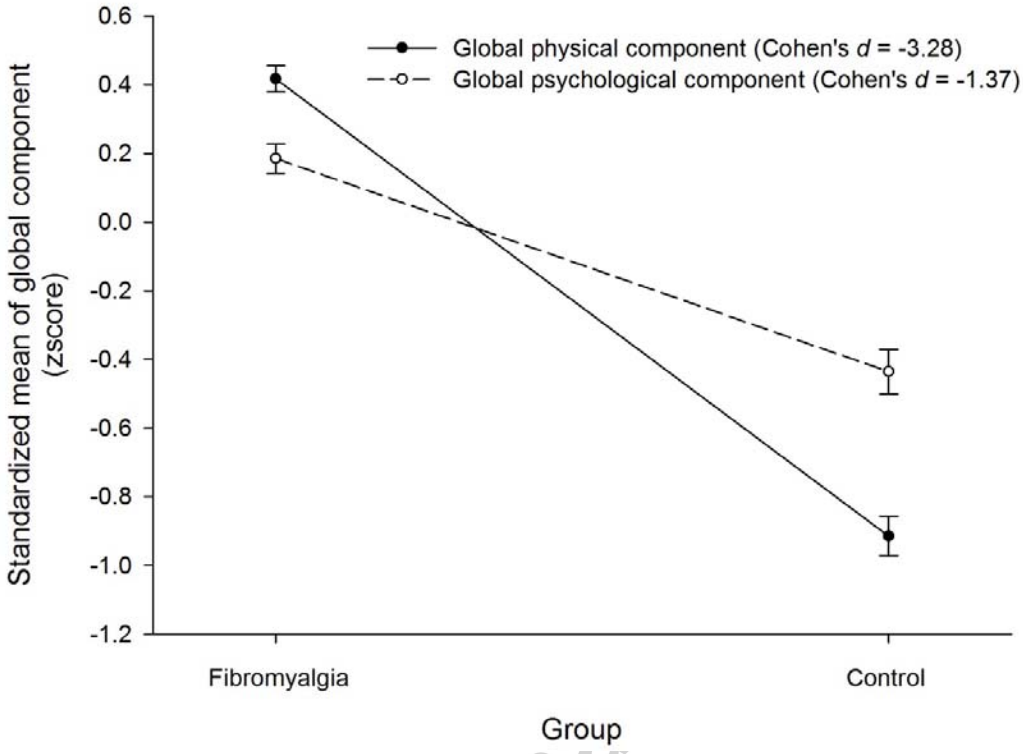

Figure 2. Graphic representation of the differences in the global physical and psychological components between the fibromyalgia and control group. An analyses of the covariance (ANCOVA) adjusted for educational status, current occupational status and body mass index was performed. The circles (black and white) represent adjusted means and error bars the 95% confidence intervals. Higher values correspond to worse state. Effect size statistics are expressed as Cohen's *d*. All P<0.001.

Supplementary table 1. Sample size by province and sex.

	Provinces[2]								
	Almería	Cádiz	Córdoba	Granada	Huelva	Jaén	Málaga	Sevilla	Total
By sex[1]	8.24%	14.82%	9.68%	10.93%	6.18%	8.07%	19.19%	22.89%	100%
Women (80%)	20	36	23	26	15	19	46	55	240
Men (20%)	5	9	6	7	4	5	12	14	60
Total	25	44	29	33	19	24	58	69	300

Source: (1) sex prevalence according to the Spanish Society of Rheumatology; (2): Andalusian population by provinces according to Multiterritorial Information System of Andalusia.

To assure representativeness of the Andalusian Region (southern of Spain), a two-phase (sex and province) proportional sampling of fibromyalgia patients was planned. We used as a reference the database of Spanish Association of Rheumatology, as well as the Census of the 8 provinces of Andalusia. The level of accuracy (*k*) was set as a fraction of the standard deviation of the population (accuracy=*k***standard deviation*). Following the common practice in clinical studies, we selected a *k* of 10-50%. Therefore, for a confidence interval of 95%, a sample consisting of 300 participants were needed to obtain an accuracy of 11%. Given this sample size, we would be able to estimate the maximum distance (in meters) that the patients are able to walk in an aerobic fitness test (the 6-minute walk) with an accuracy of 8 meters. The final sample was oversized in order to prevent loss of information.

Supplementary Table 2. Fibromyalgia and control participants' tenderness.

	Fibromyalgia (n=458)		Control (n=214)		P value	Effect size
	Mean	(SE)	Mean	(SE)		
Supraspinatus (1-8 kg/cm^2)	2.7	(0.1)	7.0	(0.1)	<0.001	3.84
Trapezius (1-8 kg/cm^2)	2.4	(0.1)	6.2	(0.1)	<0.001	3.42
Great trochanter (1-8 kg/cm^2)	2.7	(0.1)	6.4	(0.1)	<0.001	3.20
Gluteal (1-8 kg/cm^2)	2.6	(0.1)	6.4	(0.1)	<0.001	3.19
Lateral epicondyle (1-8 kg/cm^2)	3.0	(0.1)	7.1	(0.1)	<0.001	3.15
Occiput (1-8 kg/cm^2)	2.3	(0.0)	5.5	(0.1)	<0.001	3.02
Knee (1-8 kg/cm^2)	2.1	(0.1)	5.4	(0.1)	<0.001	2.78
Second rib (1-8 kg/cm^2)	2.1	(0.1)	5.1	(0.1)	<0.001	2.58
Anterior cervical (1-8 kg/cm^2)	1.7	(0.0)	4.2	(0.1)	<0.001	2.55
Algometer score (18-144 kg/cm^2)	43.2	(0.8)	106.1	(1.2)	<0.001	3.77
Total number points (0-18)	16.7	(0.1)	3.2	(0.2)	<0.001	-5.72

SE, standard error. Differences between fibromyalgia and control groups were performed using analyses of the covariance (ANCOVA) with educational status, current occupational status and body mass index entered as covariates. Effect size statistics are expressed as Cohen's *d*.

2. VALIDITY OF NEW DIAGNOSTIC CRITERIA AND UTILITY OF FITNESS TESTING AS A COMPLEMENTARY TOOL IN THE DIAGNOSIS OF FIBROMYALGIA

(Paper II and III)

II

Validation of the modified 2010 American College of Rheumatology diagnostic criteria for fibromyalgia in a Spanish population.

Segura-Jiménez V, Aparicio VA, Alvarez-Gallardo IC, Soriano-Maldonado A, Estévez-López F, Delgado-Fernández M, Carbonell-Baeza A.

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Original article

Validation of the modified 2010 American College of Rheumatology diagnostic criteria for fibromyalgia in a Spanish population

Víctor Segura-Jiménez[1], Virginia A. Aparicio[1,2], Inmaculada C. Álvarez-Gallardo[1], Alberto Soriano-Maldonado[1], Fernando Estévez-López[1], Manuel Delgado-Fernández[1] and Ana Carbonell-Baeza[3]

Abstract

Objective. The aim of this study was to validate the modified 2010 ACR preliminary criteria for FM in a Spanish population.

Methods. Five hundred and seventy-nine (550 women) FM and 294 (240 women) control participants were enrolled in the study. FM patients were previously diagnosed by a rheumatologist. All participants underwent both the 1990 ACR criteria (1990c) and the modified 2010 ACR criteria (m-2010c).

Results. The tender points count showed correlations of 0.69, 0.65 and 0.71 with the widespread pain index (WPI), symptoms severity (SS) and polysymptomatic distress (PSD) scales, respectively (all $P < 0.001$). The WPI, SS and PSD showed greater correlations with impact of FM health-related quality of life, general fatigue and depression than the tender points count. The 1990c showed sensitivity and specificity values of 84.1 and 97.6, respectively, whereas the m-2010c showed values of 88.3 and 91.8, respectively. Both criteria showed the same overall accuracy, with a value of 0.89. When the 1990c and m-2010c were combined and patients had to satisfy one of two criteria to be diagnosed with FM, the sensitivity, specificity and accuracy of questionnaires were 96.7, 89.8 and 0.94, respectively. The original cut-off points (WPI $\geqslant$ 7, SS $\geqslant$ 5 and PSD $\geqslant$ 12) showed the best test characteristics in the present study.

Conclusion. The m-2010c, with the same cut-off points as the original version, are a valid tool for the diagnosis of FM in our population. Whenever possible, the combination of the 1990c and m-2010c is recommended (patients have to meet one of the two criteria to be diagnosed), since this approach showed the best diagnostic characteristics.

Key words: tender points, questionnaire, polysymptomatic distress scale, widespread pain index, symptom severity, quality of life, impact of fibromyalgia, fatigue, sensitivity, specificity.

Introduction

FM has become a worrisome health condition in our modern society. This condition was first referred to as fibrositis and was mainly centred on diffuse pain [1]. A few years later, Yunus *et al.* [2] called it fibromyalgia and proposed a set of criteria for its diagnosis, including tender points and the presence of different symptoms. In 1990 the ACR reported the first criteria to differentiate FM from other chronic widespread pain syndromes [3]. Twenty years later, new, presumably improved ACR preliminary FM criteria have been released [4].

The 1990 ACR criteria (hereinafter referred to as 1990c) required widespread pain for at least 3 months and the presence of 11 of 18 tender points [3]. As time passed, objections to the 1990c developed, on the grounds that the presence of different tender points cannot be an objective assessment of whole body pain [5]. Furthermore,

[1]Department of Physical Activity and Sport, Faculty of Sport Sciences, University of Granada, [2]Department of Physiology, Faculty of Pharmacy, University of Granada, Granada and [3]Department of Physical Education, Faculty of Sciences Education, University of Cádiz, Cádiz, Spain.

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Correspondence to: Víctor Segura-Jiménez, Department of Physical Activity and Sport, Faculty of Sport Science, University of Granada, Carretera de Alfacar, s/n, 18011 Granada, Spain.
E-mail: vsegura@ugr.es

digital palpation instead of algometry is the most widely used method among examiners [6]. Without an objective instrument, the application of an equal pressure of 4 kg is therefore doubtful [5, 6]. Finally, FM is defined as a complex multidimensional pain disorder [4, 7] with the inclusion of equally presumably important non-pain symptoms, such as fatigue, stiffness, depression and cognitive problems, among other complaints [7, 8]. The range of these symptoms is therefore another important weakness of the 1990c [4, 5].

In 2010 the ACR released new diagnostic criteria that simplified clinical diagnosis by avoiding the requirement of examination of tender points [4]. With the new 2010 ACR criteria, FM has turned into a systemic symptom-based condition rather than the previous peripheral pain-defined condition [5]. Because most of the 2010 ACR items were obtained by self-administration, the criteria were modified in 2011 to allow complete self-administration [9]. These new criteria, which we shall call the m-2010c, eliminated the physicians' subjective assessments, thus making it a self-administered questionnaire suitable for epidemiological studies [9].

The m-2010c represent an alternative FM assessment method. However, it is not known whether the m-2010c are a valid diagnostic tool in different populations, and further investigations in different countries have been requested. To date, the 2010 ACR criteria have been validated in English- [4], Japanese- [10], French- [11] and Iranian- [12] speaking populations, whereas the m-2010c have been validated in English- [9] and Japanese- [13] speaking populations. To the best of our knowledge, no previous research has studied the validity of the m-2010c in Spain. Therefore we aimed to validate the m-2010c for FM in a representative population from southern Spain.

Patients and methods

Participants

FM patients were recruited from various FM associations via e-mail, letter or telephone. We also asked those FM patients interested in participating to recruit a healthy individual (control) of similar age, socio-demographic characteristics and demographic area in order to carry out appropriate comparisons between groups. We additionally contacted control participants via e-mail and Internet advertisements. All interested participants ($n = 960$) signed a written informed consent after receiving detailed information about the aims and study procedures. The study assessments were carried out between November 2011 and January 2013. The inclusion criteria for FM participants were (i) previous diagnosis of FM by a rheumatologist (patients were asked to provide their medical records to confirm their previous diagnosis) and (ii) no acute or terminal illness (such as cancer, stroke, recent cardiopathy, severe coronary disease, schizophrenia or any other disabling injury) or severe dementia [mini mental state examination (MMSE) < 10] [14]. The inclusion criteria for control participants were (i) no previous diagnosis of FM by a rheumatologist and (ii) no acute or terminal illness or severe dementia (MMSE < 10). A total of 39 participants were excluded from the study. One had an MMSE score <10 and the other 38 participants suffered from pain, although they had not previously visited a rheumatologist for a FM diagnosis. A total of 921 participants from southern Spain were enrolled in the study, which was reviewed and approved by the Ethics Committee of the Hospital Virgen de las Nieves, Granada, Spain.

Outcome measures

We assessed 18 tender points according to the 1990c [3] using a standard pressure algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). The mean of two measurements at each tender point was used for the analysis. A tender point scored as positive when the patient noted pain at a pressure $\leqslant 4\,kg/cm^2$. The total count of positive tender points (tender points count) was recorded for each participant. An algometer score was calculated as the sum of the minimum pain-pressure values obtained for each tender point.

The questionnaire for the m-2010c [9] is composed of two scales. The widespread pain questionnaire asked participants to grade whether (or not) they had pain or tenderness over the previous week in 19 body areas (shoulder girdle, hip, jaw, upper arm, upper leg, lower arm and lower leg, on the right and the left side of the body, separately, and additionally neck, chest, abdomen, upper back and lower back). Each item was scored as 0 or 1. The minimum total score of the widespread pain index (WPI) was 0 and the maximum total score was 19. The symptom scale questionnaire asked participants to indicate the severity of fatigue, trouble thinking or remembering and waking up tired (unrefreshed) over the previous week. The possible values were 0 (no problem), 1 (slight or mild problems, generally mild or intermittent), 2 (moderate, considerable problems, often present and/or at a moderate level) and 3 (severe, continuous, life-disturbing problems). Patients were also asked to answer whether (or not) they had had pain or cramps in the lower abdomen, depression or headache during the previous 6 months. The minimum total score of symptom severity (SS) was 0 and the maximum total score was 12. The WPI and SS were subsequently summed into a 0–31 index originally called the fibromyalgianess scale [9] and subsequently termed the polysymptomatic distress (PSD) scale [7]. The original 2010 ACR criteria study and the corresponding questionnaire have been previously translated to Spanish (see http://www.institutferran.org/documentos/WPI+SS-PACIENTES.pdf and http://www.institutferran.org/documentos/2010_ACR_FM_TRAD_FINAL.pdf). We used this questionnaire, with the exception that we adapted the second part of the SS to the m-2010c: the physicians' estimation of the SS score was eliminated and replaced with three dichotomous yes/no responses regarding the presence of pain or cramps in the lower abdomen, depression or headache during the previous 6 months, as explained above. The questionnaire was self-administered and patients obtained directions

from the researchers when they did not understand the questionnaire instructions.

The revised Fibromyalgia Impact Questionnaire (FIQR) is a self-administered questionnaire comprising 21 individual questions with a rating scale of 0–10. The questions compose three different domains: function, overall impact and symptoms score (range 0–30, 0–20 and 0–50, respectively) [15, 16]. The FIQR total score ranges from 0 to 100, with a higher score indicating a greater impact of the condition on the person's life.

The 36-item Short Form Health Survey (SF-36) is a generic instrument for assessing health-related quality of life [17, 18]. Its 36 items are grouped into eight dimensions: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role and mental health. The scores range from 0 to 100 for every dimension, and higher scores indicate better health.

The Multidimensional Fatigue Inventory (MFI) measures fatigue severity. It comprises five subscales: general fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation [19, 20]. Each subscale includes four items on a 5-point Likert scale. Scores on each subscale range from 4 to 20, with higher scores indicating greater fatigue. In the present study we only focused on general fatigue, which includes general statements about fatigue and decreased functioning.

The Beck Depression Inventory II (BDI-II) was used to assess depression severity [21, 22]. It contains 21 items and the score ranges from 0 to 63, with a higher score indicating greater depression.

The MMSE was used to assess cognitive capacity and the severity of dementia for the exclusion criteria [14, 23]. Five areas of cognitive functioning were assessed: orientation, immediate memory, attention/concentration, delayed recall and language. The score ranges from 0 to 30, with a lower score indicating a greater state of dementia.

Statistical analysis

Differences in socio-demographic variables between groups were calculated with analysis of variance (ANOVA) or the chi-square test when appropriate. Differences in clinical variables were calculated with analysis of covariance (ANCOVA), adjusting for all significant socio-demographic variables. The relationship between the tender points count, the new criteria scales and the other important study variables was studied using Pearson's correlation coefficient (r_p). Cronbach's α was used to measure the internal consistency for the m-2010c. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR) and accuracy for the 1990c, the m-2010c and the combination of both criteria were calculated. The kappa and delta indexes [24] were additionally used to measure the agreement between the gold standard (clinical/rheumatologist diagnosis) and FM criteria. New cut-off points that could represent better test characteristics than those presented in the original m-2010c were studied by means of receiving operator characteristic (ROC) analysis. Significance was set at $P < 0.05$. The Statistical Package for Social Sciences, version 20.0 (SPSS Statistics for Windows, IBM, Armonk, NY, USA) was used.

Results

A total of four participants did not assist to the tender points assessment and 44 participants did not fill out the questionnaires. The final study sample comprised 873 participants. According to the clinical (rheumatologist) diagnosis, 579 (550 women) participants became part of the FM group, whereas 294 (240 women) participants were included in the control group.

The socio-demographic characteristics of the study groups are shown in Table 1. Age, sex, educational status and occupational status were statistically different between the FM and control groups (all $P < 0.001$). The clinical characteristics of the study groups are shown in Table 2. A significant difference in all the clinical variables between the FM and control groups was observed (all $P < 0.001$), except in the MMSE ($P > 0.05$).

To further characterize the relationship between the tender points count, the new criteria scales and the study variables, Pearson correlations are shown in Table 3. The correlations between the tender points count and the WPI, SS and PSD were 0.69, 0.65 and 0.71, respectively (all $P < 0.001$). The scales of the new criteria (WPI, SS and PSD) showed greater correlations with all the study variables than the tender points count.

We applied the 1990c and the m-2010c to participants enrolled in the study. By clinical diagnosis at entry, 63.6% of the total participants were diagnosed with FM. Using 1990c, the percentage of total participants with FM was 58.4, whereas with m-2010c it was 61.0 (Table 4). Among participants completing the FM clinical diagnosis, 84.1% satisfied the 1990c and 88.3% satisfied the m-2010c. Among control participants, 2.4% were diagnosed with FM according to the 1990c and 8.2% according to the m-2010c.

The all-item internal consistency of the m-2010c showed a Cronbach's α of 0.93. The sensitivity, specificity, PPV, NPV, PLR, NLR and accuracy of the 1990c and m-2010c were calculated using the clinical diagnosis as the gold standard (Table 5). The m-2010c showed a greater sensitivity but lower specificity than the 1990c (88.3 *vs* 84.1 and 91.8 *vs* 97.6, respectively). Both criteria showed the same overall accuracy, with a value of 0.89. We further studied the combination of both the 1990c and m-2010c. When patients had to satisfy both criteria to be diagnosed (1990c + m-2010c), the sensitivity was low (75.6), despite the fact that the specificity was almost perfect (99.7). When patients had to satisfy one of the criteria to be diagnosed (1990c or m-2010c), the sensitivity and specificity were both very high (96.7 and 89.8, respectively) and the accuracy, with a value of 0.94, was higher than all the previous options. The kappa and delta values for the 1990c and m-2010c were similar and overall they were good (>0.75). The 1990c + m-2010c combination showed the lowest kappa value, whereas the 1990c or

Table 1 Socio-demographic characteristics of the study groups

	FM ($n = 579$)		Control ($n = 294$)		*P*-value
Age, mean (S.D.), years	51.9	(8.1)	49.1	(10.4)	<0.001
Sex					
Men	29	(5.0)	54	(18.4)	<0.001
Women	550	(95.0)	240	(81.6)	
Marital status					
Married	428	(73.9)	209	(71.3)	0.080
Single	58	(10.0)	46	(15.7)	
Separated	22	(3.8)	13	(4.4)	
Divorced	44	(7.6)	14	(4.8)	
Widow	27	(4.7)	11	(3.8)	
Educational status					
No studies	62	(10.7)	16	(5.4)	<0.001
Primary school	283	(48.9)	109	(37.1)	
Professional training	86	(14.9)	53	(18.0)	
Secondary school	67	(11.6)	50	(17.0)	
University medium degree	52	(9.0)	32	(10.9)	
University higher degree	29	(5.0)	34	(11.6)	
Current occupational status					
Working full time	89	(15.4)	92	(31.3)	<0.001
Working part time	61	(10.5)	36	(12.2)	
Housewife	174	(30.1)	79	(26.9)	
Student	5	(0.9)	7	(2.4)	
Retired/pensioner	23	(4.0)	16	(5.4)	
Retired/incapacity pension	79	(13.6)	13	(4.4)	
Sick leave	44	(7.6)	2	(0.7)	
Unemployed	104	(18.0)	49	(16.7)	

Values are *n* (%) unless otherwise indicated. Differences in socio-demographic variables tested by analysis of variance (ANOVA) or chi-squared test when appropriate.

Table 2 Clinical characteristics of the study groups

	FM ($n = 579$)		Control ($n = 294$)		*P*-value
	Mean	(95% CI)	Mean	(95% CI)	
Tender points count (0–18)	15	(14.4, 15.1)	3	(2.6, 3.7)	<0.001
Algometer score (18–144)	51	(49.5, 53.2)	108	(105.1, 110.5)	<0.001
WPI total (0–19)	13	(13.2, 13.8)	4	(3.6, 4.5)	<0.001
SS score total (0–12)	8	(7.7, 8.0)	2	(2.1, 2.7)	<0.001
PSD scale (0–31)	21	(20.9, 21.8)	6	(5.8, 7.1)	<0.001
FIQR total score (0–100)	64	(62.1, 65.0)	24	(15.6, 32.4)	<0.001
SF-36					
Physical function (0–100)	40	(38.8, 42.1)	79	(77.0, 81.6)	<0.001
Physical role (0–100)	35	(33.2, 36.9)	79	(76.0, 81.3)	<0.001
Bodily pain (0–100)	23	(21.1, 24.3)	65	(62.3, 66.8)	<0.001
General health (0–100)	30	(28.3, 31.2)	63	(61.1, 65.2)	<0.001
Vitality (0–100)	24	(22.6, 25.8)	62	(59.5, 64.2)	<0.001
Social functioning (0–100)	45	(42.8, 46.9)	81	(78.3, 84.2)	<0.001
Emotional role (0–100)	57	(54.4, 58.7)	84	(80.6, 86.9)	<0.001
Mental health (0–100)	46	(44.6, 48.1)	70	(67.3, 72.2)	<0.001
MFI general fatigue (4–20)	18	(17.5, 18.1)	10	(9.9, 10.7)	<0.001
BDI-II (0–63)	26	(25.1, 26.9)	10	(9.1, 11.7)	<0.001
MMSE (0–30)	28	(27.7, 28.0)	28	(27.9, 28.4)	0.057

Differences in clinical variables tested by analysis of covariance (ANCOVA), adjusting for all significant socio-demographic variables. WPI: widespread pain index; SS: symptom severity; PSD: polysymptomatic distress; FIQR: FM impact questionnaire; SF-36: 36-item Short Form Health Survey; MFI: multidimensional fatigue inventory; BDI-II: Beck depression inventory II; MMSE: mini mental state examination.

Table 3 Pearson's correlations between key study variables for all participants ($n = 871$)

	Tender points count	WPI total	SS score total	PSD scale
Tender points count	1.00	0.69	0.65	0.71
WPI total	0.69	1.00	0.77	0.97
SS score total	0.65	0.77	1.00	0.90
PSD scale	0.71	0.97	0.90	1.00
FIQR total score	0.24	0.50	0.66	0.65
SF-36 physical function	−0.61	−0.69	−0.71	−0.74
SF-36 physical role	−0.61	−0.72	−0.76	−0.78
SF-36 bodily pain	−0.66	−0.76	−0.78	−0.81
SF-36 general health	−0.61	−0.69	−0.73	−0.75
SF-36 vitality	−0.62	−0.69	−0.74	−0.75
SF-36 social functioning	−0.52	−0.61	−0.73	−0.69
SF-36 emotional role	−0.40	−0.53	−0.61	−0.59
SF-36 mental health	−0.44	−0.53	−0.61	−0.59
MFI general fatigue	0.64	0.70	0.76	0.77
BDI-II	0.51	0.60	0.70	0.67

WPI: widespread pain index; SS: symptom severity; PSD: polysymptomatic distress; FIQR: revised FM impact questionnaire; SF-36: 36-item Short Form Health Survey; MFI: multidimensional fatigue inventory; BDI-II: Beck Depression Inventory II. All *P*-values <0.001.

Table 4 FM prevalence according to clinical diagnosis and 1990, 2010 and modified 2010 ACR criteria

	FM by clinical diagnosis	FM by 1990 ACR criteria	FM by 2010 or modified 2010 ACR criteria
Spanish modified 2010 ACR criteria			
All participants ($n = 910$)	**63.6**	58.4	61.0
FM ($n = 579$)	**100**	84.1	88.3
Control ($n = 294$)	**0**	2.4	8.2
Original modified 2010 ACR criteria [9]			
All participants ($n = 7233$)	**10.1**	—	25.4
FM ($n = 729$)	**100**	—	60.0
Control ($n = 6504$)	**0**	—	21.6
Japanese modified 2010 ACR criteria [13]			
All participants ($n = 693$)	—	**66.7**	44.0
FM ($n = 462$)	—	**100**	64.0
Control ($n = 231$)	—	**0**	4.0
Original 2010 ACR criteria [4]			
All participants ($n = 514$)	**50.2**	—	38.1
FM ($n = 258$)	**100**	—	74.5
Control ($n = 256$)	**0**	—	2.0
Japanese 2010 ACR criteria [10]			
All participants ($n = 137$)	—	**68.6**	59.1
FM ($n = 94$)	—	**100**	82.0
Control ($n = 43$)	—	**0**	9.0
Iranian 2010 ACR criteria [12]			
All participants ($n = 278$)	**60.4**	47.8	38.4
FM ($n = 168$)	**100**	71.4	58.9
Control ($n = 110$)	**0**	11.7	7.2

The gold standard selected in each validation study is highlighted in bold.

m-2010c showed the best kappa and delta values from all options (see Table 5).

We analysed different cut-off points for the WPI and the SS score. We did not observed new cut-off points with better characteristics with maximal area under the curve than those provided in the original m-2010c (WPI $\geqslant 7$ and SS $\geqslant 5$ or WPI 3–6 and SS $\geqslant 9$) (data not shown). Comparisons between the FM group and the control

Table 5 Test characteristics of ACR criteria for classifying FM using clinical diagnosis as the gold standard ($n = 873$)

Criteria	Sensitivity	Specificity	PPV	NPV	PLR	NLR	Accuracy	Kappa	Delta
1990 ACR criteria	84.1	97.6	98.6	75.7	35.3	0.16	0.89	0.76	0.83
m-2010 ACR criteria	88.3	91.8	95.5	79.9	10.8	0.13	0.89	0.77	0.80
1990 or m-2010 ACR criteria	96.7	89.8	94.9	93.3	9.5	0.04	0.94	0.87	0.89
1990 + m-2010 ACR criteria	75.6	99.7	99.8	67.5	222.4	0.24	0.84	0.67	0.81

PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio; m-2010: modified 2010 ACR criteria.

Table 6 Test characteristics of the PSD scale based on receiver operator characteristics analysis ($n = 873$)

PSD	Sensitivity	Specificity	PPV	NPV	PLR	NLR	Accuracy
10	97.9	78.2	89.9	95.0	4.5	0.03	0.91
11	97.1	82.3	91.5	93.4	5.5	0.04	0.92
12	95.7	84.7	92.5	90.9	6.3	0.05	0.92
13	93.6	87.4	93.6	87.4	7.4	0.07	0.92
14	91.7	89.1	94.3	84.5	8.4	0.09	0.91
15	90.2	91.8	95.6	82.6	11.0	0.11	0.91
16	86.7	92.9	96.0	78.0	12.1	0.14	0.89

PSD: polysymptomatic distress; PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio.

group were carried out using ROC analyses for the PSD. Several cut-off scores for the PSD, together with the sensitivity, specificity, PPV, NPV, PLR, NLR and accuracy are shown in Table 6. The best cut-off scores for the PSD were 12 and 13, with a sensitivity of 95.7 and 93.6, respectively, a specificity of 84.7 and 87.4, respectively, and an accuracy of 0.92. A graphical representation of the results from the ROC analyses is presented in supplementary Fig. S1, available at *Rheumatology* Online.

All analyses were repeated with age-matched groups (35–65 years) and sex-separated groups, and the results remained unchanged.

Discussion

The present study showed acceptable validity of the m-2010c as a FM diagnostic tool. When clinical diagnosis was applied as the gold standard, the m-2010c showed greater sensitivity but lower specificity than the 1990c. The cut-off score (WPI $\geqslant 7$ and SS $\geqslant 5$ or WPI 3–6 and SS $\geqslant 9$) published in the original version perfectly fitted our sample and no different cut-off scores showed a substantial improvement. The PSD best cut-off points were 12 and 13, similar to the original version [4, 9]. The combination of both 1990c and m-2010c showed the best test characteristics for the diagnosis of FM.

Age, sex, educational status and occupational status differed between the FM and control groups. Lower levels of education have been associated with an increased prevalence of pain [25] and a higher prevalence rate of FM [26]. Furthermore, FM directly impacts work ability, which implies an indirect economic repercussion. Lower incomes have also been related to a higher prevalence of FM [25–27]. As expected, clinical variables were statistically different between the FM and control groups. Furthermore, the differences observed in tender points count, SS, WPI and PSD between the FM and control groups speaks favourably about the internal consistency of both the 1990c and the m-2010c.

Higher correlations were observed between the m-2010c and various study variables (FIQR, SF-36, MFI and BDI-II) than those obtained for the 1990c and the aforementioned study variables. In line with these results, it has been previously stated that the m-2010c and FIQR can be somewhat compared [9]. We showed a low correlation ($r_p = 0.24$) between the tender points count and FIQR, which indicates that the tender points count by itself may be a poor indicator of FM impact. These results have been shown previously with the FIQ [28, 29]. However, the correlation between the PSD and FIQR was stronger ($r_p = 0.65$) than that observed between the tender points count and the FIQR. This fact, together with the moderate to high correlation with general fatigue and depression (two other highly important FM symptoms [8]) emphasizes the concept of FM as a multisymptom dimensional condition.

There is no gold standard for the diagnosis of FM, which represents a problem when assessing the validity of new criteria. In the absence of this gold standard, an expert consensus was first adopted by Wolfe *et al*. [3] in the 1990c validation study. Subsequently this approach was used in both the 2010 original version and m-2010c [4, 9]. Following this approach, we adopted clinical diagnosis as the gold standard to study the validity of the m-2010c, as previously done in a recent FM criteria validation study in an Iranian population [12].

From the total number of FM participants recruited and diagnosed by rheumatologists, the m-2010c positively identified 88.3%, whereas the 1990 criteria positively identified 84.1%. However, the m-2010c incorrectly classified a higher percentage of control participants as having FM than the 1990 criteria (8.2 *vs* 2.4%). Compared with previous validation studies of the 2010 ACR criteria [4, 10, 12] and m-2010c [9, 13], our results were most accurate when positively identifying FM patients, whereas the incorrect classification of control participants was similar to that presented in previous studies. We further studied the possibility of using both the 1990c and the m-2010c together. Two options were available: (i) participants had to satisfy both criteria to be diagnosed as having FM or (ii) participants had to meet one of two criteria. Although the approach explained in the first option is excellent to reject those without FM (specificity = 99.7), the ability to detect patients with FM was fairly low (sensitivity = 75.6) compared with the 1990c and m-2010c by themselves, which is not acceptable. However, the second option revealed some surprising results, with a sensitivity of 96.7, specificity of 89.9 and accuracy similar for all options. The kappa and delta values for both the 1990c and m-2010c indicated good agreement between these criteria and the clinical diagnosis. Following the same pattern as above, the 1990c or m-2010c combination showed the best agreement. This combination of criteria had not previously been reported, but it seems that when the combination of the two criteria is available, satisfying one of two criteria shows the best overall characteristics to meet the diagnosis of FM. As recently shown, FM patients might not necessarily fulfil the tender points criteria to be diagnosed [30], which agrees with our findings. Furthermore, this criteria combination might help to identify more homogeneous subgroups of patients (e.g. those fulfilling only 1990c, m-2010c, or both criteria). In practice, this would imply retaining clinical and objective review of tender points examination, which would not be ideal in relation to certain types of study such as surveys and large epidemiological studies. However, this would be reasonable (and more accurate overall according to the results of the present study) in the context of clinical practice. Perhaps the m-2010c might be used a priori, due to its simplicity, quickness and self-administration; and for those patients not fulfilling these criteria, the 1990c could provide additional information in order to reach a final diagnosis.

The understanding of FM as a multidimensional disorder raises the importance of the PSD as an FM scale [7]. FM patients are a heterogeneous group and thus their symptomatology may vary between different populations, regions and/or countries [7]. Therefore we studied the possibility of new cut-off points that were able to improve the diagnostic accuracy of the m-2010c. We did not observe any improvement with different cut-off points than those proposed by Wolfe *et al.* [4] in the original version. The PSD has been identified as an important index that might allow FM to be mapped on a dimensional or continuum scale [7, 9]. We further investigated the sensitivity, specificity, PPV, NPV, PLR, NLR and accuracy of different cut-off points than those suggested in the original version [9]. The cut-off points of 12 and 13 were those that best fitted the present study. Both cut-offs showed high sensitivity, specificity and almost identical accuracy. Choosing the cut-off score of 12, the sensitivity increases by 1.9% compared with a cut-off score of 13 and the specificity only decreases by 2.7%. Moreover, this is the original cut-off score proposed for the PSD in the original m-2010c validation [9], and it perfectly fitted our population sample. Previous studies have shown an increase in accuracy with the m-2010c when the cut-off score is changed, reflecting the differences between patients with FM from different countries [10, 12, 13]. However, we found that the original cut-off score perfectly fitted our population and the m-2010c can be used in its original form.

A limitation of the current study is that we did not have an expert consensus as in Wolfe *et al.* [3] and therefore we chose the clinical diagnosis as the gold standard. It is possible that some clinical diagnoses were erroneous, since the clinical diagnosis is not a real gold standard. Although the 2010 ACR criteria have been scientifically translated to Spanish, there is not a Spanish adaptation and psychometric properties study of the m-2010c. The male sample size was low compared with the women's sample size; nevertheless, it is consistent with the general sex prevalence of FM. The study groups showed age differences and women and men were analysed together; however, we repeated all the analyses with age-matched and sex-separated groups, obtaining the same results showed in the present study. The main strength of the present study is its large sample size, which was from southern Spanish population with FM. We also used both the 1990c and the m-2010c in our study sample, which allowed us to compare both criteria and study the usefulness of criteria combinations.

Conclusions

The present study showed the validity of the m-2010c as a FM diagnostic tool in Spain. We suggest using the same cut-off points as the original version. However, the results suggest that using both the 1990c and the m-2010c, and meeting one of the two criteria, might be a better option than using the m-2010c alone. Future studies should examine this combination of criteria.

Rheumatology key messages

- The modified 2010 ACR preliminary criteria are valid for use to diagnose FM in the Spanish population.
- For FM diagnosis, we recommend use of the cut-off points suggested in the modified 2010 ACR preliminary criteria.
- Combination of 1990 and modified 2010 ACR criteria showed the best characteristics for FM diagnosis.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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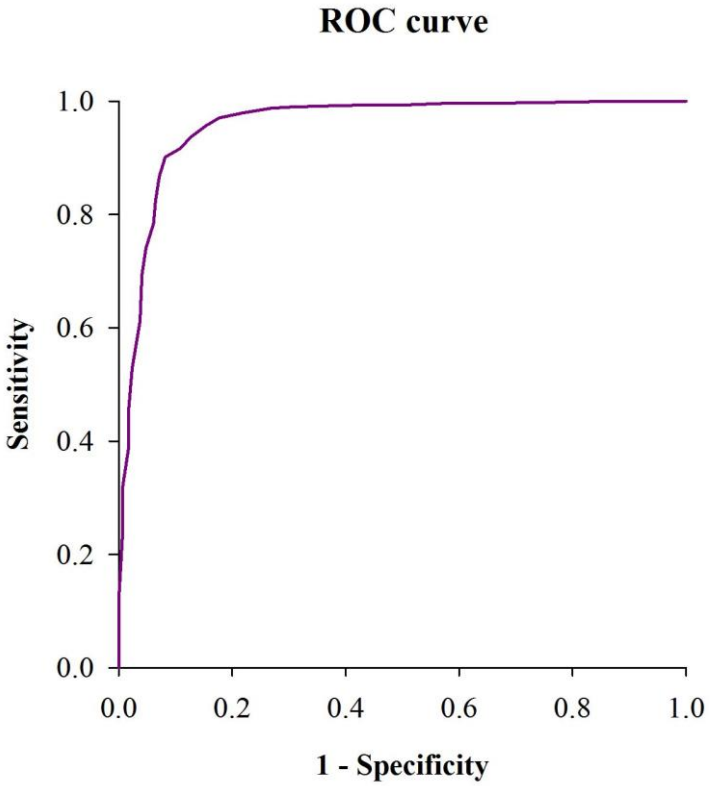

Supplementary Fig. S1. Receiver operator characteristics (ROC) curve for the Polysymptomatic Distress Scale (PSD). The area under the curve (95% confidence intervals) is 0.958 (0.944-0.973), P<0.001.

Fitness Testing in the Fibromyalgia Diagnosis: the al-Ándalus Project.

III

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[1]Department of Physical Education and Sport, Faculty of Sports Sciences, University of Granada, Spain; [2]Department of Physiology and Institute of Nutrition and Food Technology, Faculty of Pharmacy, University of Granada, Spain; [3]Department of Physical Education, Faculty of Education Science, University of Cádiz, Spain

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[1]Department of Physical Education and Sport, Faculty of Sports Sciences, University of Granada, Spain; [2]Department of Physiology and Institute of Nutrition and Food Technology, Faculty of Pharmacy, University of Granada, Spain; [3]Department of Physical Education, Faculty of Education Science, University of Cádiz, Spain

Address correspondence: Virginia Ariadna Aparicio. Department of Physiology. School of Pharmacy and Faculty of Sport Sciences. University of Granada. Campus Universitario de Cartuja s/n. Granada. 18071 (Spain). Telephone: 34-958-243882; Fax: 34-958-248959; E-mail: virginiaparicio@ugr.es.

ABSTRACT

Purpose. To determine the ability of a set of physical fitness tests to discriminate presence/absence of fibromyalgia in women. ***Methods.*** The sample comprised 487 women with fibromyalgia (52.1±8 years) and 250 control women (49.3±9 years). We assessed physical fitness by means of the arm-curl, 30-s chair-stand, handgrip strength, 8-feet up&go, 6-min walk, chair sit&reach and the back-scratch tests. The revised fibromyalgia impact questionnaire was used to assess fibromyalgia severity and symptomatology. ***Results.*** Fibromyalgia patients performed worse than control women in all the fitness tests studied (all, P<0.001). The ROC analysis showed that all the fitness tests were able to discriminate between presence/absence of fibromyalgia (all, P<0.001). The area under the curve ranged from 0.708 to 0.910 (all, P<0.001). Among the fitness tests studied, the arm-curl test, followed by the 30-s chair-stand and handgrip strength tests showed the highest capacity discriminating between the presence/absence of fibromyalgia. An arm-curl test score of <20 repetitions was associated with an increased odds of having fibromyalgia (odds ratio (OR): 35.6; 95% confidence interval [CI]: 12.6-101) in women aged 35-44. An arm-curl test score of <16 repetitions was associated with an increased odds of having fibromyalgia (OR: 23.7; 95% CI: 10.3-54.0) in women aged 35-44. In the group of women aged 55-65, the highest OR was observed for the handgrip strength test and the odds of having fibromyalgia was 17 times greater in those patients who performed at less than 19 kg. ***Conclusions.*** The arm-curl, 30-s chair-stand and handgrip strength tests powerfully discriminated women with fibromyalgia from healthy women. Identification of women who fail to meet the suggested standards can help to easily, quickly and cheaply rule out the presence of the disease, especially in primary care settings.

Key-words: arm-curl, 30-s chair-stand, handgrip strength, women, functional capacity.

INTRODUCTION

Fibromyalgia is a complex multidimensional disorder with pain as its main symptom, but with other relevant non-pain symptoms, such as fatigue, stiffness, memory and cognitive difficulties, among others (1, 32, 39). An equally important feature of fibromyalgia is low physical capacity and functionality, which limit the patients' daily activities and reduces their quality of life (25, 31). The prevalence of comorbidities among fibromyalgia patients is extremely high (38), which increases the patients' needs for appropriate clinical management. This increases healthcare system utilization and implies high treatment consuming and economic burdens (21). Therefore, fibromyalgia has become a recurring health condition with a high prevalence among females between the ages of 40 and 59 years (25).

Fibromyalgia is challenging to diagnose, especially in primary care settings (12, 17, 24). Since the first diagnosis criteria, developed by the American Colleague of Rheumatology (ACR) in 1990 (which was mainly based on the identification of tender points) (39), the diagnosis of fibromyalgia is still a dynamic process where different clinical, psychosocial and functional assessments are implicated (9, 17, 29, 32, 37, 40). Indeed, as time has passed, several objections to the first ACR criteria were noted, highlighting the fact that tender points cannot be an objective assessment of whole bodily pain (2, 37). Moreover, it became increasingly clear that the tender point count was rarely performed in primary care settings where most fibromyalgia diagnoses occurred and were oftentimes performed incorrectly (17). Furthermore, digital palpation instead of algometry was the most widely used method among examiners (17). Therefore, without an objective instrument, the application of equal pressure of 4 kg is doubtful (17, 29). For this reason, in 2010, the ACR released new diagnostic criteria avoiding the requirement of tender points examination (37). Therefore, various instruments and criteria are

currently being used for fibromyalgia diagnosis and monitoring. While fibromyalgia remains an integral part of rheumatology, it is not an exclusive rheumatic condition and spans a broad range of medical disciplines (18).

In 2006, Mannerkopi et al. (23) suggested that fitness testing (especially the handgrip strength and the 6-min walk tests) might complement the previously used tools used in the clinical examination when planning treatment for fibromyalgia patients. In 2007, Bush et al. (11) highlighted the importance of a better characterization of fibromyalgia patients' physical fitness/functional capacity levels. Consequently, our group studied the usefulness of fitness testing for the assessment and monitoring of fibromyalgia (3, 6), and its relationship with fibromyalgia severity and symptomatology (14, 15). We concluded that worse functional capacity is associated to the fibromyalgia-related symptomatology (14, 15), and that the handgrip strength and the 30-s chair stand tests are useful complementary tools for the diagnosis and monitoring of the disease (3, 6). However, we did not propose fitness cut-off points for different age groups. Because older age is associated to lower fitness levels, (8) we hypothesize that the cut-off points might differ across age ranges.

Practitioners need practical tools for the correct diagnosis of fibromyalgia, to complete the patient's overall health status, and to test the effectiveness of specific treatments. Therefore, we have replicated our preliminary study (3, 6) with a larger sample size and with age-specific analyses in order to establish new cut-off points capable to enhance the current diagnosis accuracy. Therefore, the present study aimed to determine the ability of a set of seven physical fitness tests to discriminate between the presence or absence of fibromyalgia in women of different ages.

MATERIALS AND METHODS

Study sample and design

Fibromyalgia patients were recruited from different fibromyalgia associations via e-mail, letter or telephone. We also recruited a representative group of control women and men with similar ages, socio-demographic characteristics and demographic area, via e-mail and internet advertisements, in order to carry out appropriate comparisons between groups. All interested participants signed a written informed consent after receiving detailed information about the aims and study procedures. The inclusion criteria for fibromyalgia participants were: i) to be previously diagnosed by a rheumatologist (patients were asked to provide their medical records to confirm their previous diagnosis); ii) to meet the 1990 ACR fibromyalgia criteria: widespread pain for more than 3 months and pain $\leq$4 kg/cm^2 of pressure for 11 or more of 18 tender points (39); iii) not to have acute or terminal illness (such as cancer, stroke, recent cardiopathy, severe coronary disease, schizophrenia, or any other disabling injury), or severe dementia (Mini Mental State Examination (MMSE) <10) (33); iv) to meet age criteria: 35-65 years old. The inclusion criteria for control women were: 1) not to meet the 1990 ACR fibromyalgia criteria; 2) not to have acute, terminal illness, or severe dementia (MMSE <10) (33); 3) to meet age criteria: 35-65 years old. From an initial sample of 960 participants, the following subjects were excluded: 38 fibromyalgia participants had not been previously diagnosed by a rheumatologist, 1 fibromyalgia women presented severe dementia, 101 fibromyalgia participants did not meet the 1990 ACR criteria, whereas 7 control participants met it. Finally, we decided to exclude 65 men (21 fibromyalgia and 44 control men) for the present data analysis due to the low male fibromyalgia sample size recruited. To ensure that all tests had the same statistical power, only those subjects who had valid data in all physical fitness tests were included in the analyses. Therefore, the final

study sample comprised 487 (52.1±8.0 years) female fibromyalgia patients vs. 250 (49.3±9.9 years) region-matched control women.

All the measurements were performed by the same trained research team in order to reduce inter-examiner error. The present project was reviewed and approved by the Ethics Committee of the Hospital Virgen de las Nieves, Granada (Spain). Moreover, the present study has been conducted in conformance with the policy statement of the ACSM as published by *Medicine & Science in Sports & Exercise*®.

Material and procedures

Anthropometry and body composition

We used a portable eight-polar tactile-electrode impedanciometer (InBody R20, Biospace, Seoul, Korea) to measure body weight (kg), body fat (kg and %) and skeletal muscle mass (kg). Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). Body mass index (BMI) was calculated as weight (kg) divided by squared height (m^2). Waist circumference (cm) was measured with the participant standing at the middle point between the ribs and ileac crest (Harpenden anthropometric tape, Holtain Ltd).

Sociodemographic and clinical data acquisition

Sociodemographic information was recorded using a self-report instrument that included date of birth, marital status, educational status, current occupational status and time since fibromyalgia diagnosis, among other questions. Participants received instructions on how to complete such self-administered questionnaire. Smoking status and questions regarding pharmacology or the presence of other diseases were asked to all the participants by an examiner through an initial survey.

The Mini Mental State Examination

The Spanish version of the MMSE (33) was administered to participants confidentially by trained interviewers to assess cognitive function and severity of dementia. Five areas of cognitive functioning were assessed: orientation, immediate memory, attention/concentration, delayed recall and language.

The modified 2010 ACR fibromyalgia diagnostic criteria

This questionnaire (36) is composed by two scales: 1) The widespread pain scale asking participants to grade whether (or not) they had pain or tenderness in the previous week in 19 body areas and, 2) The symptom severity scale asking participants to indicate the severity of fatigue, trouble thinking or remembering, and waking up tired (unrefreshed) over the previous week. Patients were also asked to answer whether they had had pain or cramps in the lower abdomen, depression, or headache during the previous 6 months. The widespread pain index and the symptom severity scale were subsequently summed into an index called "polysymptomatic distress scale" (35). We used the Spanish version, which has shown high sensitivity and specificity for fibromyalgia diagnosis (30).

Tenderness

We assessed 18 tender points according to the 1990 ACR criteria for classification of fibromyalgia (39) using a standard pressure algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). The mean of the two measurements at each tender point was used for the analysis. A tender point was scored as positive when the patient noted pain at pressure ≤ 4 kg/cm^2. The total count of positive tender points (tender points count) was recorded for each participant. An algometer score was calculated as the sum of the minimum pain-pressure values

obtained for each tender point. The average score of two measurements for each tender point was used in the analysis.

Fibromyalgia Impact

The revised Fibromyalgia Impact Questionnaire (FIQR)(22) is a self-administered questionnaire, comprising 21 individual questions with a rating scale of 0 to 10. These questions compose 3 different domains: function, overall impact and symptoms (ranging 0-30, 0-20 and 0-50, respectively). The FIQR total score ranges from 0 to 100, with higher score indicating greater impact of the disease.

Physical fitness testing

The Functional Senior Fitness Test battery was used because it is relatively easy to administer, safe, and requires minimal equipment and space (27). It has shown no ceiling and floor effects, which is a relevant aspect for this study due to the heterogeneity of fibromyalgia patients (34). Therefore, the tests used are feasible to perform in clinical and community settings. Additionally, we also measured the handgrip strength test which is commonly used in fibromyalgia patients (13). The main functional capacity components studied were:

Lower-body muscular strength. The "30-s chair-stand test" involves counting the number of times within 30 seconds that an individual can rise to a full stand from a seated position with back straight and feet flat on the floor, without pushing off with the arms. The arms were crossed at the chest level (27).

Upper-body muscular strength. The handgrip strength was assessed using a hand dynamometer with adjustable grip (TKK 5101 Grip D; Takey, Tokio Japan). The subject continuously and gradually squeezes for at least two seconds, using optimal grip-span, which was calculated using the formula by Ruiz et al. (28): $y = x/5 + 1.5$; "x" being the hand size, and

"y" the grip length. Each patient completed two attempts with each hand, with the arm fully extended, forming an angle of 30° with respect to the trunk (28). The maximum score in kilograms for each hand was recorded and the mean score of left and right hands was was used in the analyses. We also included the "Arm-curl test", which measures the number of times that with the person seated, a hand weight (2.3 kg for women) can be curled through a full range of motion within 30s (27). Patients performed one trial with both hands and the average was used in the analyses.

Lower-body flexibility. In the "chair sit & reach test", the patient seated with one leg extended, slowly bends forward sliding the hands down the extended leg in an attempt to touch (or pass) the toes (27). The number of centimetres short of reaching the toe (minus score) or reaching beyond it (plus score) was recorded. Two trials with each leg were performed, and the best value for each leg was recorded. The average of both legs was used in the analysis.

Upper-body flexibility. The "back-scratch test", a measure of overall shoulder range of motion, involves measuring the distance between (or overlap of) the middle fingers behind the back with a ruler (27). This test was assessed twice, alternately with both hands, and the best value was recorded. The average of both hands was used in the analysis.

PARAGRAPH 18: *Motor agility/dynamic balance*. The "8-feet up & go" test" consists in standing up from a chair, walking 8-feet (2.44 meters) to and around a cone, and returning to the chair in the shortest possible time (27). The best time (in seconds) of two trials was recorded and used in the analysis.

Aerobic endurance/cardiorespiratory fitness. This test was assessed by the "6-min walk test". This test involves determining the maximum distance (meters) that can be walked in 6 min along a 45.7 meters rectangular course (27).

Statistical analysis

The comparisons between women with fibromyalgia and controls were performed using one-way analysis of covariance (ANCOVA) after adjustment for age and BMI. We adjusted all the models for age and BMI due to the fact that both are inversely related to fitness and fibromyalgia symptomatology (4, 5, 20). The occupational and educational status and the intake of painkillers, stimulants and antidepressants were further added as covariates to test their potential confounder effect on body composition and physical fitness. Differences in categorical variables were assessed with the Chi-square test. The relationships between all fitness tests and FIQR, the modified 2010 ACR fibromyalgia diagnostic criteria and tenderness in fibromyalgia patients were analyzed by partial correlations after adjustment for age and BMI.

We further categorized the sample by age-specific groups (women aged 35-44, 45-54 and 55-65 years old). The fitness test thresholds that best discriminated between presence and absence of fibromyalgia for the entirely sample and for each age-specific group were determined using receiver operating characteristic (ROC) curve analysis (41). To identify the best threshold, the distance between the perfect test and each sensitivity and 1-specificity pair was calculated, and then, the pair closest to 1 was chosen. We also calculated the area under the curve (AUC) and 95% confidence intervals (CI). The AUC represents the ability of the specific fitness test to correctly classify subjects as having vs. not having fibromyalgia. The values of AUC range between 1 (perfect test) to 0.5 (worthless test). Binary logistic regression was used to further study the relationship between fitness testing and presence/absence of fibromyalgia for the entirely sample and for each age-specific group, after adjustment for age and BMI. All the analyses were performed using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 20.0; Armonk, NY) and the level of significance was set at $P<0.05$.

RESULTS

Socio-demographic and clinical characteristics of the study sample by groups are presented in **table 1**. No differences between groups were observed on marital status and smoking status. Age, tender points count, FIQR, educational status and current occupational status differed between groups (all, $P<0.001$). Regarding medication, fibromyalgia patients consumed more painkillers, laxatives, antidepressants and stimulants in the last two weeks than the control group (all, $P<0.001$).

Anthropometric and fitness characteristics of the study sample by presence/absence of fibromyalgia after adjustment for age are shown in **table 2**. Body mass index, waist circumference and fat percentage were higher, whereas height was lower in fibromyalgia compared to the control group (all, $P<0.001$). The fibromyalgia group performed worse in all the fitness tests compared to their healthy peers (all, $P<0.001$). After further adjustment for age, educational status, occupational status, BMI and medication, the results remained unchanged (all, $P<0.001$).

Partial correlations between fitness testing and the FIQ-R, the modified 2010 ACR fibromyalgia diagnostic criteria, and tenderness among fibromyalgia patients, are shown in **table 3**. Most of fitness tests were inversely correlated with the FIQR total score, the modified 2010 ACR fibromyalgia diagnostic criteria and all the FIQR dimensions (except for the tenderness level). The 30-s chair-stand and the arm-curl tests were the most correlated with the FIQR total score and the FIQR dimensions, the Widespread Pain Index, the Symptom Severity, and the Polysymptomatic Distress Scale. The arm-curl test, followed by the 30-s chair-stand, the chair sit & reach, and the handgrip strength, were those more strongly associated to the tender points count and the algometer score (all, $P<0.001$).

Table 4 shows the capacity of each fitness test to discriminate between presence/absence of fibromyalgia. The ROC analysis showed that all the studied fitness tests were able to discriminate between presence and absence of fibromyalgia for the entire sample and for age-specific groups. The AUC for the whole study sample ranged from 0.741 to 0.893. The age-specific analyses revealed an AUC ranging from 0.793 to 0.910 for women aged 35-44 years, from 0.726 to 0.901 for women aged 45-54 years, and from 0.708 to 0.846 for women aged 55-65 years old.

The arm-curl, followed by the 30-s chair-stand and the handgrip strength tests, showed the highest capacity to discriminate presence/absence of fibromyalgia for the entire study sample (AUC=0.89, 0.87 and 0.83, respectively, all, P<0.001). The same trend was observed for the age-specific groups, except for the handgrip strength test, that showed a lower capacity than other tests for the group of women 35-44 years but a high ability identifying fibromyalgia in women aged 55-65 years.

Table 5 shows the cut-off points, OR and 95% CI of the physical fitness tests to identifying fibromyalgia presence/absence after adjusting for age and BMI. The arm-curl and 30-s chair stand tests showed the highest ability to discriminate fibromyalgia presence/absence. The optimal cut-off point to discriminate between fibromyalgia presence/absence with the arm-curl test in women aged 35-44 years was <20 repetitions. An arm-curl test <20 repetitions was associated with an increased odds of having fibromyalgia (OR: 35.6; 95% CI: 12.6–101) in women aged 35-44 years. The optimal cut-off point to discriminate between fibromyalgia presence/absence with the 30-s chair-stand test in women aged 35-44 years was <13 repetitions. A 30-s chair-stand test <13 repetitions was associated with an increased odds of having fibromyalgia (OR=22.0; 95% CI: 7.6–63.8) in women aged 35-44 years. The optimal cut-off

point to discriminate between presence/absence of fibromyalgia for the arm-curl test in women aged 45-54 years was <16 repetitions. An arm-curl test <16 repetitions was associated with an increased odds of having fibromyalgia (OR: 23.7; 95% CI: 10.3–54.0) in women aged 45-54 years. The optimal cut-off to discriminate between presence/absence of fibromyalgia for the 30-s chair-stand test in women aged 45-54 years was <12 repetitions. A 30-s chair-stand test <12 repetitions was associated to an increased odds of having fibromyalgia (OR=19.9; 95% CI: 9.4–42.1) in women aged 45-54 years. In the group of women aged 55-65 the higher ORs were observed for the handgrip strength test. A handgrip strength test score <19 kg was associated with an increased odds of having fibromyalgia (OR=17.0; 95% CI: 6.4-44.8).

DISCUSSION

The main findings of the present study indicate that fitness testing is a powerful tool to discriminate between presence/absence of fibromyalgia in women, regardless of the age range of the women. These results support our previous findings, and highlight the importance of implementing fitness testing as a complementary tool for the diagnosis and monitoring of fibromyalgia (3, 6). The arm-curl, 30-s chair-stand and handgrip strength tests were those that more potently discriminated women with fibromyalgia from healthy women. An arm-curl test score of <20 repetitions, was associated to 36 times greater increased odds of having fibromyalgia in women aged 35-44. An arm-curl test score <16 repetitions, was associated to 24 times greater increased odds of having fibromyalgia in women aged 45-54. In the group of women aged 55-65, the highest OR were observed for the handgrip strength test. The odds of having fibromyalgia was 17 times greater in those patients who performed <19 kg. In agreement with previous studies from our group (3, 6), we recommend the use of fitness testing in clinical setting as a quick and complementary tool for the fibromyalgia diagnosis.

As expected, we observed that fibromyalgia patients to have lower functional capacity than healthy women in all the studied physical fitness tests. Therefore, we confirm that physical fitness is clearly decreased in people with fibromyalgia compared to age-matched healthy peers (14, 23, 31), and is similar to healthy older adults (14, 26). Hence, fibromyalgia patients have an impaired functional capacity with a high risk of disability and difficulties on doing tasks associated with staying physically independent (26). Patients with chronic pain use to reduce their physical activity and thus display a deconditioned fitness status (10, 14). Indeed, in the recent study by Bjornsdottir et al. (10) the authors studied the consequences of chronic pain in 5906 Icelanders aged 18-79 years reporting chronic low back pain, chronic neck symptoms, and/or fibromyalgia with the aim of analyze the global burden imposed by chronic pain conditions. Several symptoms and functional limitations in daily life were strongly associated with chronic pain, including deficient energy and muscular discomfort, physical mobility limitations, lifting groceries, climbing stairs, and stooping (10). The authors also found that women, but not men, with chronic pain tended to refrain from physical activity (10).

Pain is the more predominant symptom in fibromyalgia and can be on the basis of the lower functional capacity observed (10, 14). Our group previously examined the association between pain and functional capacity levels in a smaller sample of similar age and region (14). We observed an inverse association of tender points count with the 30-s chair-stand and the distance covered in the 6-min walk tests, and a positive association of the algometer score with the 30-s chair-stand, the 6-min walk and the back scratch tests. However, we did not assess the arm-curl test and we found that weight status seems to play a role in these associations. This is the reason why all the analysis performed in the present study related to fitness were adjusted for BMI. Our results concur with these studies suggesting that the higher the muscle strength the

lower the pain and symptomatology reported (7, 19). Hooten et al. (19) found that higher knee extensor isometric and isokinetic strength was associated with lower pressure pain threshold. Similarly, Assumpção et al. (7) observed that muscle strength (knee and elbow extension) was related to pain threshold and pain on a visual analogue scale. However, the association of aerobic fitness with pain and symptomatology in women with fibromyalgia is not clear, with some studies reporting a certain degree of association (14, 15), while other reporting lack of relationship (19).

Our first study analysing the utility of physical fitness testing for the diagnosis and monitoring of fibromyalgia was solely performed assessing the handgrip strength test in 81 female fibromyalgia patients and 44 control women (6). We observed that a score lower to 23 kg was associated with 34 times higher odds of having fibromyalgia, after adjustment for age (6). In the present study, this association was lower but we have included higher sample size and further adjusted for age, BMI and medication, and thus, gained in accuracy. In our subsequent study (3), the sample comprised 94 female fibromyalgia patients and 66 healthy controls. That time, we assessed the same physical fitness tests battery than in the present study, except for the inclusion of the arm-curl test and the exclusion of the 30-s blind flamingo test (static balance) this time. We observed that all fitness tests, except the back-scratch test, were able to discriminate between presence/absence of fibromyalgia (3). We found that the 30-s chair-stand test showed the highest ability to discriminate presence/absence of fibromyalgia (we did not assess the arm-curl test) (3). A chair-stand test lower to <10 repetitions was then associated to 52 times higher odds of having fibromyalgia whereas in the present study we have modified the cut-off up to <12 repetitions for the entirely sample size. This time we have also proposed a cut-off point <13 for women aged 35-44 and <11 for women aged 55-65. Therefore, the 30-s chair-stands test showed a remarkable

discriminative capacity to identify fibromyalgia presence (being now the second proposed test). Indeed, muscle strength, as measured by the arm-curl, the 30-s chair-stand and the handgrip strength tests appear to be the most discriminative fitness tests in order to establish fibromyalgia presence/absence.

As recently shown, fibromyalgia patients might not necessarily fulfill the tender points criteria to be diagnosed (9, 37), which concurs with our proposal of including new clinical tools for the diagnosis of the fibromyalgia. In fact, in an attempt to avoid the requirement of the tender points examination, the ACR released new diagnostic criteria in 2010 (37) which is gaining widespread acceptance. Recently, a study displayed that the combination of the 1990 criteria and the modified 2010 ACR criteria showed a higher sensitivity and specificity for fibromyalgia diagnosis than the 1990 or the modified 2010 ACR criteria independently (30). Due to the unknown etiology of fibromyalgia, there is not a gold standard instrument for its diagnosis. Consequently, the study by Segura et al. (30) showed that the use of different validated diagnostic tools together might enhance the accuracy of the fibromyalgia diagnosis. This highlights the need for additional diagnostic tools in fibromyalgia. In this context, fitness testing assessment might improve the diagnostic accuracy of fibromyalgia syndrome and supplement current diagnostic tools, which in turns might also help to identify more heterogeneous subgroups of patients (e.g. those fulfilling only ACR-1990, or ACR-2010 or both criteria). In the present study, we found a positive relationship between better fitness tests scores and lower global score of FIQR, FIQR dimensions and the modified 2010 ACR criteria. Furthermore, most of the studied tests were also correlated with tender points count and algometer score, which reinforces the utility of fitness testing instead of the classical, and more complicated, tender points assessment (17).

Fatigue has been shown as the second most reported symptom in fibromyalgia (32). We have observed the highest correlations between FIQR-energy rating/fatigue and fitness testing thorough the 30-s chair-stand test (lower body muscle strength), followed by the arm-curl test (upper-body muscle strength), which strengthen the idea that the muscle strength tests proposed in the present study are also sensitive to other important fibromyalgia's key symptoms.

Some limitations need to be mentioned. First, the male sample size was too small to perform the present statistical approach and most of the statistical analysis tests would not be possible or representative (i.e. partial correlations, AUC and ROC analysis, binary logistic regression analysis, and of course classifications by age-groups), so this study was carried out only in women, and future studies should replicate this analysis in larger samples in men with fibromyalgia. Moreover, as physical fitness levels clearly differ between genders we could not merge both groups. Second, the higher pain observed in the participants with lower fitness levels could have been influenced by the fear of pain phenomena (16). Third, we have not objectively assessed physical activity levels among the sample. Finally, in the same way that tender points and the new 2010 diagnosis criteria may erroneously classify people with fibromyalgia when they are healthy, fitness testing can also make that error, classifying a healthy person with little fitness as a person with fibromyalgia. Therefore, the proposed tests should be used just as additional tools for the diagnosis and not as the only source of criteria. On the other hand, compared to previous literature, the present study involved a large and representative sample (almost five hundred female fibromyalgia patients and two hundred and a half age-matched controls women from the same geographical area). Furthermore, this study examined a complete range of functional capacity parameters in a single report, which allowed us to make comparisons between fitness tests. Finally, due to the high sample size recruited in the present

replication study, we could further establish age-specific fitness cut-off points (i.e. for women aged 35-44, 45-54 and 55-65 years old).

Clinical Implications

The present study has several clinical implications to highlight. These results reinforce our previous hypothesis that physical fitness could be set as a complementary tool for the diagnosis and monitoring of fibromyalgia in clinical settings. The high capacity of the proposed fitness tests to discriminate between presence or absence of fibromyalgia and the fact that they are inexpensive and easily accessible facilitates the inclusion of fitness testing as a complementary fibromyalgia diagnostic tool. This, in turn, might also assist the clinician in targeting treatment. Particularly, the arm-curl and the 30-s chair-stand tests have a great potential in a clinical setting for several reasons: First, a dumbbell or a chair and a stopwatch is all the equipment needed to perform them, so they are extremely cheap. Second, the time needed to perform these test is just 30s (2-3 minutes in total), which is a fundamental issue for clinicians who are usually under time constrains. Third, other fitness tests, such as the 6-min walk test, require larger spaces, while the arm-curl and the 30-s chair-stand tests can be performed in any room without any special requirement. Forth, the procedures for these test are simple and do not require any particular training. In addition to these tests, we suggest the use of the handgrip strength test for women aged 55-65 years old (but a hand dynamometer is required).

CONCLUSION

We observed that physical fitness in general, and particularly the arm-curl and the 30-s chair-stand tests, powerfully discriminate the presence/absence of fibromyalgia in women. We found other test able to discriminate between presence/absence of fibromyalgia; and based on the results, we also suggest the use of the handgrip strength test for a more thorough evaluation,

mainly among women aged 55-65 years old. Fitness testing can serve as a complement to the current fibromyalgia diagnosis criteria in order to achieve a better discrimination between healthy status and fibromyalgia presence. Identification of women who fail to meet the proposed cut-off points can help to easily, quickly and cheaply discriminate and rule out the presence of the disease, especially in primary care settings.

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Competing interests

None of the authors have any conflict of interests.

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Table 1.Socio-demographic and clinical characteristics of the study sample by groups.

	Fibromyalgia patients	Healthy women	P
	Mean (SD)	**Mean (SD)**	
Age (years)	51.9 (8.3)	49.3 (9.9)	<0.001
Tender points count (kg/cm^2)	16.8 (1.9)	2.8 (2.9)	<0.001
Algometer score	42.8 (13.4)	109.9 (22.3)	<0.001
FIQ-R	64.5 (16.7)	27.0 (8.5)	<0.001
	N (%)	**N (%)**	
Marital status			
Married	367 (75.5)	175 (70.3)	
Single	40 (8.2)	34 (13.7)	
Separated	15 (3.1)	13 (5.2)	0.138
Divorced	38 (7.8)	16 (6.4)	
Widow	26 (5.3)	11 (4.4)	
Educational status			
No studies	53 (10.9)	17 (6.8)	
Primary school	233 (47.9)	93 (37.2)	
Professional training	75 (15.4)	39 (15.6)	0.022
Secondary school	59 (12.1)	43 (17.2)	
University medium degree	42 (8.6)	32 (12.8)	
University higher degree	24 (4.9)	26 (10.4)	
Current occupational status			
Working	121 (24.9)	100 (40.0)	
Unemployed	85 (17.5)	40 (16.0)	
Sick leave	35 (7.2)	2 (0.8)	<0.001
Retired/pensioner	85 (17.5)	15 (6.0)	
Student	5 (1.0)	8 (3.2)	
Housewife	155 (31.9)	85 (34.0)	
Medication (last two weeks)			
Painkillers	435 (89.7)	132 (53.2)	<0.001
Laxatives	99 (20.4)	22 (8.9)	<0.001
Antidepressants	280 (57.7)	25 (10.1)	<0.001
Stimulants	35 (7.2)	1 (0.4)	<0.001
Contraceptives	13 (2.7)	11 (4.4)	0.134
Hormonal replacement for menopause	12 (2.5)	8 (3.2)	0.539
Medication for losing weight	12 (2.5)	4 (1.6)	0.533
Time since diagnosis			
Less than 1 year	33 (6.8)	-	
Between 1 and 5 years	166 (35.3)	-	
More than 5 years	274 (57.9)	-	
Smoking everyday	121 (24.9)	51 (20.6)	0.902

SD, standard deviation; FIQR, Revised Fibromyalgia Impact Questionnaire.

Table 2: Anthropometric and functional capacity of the study samples.

	Fibromyalgia patients (n=487)	**Healthy women (n=250)**	**P[a]**	**P[b]**
Weight (kg)	71.3 (14.0)	67.8 (12.7)	0.049	0.002
Height (m)	157.8 (6.0)	159.8 (6.2)	<0.001	<0.001
Body mass index (kg/m^2)	28.6 (5.4)	26.5 (4.6)	<0.001	<0.001
Muscle mass (kg)	22.7 (3.3)	23.0 (3.3)	0.050	0.064
Fat mass (%)	40.1 (7.7)	36.7 (7.5)	<0.001	<0.001
Waist circumference (cm)	90.6 (13.1)	85.4 (12.5)	<0.001	<0.001
Physical fitness tests				
Arm-curl (rep.)	14.3 (4.96)	22.7 (4.62)	<0.001	<0.001
30-s chair-stand (rep.)	10.3 (3.32)	15.3 (3.05)	<0.001	<0.001
Handgrip strength (kg)	19.7 (7.59)	29.6 (8.06)	<0.001	<0.001
8-feet up & go # (s)	7.02 (2.34)	5.27 (1.03)	<0.001	<0.001
6-min walk (m)	483.5 (89.6)	586.3 (73.3)	<0.001	<0.001
Chair sit & reach (cm)	-11.4 (12.1)	2.49 (10.7)	0.001	<0.001
Back-scratch (cm)	-14.5 (12.7)	-5.70 (9.82)	<0.001	<0.001

Values are expressed as mean (standard deviation); # Lower scores indicate better performance. P[a] values are shown after adjusting the model for age. P[b] Model adjusted for age, occupational status, educational status and medication. Physical fitness was further adjusted for body mass index.

Table 3. Partial correlations between fitness testing and the Revised Fibromyalgia Impact Questionnaire (FIQ-R), the modified American Colleague of Rheumatology (ACR) 2010 fibromyalgia diagnostic criteria and tenderness in the fibromyalgia patients group.

	Chair sit & reach	Back scratch	Handgrip strength	Chair stand	8-feet up & go #	Arm-curl	6-min walk
FIQR							
FIQR total score	-0.318 ‡	-0.291 ‡	-0.221 ‡	-0.357 ‡	-0.245 ‡	-0.336 ‡	-0.344 ‡
FIQR symptoms	-0.307 ‡	-0.303 ‡	-0.230 ‡	-0.315 ‡	-0.229 ‡	-0.277 ‡	-0.307 ‡
FIQR overall impact	-0.270 ‡	-0.226 ‡	-0.119†	-0.275 ‡	-0.177 ‡	-0.267 ‡	-0.278 ‡
Pain rating	-0.233 ‡	-0.223 ‡	-0.180 ‡	-0.224 ‡	-0.168 ‡	-0.225 ‡	-0.232 ‡
Energy rating/fatigue	-0.225 ‡	-0.212 ‡	-0.207 ‡	-0.301 ‡	-0.195 ‡	-0.253 ‡	-0.253 ‡
Stiffness rating	-0.282 ‡	-0.239 ‡	-0.146 ‡	-0.180 ‡	-0.123†	-0.167 ‡	-0.174 ‡
Sleep quality/problems	-0.198 ‡	-0.161 ‡	-0.155†	-0.157†	-0.132†	-0.106*	-0.132†
Depression level	-0.262 ‡	-0.251 ‡	-0.159 ‡	-0.246 ‡	-0.220 ‡	-0.232 ‡	-0.287 ‡
Memory problems	-0.166 ‡	-0.188 ‡	-0.122†	-0.210 ‡	-0.109*	-0.165 ‡	-0.214 ‡
Anxiety level	-0.195 ‡	-0.230 ‡	-0.125†	-0.153†	-0.155†	-0.184 ‡	-0.196 ‡
Tenderness level	-0.037	-0.053	-0.040	-0.134†	-0.083	-0.101*	-0.099*
Balance problems	-0.195 ‡	-0.192 ‡	-0.185 ‡	-0.259 ‡	-0.183 ‡	-0.210 ‡	-0.240 ‡
Environmental sensitivity	-0.131†	-0.134†	-0.144†	-0.105*	-0.040	-0.075	-0.056
Modified ACR-2010 fibromyalgia diagnostic criteria							
Widespread Pain Index	-0.150†	-0.134†	-0.110*	-0.132†	.145†	-0.123†	-0.121†
Symptom Severity Score	-0.192‡	-0.186‡	-0.120†	-0.228‡	.176‡	-0.209‡	-0.187‡
Polysymptomatic Distress	-0.201‡	-0.178‡	-0.135†	-0.202‡	.187‡	-0.189‡	-0.175‡
Tenderness							
Number of tender points	-0.178 ‡	-0.113*	-0.177 ‡	-0.169 ‡	-0.103*	-0.204 ‡	-0.129†
Algometer score	0.224 ‡	0.125†	0.178 ‡	0.245 ‡	0.207 ‡	0.271 ‡	0.173 ‡

* P<0.05, † P< 0.01, ‡ P<0.001; # Lower score indicates better performance; Model adjusted for age and body mass index.

Table 4. Ability (receiver operating characteristics curve analysis) of different fitness tests to discriminate between presence/absence of fibromyalgia.

Presence/absence of fibromyalgia	**All age groups** (487 fibromyalgia patients vs. 250 control women)		**Women aged 35-44 years** (102 fibromyalgia patients vs. 72 control women)		**Women aged 45-54 years** (211 fibromyalgia patients vs. 114 control women)		**Women aged 55-65 years** (174 fibromyalgia patients vs. 64 control women)	
Fitness Tests	**AUC (SEM)**	**95% CI**	**AUC (SEM)**	**95% CI**	**AUC (SEM)**	**95% CI**	**AUC (SEM)**	**95% CI**
Arm-curl	0.893 (0.01)	0.869-0.916	0.910 (0.02)	0.865-0.955	0.901 (0.02)	0.866-0.935	0.846 (0.03)	0.786-0.906
30-s chair-stand	0.866 (0.01)	0.839-0.894	0.919 (0.02)	0.879-0.959	0.863 (0.02)	0.822-0.904	0.825 (0.03)	0.763-0.888
Handgrip strength	0.834 (0.01)	0.806-0.862	0.798 (0.03)	0.730-0.866	0.855 (0.02)	0.813-0.897	0.811 (0.03)	0.752-0.870
8-feet up & go	0.832 (0.02)	0.802-0.860	0.871 (0.02)	0.817-0.925	0.858 (0.02)	0.815-0.901	0.778 (0.03)	0.711-0.845
6-min walk	0.820 (0.02)	0.791-0.846	0.816 (0.02)	0.753-0.880	0.838 (0.02)	0.794-0.882	0.748 (0.03)	0.674-0.822
Chair sit & reach	0.811 (0.02)	0.778-0.844	0.836 (0.03)	0.775-0.896	0.799 (0.03)	0.745-0.852	0.796 (0.03)	0.729-0.862
Back-scratch	0.741 (0.02)	0.703-0.779	0.793 (0.02)	0.724-0.863	0.726 (0.02)	0.668-0.783	0.708 (0.03)	0.634-0.783

AUC, area under de curve; SEM, standard error of the mean; CI, confidence interval. All, $P<0.001$.

Table 5. Binary logistic regression statistics testing the predictive capacity of the fitness testing thresholds derived from the receiver operating characteristic curve analysis for presence/absence of fibromyalgia.

		Low fitness (based on the cut-off)											
		All age groups (487 fibromyalgia patients vs. 250 control women)			**Women aged 35-44 years** (102 fibromyalgia patients vs. 72 control women)			**Women aged 45-54 years** (211 fibromyalgia patients vs. 114 control women)			**Women aged 55-65 years** (174 fibromyalgia patients vs. 64 control women)		
	Fitness test	**Cut-off point**	**OR**	**95% CI**	**Cut-off point**	**OR**	**95% CI**	**Cut-off point**	**OR**	**95% CI**	**Cut-off point**	**OR**	**95% CI**
Presence/ absence of fibromyalgia	*Arm-curl (rep.)*	<16	20.4	11.9-34.7	<20	35.6	12.6-101	<16	23.7	10.3-54.0	<16	12.6	5.3-27.7
	30-s chair-stand (rep.)	<12	16.7	10.2-27.3	<13	22.0	7.6-63.8	<12	19.9	9.4-42.1	<11	12.9	5.2-31.8
	Handgrip strength (kg)	<20.9	14.7	8.9-24.6	<22.1	17.3	6.1-49.1	<21.6	17.5	8.2-37.0	<19.1	17.0	6.4-44.8
	8-feet up & go # (s)	≥5.3	9.9	6.8-14.4	≥5.1	12.0	5.6-25.8	≥5.3	12.6	6.9-23.1	≥5.9	7.3	3.9-13.7
	6-min walk (m)	<510	8.3	5.3-12.8	<551	8.1	3.3-19.6	<504	12.5	5.9-26.5	<500	5.3	2.7-10.5
	Chair sit & reach(cm)	<-6.7	10.4	6.8-15.7	<-5.7	19.2	7.3-50.1	<-6.7	9.9	5.3-18.3	<-9.7	12.1	5.3-27.5
	Back-scratch (cm)	<-10	4.7	3.2-6.8	<-8.7	7.5	2.8-19.8	<-8.9	3.7	2.1-6.5	<-11.7	4.5	2.3-8.9

High fitness was used as reference; # A score above the threshold indicates a lower fitness, opposite to the rest of the tests; OR, odds ratio; CI, confidence interval.

3. THE USEFULNESS OF SELF-REPORTED PHYSICAL ACTIVITY QUESTIONNAIRES IN FIBROMYALGIA

(Paper IV and V)

Comparison of physical activity using questionnaires (LTPAI and PAHWI) and accelerometry in fibromyalgia patients: the al-Ándalus project.

Segura-Jiménez V, Alvarez-Gallardo IC, Romero-Zurita A, Camiletti-Moirón D, Munguía-Izquierdo D, Carbonell-Baeza A, Ruiz JR.

IV

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ORIGINAL ARTICLE

Comparison of Physical Activity Using Questionnaires (Leisure Time Physical Activity Instrument and Physical Activity at Home and Work Instrument) and Accelerometry in Fibromyalgia Patients: The Al-Ándalus Project

Víctor Segura-Jiménez, BSc,[a] Inmaculada C. Álvarez-Gallardo, BSc,[a] Alejandro Romero-Zurita, PhD,[a] Daniel Camiletti-Moirón, BSc,[a,b] Diego Munguía-Izquierdo, PhD,[c] Ana Carbonell-Baeza, PhD,[d] Jonatan R. Ruiz, PhD[a]

From the [a]Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada; [b]Department of Physiology, Faculty of Pharmacy, University of Granada, Granada; [c]Department of Sports and Informatics, Section of Physical Education and Sports, Faculty of Sport, University Pablo de Olavide, Seville; and [d]Department of Physical Education, Faculty of Sciences Education, University of Cádiz, Cádiz, Spain.

Abstract

Objective: To compare the levels of physical activity (PA) assessed with questionnaires (Leisure Time Physical Activity Instrument [LTPAI], Physical Activity at Home and Work Instrument [PAHWI]) and accelerometry in patients with fibromyalgia; and to analyze the test-retest reliability of these questionnaires.

Design: Cross-sectional study.

Setting: Local fibromyalgia association.

Participants: Participants (N=99; 5 men) with fibromyalgia with a mean age of 50.2±9.5 years.

Interventions: Not applicable.

Main Outcome Measures: Participants carried an accelerometer for 1 week and completed the LTPAI and PAHWI twice (separated by a 1-wk interval). The LTPAI and PAHWI were summed to obtain overall values of PA.

Results: Time spent in total, moderate, and moderate-vigorous PA was higher ($P<.01$) when assessed by the LTPAI and PAHWI compared with accelerometry. The Bland-Altman method showed an absence of agreement between the LTPAI and PAHWI and the accelerometer for moderate, moderate-vigorous, and total PA. The test-retest reliability for the workplace subscale and total score of the PAHWI showed high and moderate intraclass correlation coefficients (ICCs), respectively, but also manifested high SE of measurements (up to 179min/d). The LTPAI showed low to moderate ICCs and high SE of measurements (up to 79min/d). For the LTPAI and PAHWI, the ICCs for total activity across the population were low to moderate, and the Bland-Altman method confirmed this lack of agreement.

Conclusions: The LTPAI and PAHWI and the accelerometer differ greatly when assessing PA. Furthermore, the LTPAI and PAHWI did not show good levels of test-retest reliability. Therefore, the self-administered LTPAI and PAHWI show questionable usefulness to assess PA in populations with fibromyalgia.

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Fibromyalgia is a systemic chronic musculoskeletal pain disorder characterized by multiple tender points in all body quadrants[1] and widespread pain.[2] Fibromyalgia is also typically accompanied by a wide variety of symptoms (eg, sleep disturbances, reduced physical work capacity, fatigue,[1] stiffness, mood disorders,[3] cognitive disturbances[4]).

Patients with fibromyalgia can benefit from physical activity (PA) to maintain or improve their health.[5] Several studies showed the benefits of PA on pain,[6-10] general symptomatology,[9-11] psychological outcomes,[11] global well-being,[12,13] and physical fitness[6,9,10] in patients with fibromyalgia. Despite the proven benefits of PA on their symptomatology, women with fibromyalgia are usually less physically active than healthy controls.[14]

Self-reported questionnaires are easy and inexpensive to administer, which makes them suitable to assess PA at the population level. However, PA information derived from self-reports is potentially subjected to response bias.[15] In fact, overreporting is common in all populations with the use of PA questionnaires.[15-18] People with fibromyalgia are known to have memory and cognitive difficulties.[19] This fact, together with the wide symptomatology of the condition,[2] makes PA difficult to recall, which may partially explain the limitation of self-report methods, especially in this population.[20]

The Leisure Time Physical Activity Instrument (LTPAI) and Physical Activity at Home and Work Instrument (PAHWI) have been used to estimate PA in people with fibromyalgia.[19,21-23] The LTPAI focuses on leisure activities, whereas the PAHWI focuses on activities at home and in the workplace. When used together (LTPAI and PAHWI), these questionnaires assess the time spent in different intensities and total PA during the week. The LTPAI and PAHWI were originally designed to be used together and validated among women with fibromyalgia in 2005.[21] Both instruments were later transculturally adapted into Spanish in 2011,[19] and their psychometric characteristics were studied.[19] There is a need to examine whether the questionnaires used to assess PA in a population with fibromyalgia are valid and reliable. Studies examining the LTPAI and PAHWI construct validity and test-retest reliability in Spanish populations with fibromyalgia are scarce.[19] Furthermore, there are no studies, to our knowledge, comparing differences between the LTPAI and PAHWI data and an objective measure of PA (eg, accelerometry in women with fibromyalgia). Therefore, we aimed to compare PA estimated by the LTPAI and PAHWI with PA measured by accelerometry in a convenience sample of Spanish patients with fibromyalgia. We also studied the test-retest reliability of the LTPAI and PAHWI.

Methods

Participants

We contacted a local association of patients with fibromyalgia from Granada (Southern Spain) to recruit participants, and 116 potential participants responded. One hundred gave their written informed consent after receiving detailed information about the aims and study procedures in an informative session. Participants were excluded from the study if they did not meet the American College of Rheumatology criteria (widespread pain for >3mo and pain with 4kg/cm^2 of pressure reported for ≥11 of 18 tender points[1]), had acute or terminal illness, or had severe dementia (Mini-Mental State Examination [MMSE] scores <10).[24] One participant had <11 tender points. The final study sample consisted of 94 women and 5 men with fibromyalgia. The study protocol was reviewed and approved by the Ethics Committee of the Hospital Virgen de las Nieves (Granada, Spain).

List of abbreviations:

BMI	**body mass index**
CI	**confidence interval**
ICC	**intraclass correlation coefficient**
LTPAI	**Leisure Time Physical Activity Instrument**
MMSE	**Mini-Mental State Examination**
PA	**physical activity**
PAHWI	**Physical Activity at Home and Work Instrument**
r_c	**concordance correlation coefficient**

Procedures

At the first visit, the tender points count and body mass index (BMI) were estimated. The MMSE, demographic data, and LTPAI and PAHWI were completed in the assessment setting. Participants were asked to wear an accelerometer for 9 consecutive days, starting the same day they received the monitor. They were instructed to wear the accelerometer on their lower back, which was attached by an elastic belt, over the whole day (24h) and were advised to keep on with their normative life. To protect the accelerometers, participants were asked to take them off while bathing. Participants had a second visit to complete the LTPAI and PAHWI questionnaires (retest) and return the accelerometers to the researchers.

Measures

Tender points count

We assessed the 18 fibromyalgia-related tender points according to the American College of Rheumatology criteria for classification of fibromyalgia[1] using a standard pressure algometer (FPK 20[a]). The total count of positive tender points was recorded for each participant.

Body mass index

We measured weight with an 8-polar tactile-electrode impedanciometer (portable InBody R20[b]). Height (cm) was measured using a stadiometer (seca 22[c]). BMI was calculated as weight (kg) divided by height (m) squared.

Mini-Mental State Examination

The MMSE[24] was used to assess severity of dementia for the exclusion criteria. The MMSE is a brief cognitive screening test, which contains questions that assess 5 areas of cognitive functioning: orientation, immediate memory, attention/concentration, delayed recall, and language.

Leisure Time Physical Activity Instrument

The LTPAI[19,21] comprises 4 items with 3 activity levels: light, moderate, and vigorous. Participants were asked to recall the average number of hours a week during the previous 4 weeks that they had engaged in a particular type of leisure PA and the activity level. The scale is simplified into the following 3 steps: (1) 0.5 to 1.5 hours a week, (2) 2 to 4 hours a week, and (3) >4 hours a week. When the participant marked step 1 or 2, the mean value of the range was used in the calculation of the total score. When step 3 was marked, participants were asked to provide the answers in hours. When no step was selected, the number of hours for the category was 0. The number of hours indicated by the participants

for each intensity category was summed to obtain the leisure time PA level for 1 week. Nonoccupation or work-related activity was emphasized with this tool. The Spanish version of the LTPAI has shown low to moderate construct validity and satisfactory reliability.[16]

Physical Activity at Homework or Workplace Instrument

The PAHWI[19,21] comprises 7 items with 3 categories for work performed at home (light, moderate, and heavy activity) and 4 categories for employment (sedentary, light, moderate, and heavy activity). A short description of each category was presented. Participants were asked to report the average number of hours a week during the previous 4 weeks working in the given activity category. The hours for each category were summed to obtain the total score. The Spanish version of the PAHWI has shown poor construct validity, satisfactory reliability for the workplace subscale, and moderate reliability for the housework subscale and total score.[16]

The LTPAI and PAHWI were self-reported. Participants received instructions only if after reading they did not understand the instructions or did not know how to classify their activities. Although they are presented as 2 different questionnaires, the LTPAI and PAHWI are different sections of a unique questionnaire (LTPAI and PAHWI) covering the whole complex of PA during the day: leisure time, homework, and workplace. The 3 categories (light, moderate, moderate vigorous) of both the LTPAI and PAHWI were summed and combined to obtain the total PA minutes per week. Then, the final scores were divided by 7 to obtain the total PA (min/d) and therefore allow comparison with accelerometry.

Accelerometry

An accelerometer (Actigraph GT1M[d]) was used to measure PA.[25] Accelerometers were initialized as described by the manufacturer, and data were saved in 5-second epochs. Participants wore the device on the lower back, secured with an elastic belt, underneath clothing, and near to the center of gravity. Data were downloaded onto a computer using the manufacturer software. Data reduction, cleaning, and analyses were performed using the MAHUffe program.[e]

Monitor wearing time was calculated by subtracting the sleeping reported time (recorded through a diary) from the total registered time for the entire day (ie, 1440min). Bouts of 60 continuous minutes of 0 activity intensity counts were also excluded from the analysis, considering these periods as nonwearing time.[26] In addition, a recording of >20,000 counts per minute was considered as a potential malfunction of the accelerometer or measuring accelerations other than those caused by the wearer's volitional movements (eg, vibrations from being in a car), and the value was excluded from the analyses.[26] These exclusion criteria have also previously been used in a recent fibromyalgia study using accelerometry.[27] There was no recording of >20,000 counts per minute in our study. The first day (to avoid reactivity) and last day (return back device) were excluded from the analysis. A total of 7 days of recording with a minimum of ≥10 hours of registration per day was necessary to be included in the study analysis.

PA levels were set as time (min/d) engaged in light, moderate, and moderate-vigorous PA intensity based on a standardized cut off of 100 to 1951, 1952 to 5724, and ≥1952 counts per minute, respectively.[28] We also calculated the total PA as the sum of the light, moderate, and moderate-vigorous PA intensity, expressed as minutes per day.

Statistical analysis

To examine any systematic difference between the measured and estimated PA, we performed a paired t test. The concordance between the LTPAI and PAHWI and the accelerometry scores was studied with the concordance correlation coefficient (r_c) because it is more adequate than other correlation methods with similar purpose for assessing intermethod agreement.[29] Pearson correlation coefficient was used as additional information for the r_c value. The measurement error between the measured (accelerometry) and estimated (LTPAI and PAHWI) PA was assessed following Bland-Altman plots.[30] The mean difference, 95% confidence intervals (CIs) of the difference, and 95% limits of agreement (mean difference ±1.96 SD of the differences) were calculated. We also examined heteroscedasticity.

To study the test-retest reliability of the LTPAI and PAHWI, we calculated the SD of the mean differences, 95% CI for the mean difference, 2-way mixed average measures intraclass correlation coefficient (ICC),[31,32] 95% CI for the ICC, SE of measurement estimated as the square root of the mean square error term from the analysis of variance,[32,33] and intraindividual SD.[34] The measurement error between test and retest was also studied following the Bland-Altman method,[30] as previously explained. We also applied a logarithmic transformation to the data as explained in the Bland-Altman method for test-retest agreement.[30]

We used a parametric statistic because of the large sample size; however, the study variables were nonnormally distributed. We repeated the analyses using a nonparametric statistic, and the results did not materially change. All analyses were performed using SPSS version 20.0,[f] and the level of significance was set at $P<.05$.

Results

The clinical and sociodemographic characteristics of the sample are summarized in table 1.

The LTPAI and PAHWI estimations were higher in total PA and in light, moderate, and moderate-vigorous PA intensity (mean difference, 87, 16, 49, and 71min/d, respectively) compared with the accelerometry data. Table 2 illustrates PA levels according to the LTPAI and PAHWI and accelerometry divided by age and BMI. The LTPAI and PAHWI showed higher minutes per day of total PA and all the PA intensities compared with the accelerometer across all the stratified variables. The older age group (>50y) and those with BMI <30kg/m^2 showed the highest discrepancy between the objective and subjective measure in total PA and all the PA intensities (P values, .024 to <.001), except in light PA (all, $P>.05$).

A very low correlation was observed between self-reported (LTPAI and PAHWI) and objective (accelerometry) PA levels, whereas no correlation was found in light PA intensity. The r_c value between the LTPAI and PAHWI and accelerometry ranged from .06 to .12 (table 3), whereas the Pearson order correlations ranged from .21 to .32.

Figure 1 shows the scatterplots for total PA and moderate-vigorous PA intensity assessed by the LTPAI and PAHWI versus accelerometry. There was a lack of association between the LTPAI and PAHWI and the accelerometer. The Bland-Altman plots for intermethod agreement between the LTPAI and PAHWI and accelerometry are shown in figure 2. The same procedure was followed for light and moderate PA intensity, which is shown in supplemental figure S1 and supplementary figure S2 (available

Table 1 Sociodemographic characteristics of the fibromyalgia sample (N=99)

Variable	Value
Tender points	17.2±1.7
MMSE*	27.8±2.1
Sex	
Women	94 (94.9)
Men	5 (5.1)
BMI (m/kg^2)†	
<25	31 (32.0)
25–29.9	38 (39.20)
>30	28 (28.8)
Age (y)	
35–50	45 (45.5)
51–73	54 (54.5)
Years since clinical diagnosis†	
≤5	48 (50.0)
>5	48 (50.0)
Marital status	
Married	75 (75.7)
Unmarried	15 (15.2)
Separated/divorced/widowed	9 (9.1)
Educational status*	
Unfinished studies	3 (3.1)
Primary school	39 (39.8)
Secondary school	32 (32.6)
University degree	24 (24.5)
Occupational status†	
Working	29 (34.5)
Unemployed	28 (33.3)
Retired	27 (32.2)

NOTE. Values are n (%) or mean ± SD.
* One missing datum.
† Various missing data.

online only at http://www.archives-pmr.org/). The scatter of the differences increased as PA minutes per day increased.

The test-retest mean difference and SD, 95% CI of the mean difference, ICC, 95% CI of the ICC, SE of measurement, and intraindividual SD are shown in table 4. No systematic differences were found between test-retest, except for the LTPAI light PA intensity (P=.047). The ICCs were overall moderate for the PAHWI total score, LTPAI and PAHWI total score, LTPAI and PAHWI light, moderate, and moderate-vigorous PA (overall range, .42–.63), and satisfactory for the workplace subscale of the PAHWI (ICC=.81). The SEs of measurements were overall high, with values for the LTPAI and PAHWI total PA and all the PA intensities ranging from 96 to 205min/d. Mean differences between test and retest were lower than the SE of measurement for the LTPAI and PAHWI total PA and for all the PA intensities (range, −14 to 16min/d).

Figure 3 shows the Bland-Altman plot for the test-retest total PA and moderate-vigorous PA intensity of the LTPAI and PAHWI before and after logarithmic transformation. The same procedure was followed for light and moderate PA intensity, which is shown in supplementary figure S3. There was no systematic error (all P values >.05) between total, light, moderate, and moderate-vigorous PA test-retest comparisons. Random bias was large for total PA and for all PA intensities. The antilogarithms[30] of the total

Table 2 Descriptive PA data from the LTPAI and PAHWI and accelerometry by age and BMI

	Total PA			Light			Moderate			Moderate Vigorous		
Participants	LTPAI and PAHWI (min/d)	Accelerometry (min/d)	P	LTPAI and PAHWI (min/d)	Accelerometry (min/d)	P	LTPAI and PAHWI (min/d)	Accelerometry (min/d)	P	LTPAI and PAHWI (min/d)	Accelerometry (min/d)	P
All (N=99)	317±273	230±58	.001	196±171	179±41	.335	99±118	50±26	<.001	121±165	51±27	<.001
Age (y)												
21–50 (n=45)	277±224	234±56	.189	182±143	183±44	.973	72±97	50±22	.143	95±159	51±22	.075
51–73 (n=54)	350±306	227±60	.003	207±191	176±39	.239	121±129	49±29	<.001	143±168	50±30	<.001
BMI (kg/m^2)												
<25 (n=31)	315±292	221±53	.064	157±137	164±36	.769	120±141	55±27	.012	158±220	57±28	.013
25–29.9 (n=38)	365±314	249±56	.024	236±207	196±38	.226	110±123	52±24	.005	129±155	53±25	.004
>30 (n=28)	270±176	220±61	.149	193±143	177±44	.576	67±71	42±26	.063	77±91	43±27	.050

NOTE. Values are mean ± SD. The difference of LTPAI and PAHWI versus accelerometry is shown for total PA and light, moderate, and moderate-vigorous PA intensity using a paired t test.

Table 3 Values of r_c and Pearson r for total PA and time spent in PA intensities from the LTPAI and PAHWI and accelerometry (N = 99)

LTPAI and PAHWI	Accelerometry	r_c	r	$P_{Pearson}$
Light	Light	.10	.21	.034
Moderate	Moderate	.10	.27	.007
Moderate-vigorous	Moderate-vigorous	.06	.24	.017
Total PA	Total PA	.12	.32	.001

Abbreviations: $P_{Pearson}$, P value for Pearson correlation coefficient; r, Pearson correlation coefficient; r_c, concordance correlation coefficient.

PA and light, moderate, and moderate-vigorous PA intensity limits of agreement were (.18, 5.61), (.15, 5.66), (.11, 11.22), and (.11, 11.65), respectively.

Discussion

The present study showed a low agreement in all PA intensities and total PA when the self-administered LTPAI and PAHWI were compared with measured PA (accelerometry) in a convenience sample of patients with fibromyalgia. Additionally, the test-retest analysis suggested that the LTPAI and PAHWI have a low degree of reliability in the population studied.

Other studies compared the LTPAI and PAHWI with different PA assessment methods in people with fibromyalgia using the Spearman rank correlation coefficient only. They observed a moderate association of the LTPAI with the 6-minute walk test[21] ($\rho = .40$) and other PA questionnaires[19,21] ($\rho = .39$ and .61), but this association was lower when compared with the active energy expenditure of an objective body monitoring device ($\rho = .27$). The absence of satisfactory concordance measured by the r_c value indicated a low relation between the objective and subjective method in the present study. Similarly, the Pearson correlation coefficient between the LTPAI and PAHWI and the accelerometer scores ranged from .21 to .32, indicating a poor relation between both instruments. We calculated this correlation coefficient to compare our results with previous studies, but this technique has previously been criticized in the analysis of measurement method comparison data.[30,33] Alternatively, the Bland-Altman method[30] has been proposed to study the degree of agreement between different methods.

The LTPAI and PAHWI showed higher values of total PA and in all the intensity categories of PA when compared with accelerometry. Contrary to the youngest group, the oldest group exhibited significant differences between both methods, indicating that older individuals could present more difficulties when reporting their PA levels, as previously reported.[17] Our results concur with the body of literature, which affirms that the validity of questionnaires is higher in younger subjects.[35] Cognitive dysfunction increases with age, which could impair the ability of self-report. Otherwise, older and young adults may not have the same variety of activities; therefore, the questionnaires would not similarly fit in both age groups. Both the subjective and objective measures showed that the group with the highest BMI was the least active, and the higher the BMI the lower the PA at moderate and moderate-vigorous intensity. Unlike the other groups of BMI, those with the highest BMI did not show significant differences in total and all PA intensities, highlighting that this group may be aware of their low involvement in PA. In turn, those with lower BMI tend to have a higher general perception of their health[36] and might interpret their lower BMI as a proof of adequate activity levels,[36] therefore resulting in an overreporting of their PA.[35,36] To explore the relation between age, BMI, and misreporting, longitudinal designs would be helpful.

The scatterplot of the LTPAI and PAHWI versus accelerometry showed no association between both instruments and an extreme

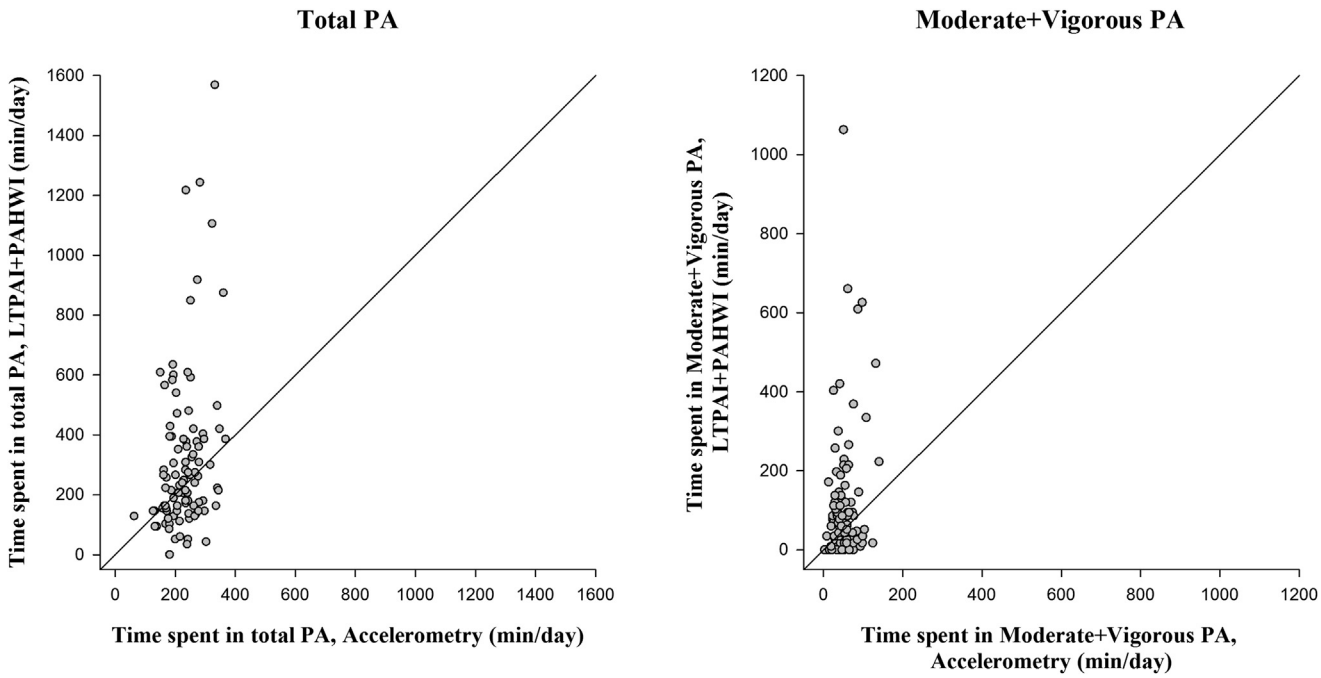

Fig 1 Scatterplots of total PA and moderate-vigorous PA intensity of the LTPAI and PAHWI versus accelerometry. The 45° of equality line is shown. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.

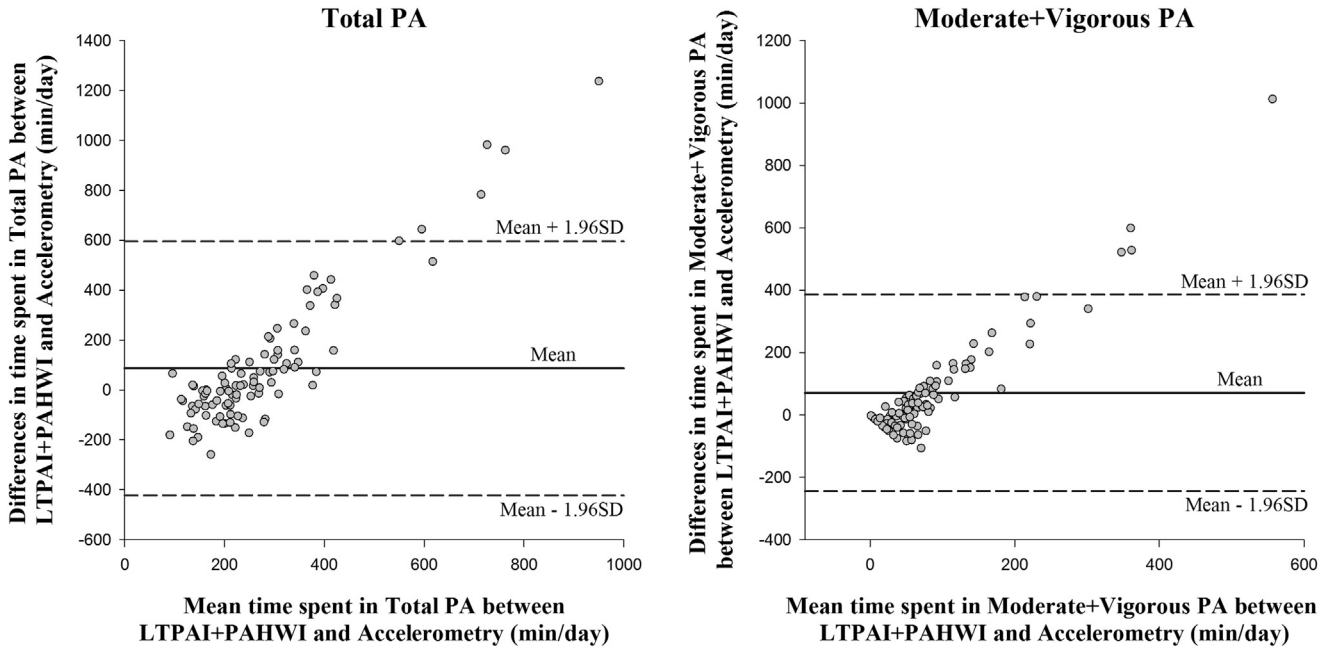

Fig 2 Bland-Altman plots (total PA and moderate-vigorous PA intensity) for intermethod agreement between the LTPAI and PAHWI and accelerometry. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.

difference in variability. An examination of the Bland-Altman plots displayed a large measurement error between the accelerometer and questionnaires, with discrepancies up to around 500min/d in total PA. Furthermore, the results indicated that the greater the time spent in a certain level of PA measured by the accelerometer, the greater the difference between the 2 methods. This may reflect overreporting, failure to recall time well, or rounding up of time for the LTPAI and PAHWI data. Furthermore, the LTPAI and PAHWI ask for time and frequency spent in light, moderate, and vigorous PA intensity, which is a subjective rating of intensity. Individuals usually do not know how to classify their activities. Patients with fibromyalgia usually have a rate of perceived effort higher than healthy people[37]; therefore, they might tend to misclassify their activities. It might also be possible that people with low aerobic capacity would perceive intensity as higher than trained people or those with a higher aerobic capacity.[38] The lack of agreement between the LTPAI and PAHWI and the accelerometer could suggest that: 1) there is a greater variability in the fibromyalgia patients' reported responses when compared to objective measures of PA[14]; 2) the LTPAI and PAHWI do not properly assess PA in patients with fibromyalgia, as well as previously shown with other PA questionnaire in this population.[39] On the other hand, although the Actigraph GT1M is a valid measure currently used to objectively assess PA in large population and fibromyalgia studies,[18,27,40] activities (eg, heavy manual work, bicycling, weight lifting) can be underestimated by

Table 4 Test-retest agreement and measurement errors for the LTPAI and PAHWI

Variable	Test 1	Test 2	Difference (Test 1—Test 2)	95% CI Mean Difference	Intraindividual SD	SEM	ICC	95% CI for ICC
LTPAI, total score (min/d)	51±42	70±110	−19±111	−41 to 3	135	79	.19	−.21 to .45
Light (min/d)	26±24	35±45	−10±48*	−19 to 0	68	34	.20	−.20 to .46
Moderate (min/d)	18±19	25±54	−7±51	−17 to 4	47	36	.33	.00 to .55
Vigorous (min/d)	7±13	10±34	−3±36	−10 to 4	20	25	.08	−.37 to .38
PAHWI, total score (min/d)	314±247	297±240	17±253	−34 to 67	118	179	.63	.45 to .75
Home (min/d)	198±146	186±168	12±205	−29 to 53	85	145	.26	−.10 to .51
Work place (min/d)	116±199	112±177	5±150	−25 to 35	32	106	.81	.72 to .88
LTPAI and PAHWI, total score (min/d)	320±235	318±274	2±290	−57 to 60	11	205	.52	.29 to .68
Light (min/d)	183±136	196±171	−14±187	−51 to 24	98	132	.42	.14 to .61
Moderate (min/d)	110±113	99±118	11±136	−17 to 38	74	96	.47	.20 to .64
Moderate vigorous (min/d)	137±151	122±166	16±174	−19 to 51	109	123	.57	.35 to .71

NOTE. Values are mean ± SD or as otherwise indicated. Differences between the test and retest from the LTPAI and PAHWI are tested for PA from paired *t* test.

Abbreviation: SEM, SE of the measurement.

* $P = .047$.

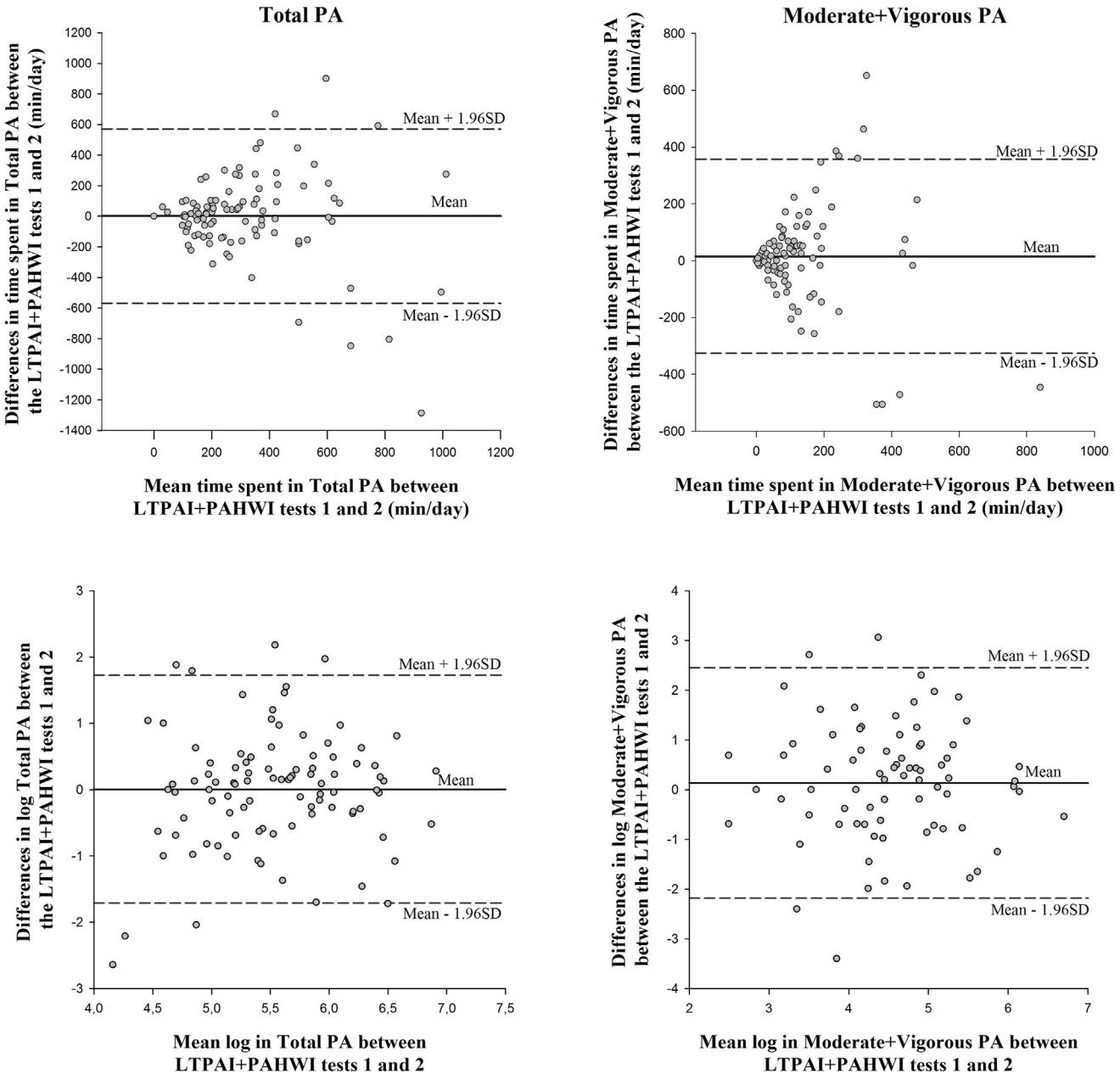

Fig 3 Bland-Altman plots of test-retest total PA and moderate-vigorous PA intensity for the LTPAI and PAHWI before and after logarithmic transformation. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.

this device.[41] However, because of the low functional capacity levels in this population, this profile of activities is unusual.[42] In spite of this, both the self-report and objective measures are likely to contribute to the discrepancies in PA levels observed between the 2 tools.

The test-retest reliability showed better results when the LTPAI and PAHWI were summed. The ICC scores indicated satisfactory stability for the workplace subscale of the PAHWI, for the total score, and all the PA intensities of the LTPAI and PAHWI. However, the SE of measurement scores were very high in all the categories, indicating a large bias of the questionnaires. The ICC values reported in the present study were lower than those determined in the original version[21] and Spanish transcultural adaptation,[19] even though the test-retest interval was the same (7d). As previously stated, participants received instructions only when they did not understand the instructions or did not know how to classify their activities. Therefore, following the original articles' instructions, the questionnaires were self-reported as much as possible to avoid any interviewer bias. We do not know whether the previous studies offered greater help to participants, which could influence the results and might explain the differences between studies. Our results concur with those of Cancela et al[17] with older women participants, which affirmed that reliability of the instruments was stronger when the LTPAI and PAHWI scores were added, which speaks favorably of the structure and organization of both tools.

The fanning effect observed in the Bland-Altman plots indicated that the reproducibility of the questionnaire decreases as the

amount of reported PA increases. We observed a large measurement error between the questionnaires test-retest, with discrepancies up to around 500min/d in total PA. Logtransformed data showed wide limits of agreement, reflecting the lack of reproducibility. The limits showed that in 95% of cases, the retest measure will be between about .17 and 5.64 times the test measure for total PA and light PA intensity, whereas values correspond to around .11 and 11.45 for moderate and moderate-vigorous PA intensity. This fact highlights the absence of precision of the questionnaires in the population studied. The lack of test-retest reliability could also be explained by changes in PA between the first and second time points. However, test-retest differences were so high that this fact is unlikely. Furthermore, fear of pain and activity in the population with fibromyalgia limits voluntary physical activities[43]; therefore, their PA patterns remain stable through time, and they mostly spent their time in sedentary behaviors.[27,43]

Study limitations and strengths

As previously mentioned, uniaxial accelerometers are known to underestimate certain types of PA.[41] However, they might also measure accelerations other than those caused by the wearer's volitional movements, resulting in higher counts per minute than those corresponding to the true individual's motions. We do not know whether and how often there may be this kind of movement in our valid data (<20,000 counts/min). To enhance the assessment of various PA intensities with the Actigraph, we chose cut points recommended by Freedson et al.[28] Comparisons of accelerometer-based PA estimates using different cut-off levels have shown that they produce varying results with none of the cut-off points being ideal.[44] Therefore, results observed between the LTPAI and PAHWI and the accelerometer need to be interpreted keeping this in mind. We do not know whether participants modified their habitual sedentary behavior or PA during the days they were monitored despite being advised to keep on with their normative life. The sampling method (convenience sample) is another limitation of the present study. We do not know whether sampling differences can explain differences between the present and previous studies; however, participants' education was similar to those presented in the original version and Spanish adaptation.[19,21] The relatively low number of men included in the study limits the present study findings in this population; therefore, future studies should analyze PA in a larger sample of men with fibromyalgia. Additionally, we have no data on an age-matched group of healthy people; therefore, direct comparisons cannot be made. Finally, it must be mentioned that accelerometry is not the criterion standard to measure PA; therefore, future studies using doubly labeled water are warranted, so it could clarify our findings. On the other hand, strengths of the present study were the large sample size studied (the highest to our knowledge to date) and the collection of accelerometer data during 7 consecutive valid days.

Conclusions

The present study shows large discrepancies in all PA intensities and in total PA between the LTPAI and PAHWI and objectively measured PA (accelerometry) in a Spanish sample of patients with fibromyalgia. Moreover, we observed a low reliability of the LTPAI and PAHWI in our population. Taken together, the results suggest that the self-administered LTPAI and PAHWI might not be an appropriate tool to assess PA in a population with fibromyalgia.

Suppliers

a. Wagner Instruments, PO Box 1217, Greenwich, CT 06836-1217.
b. Biospace, Biospace Building 54, Nonhyeon-ro 2-gil, Gangnam-gu, Seoul 135-960, Korea.
c. seca, Hammer Steindamm 9-25, 22089 Hamburg, Germany.
d. Actigraph LLC, 49 E Chase St, Pensacola, FL 32502.
e. MRC Epidemiology Unit in Cambridge. Available at: www.mrc-epid.cam.ac.uk.
f. IBM, 1 New Orchard Rd, Armonk, NY 10504-1722.

Keywords

Accelerometry; Reliability of results; Physical activity; Fibromyalgia; Pain

Corresponding author

Víctor Segura-Jiménez, BSc, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Carretera de Alfacar, s/n, 18011, Granada, Spain. *E-mail address:* vsegura@ugr.es.

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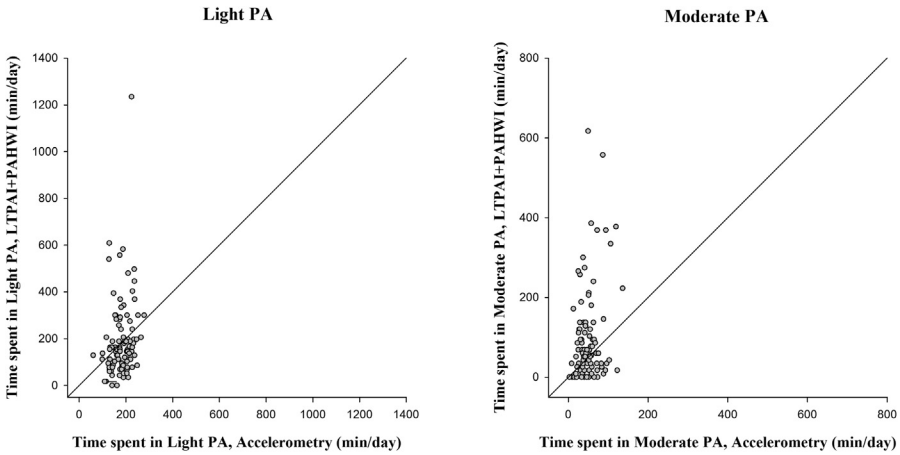
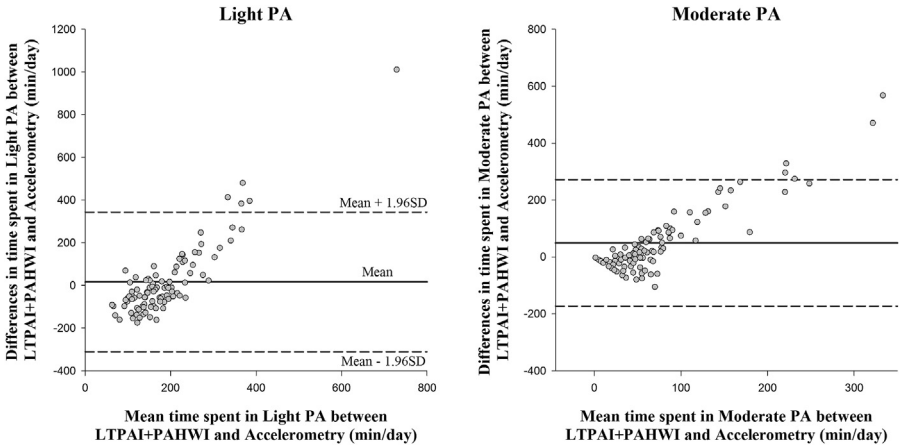
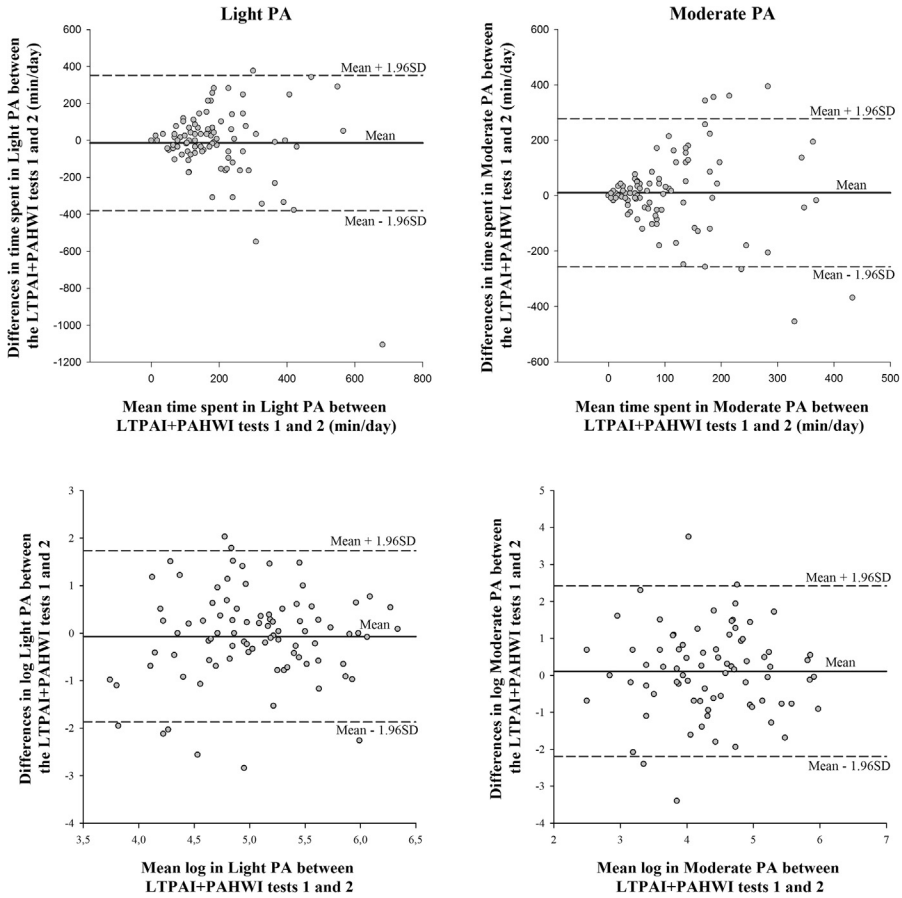


Supplemental fig S1 Scatterplots of light and moderate PA intensity of the LTPAI and PAHWI versus accelerometry. The 45° of equality line is shown. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.



Supplemental fig S2 Bland-Altman plots (light and moderate PA intensity) for intermethod agreement between the LTPAI and PAHWI and accelerometry. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.



Supplemental fig S3 Bland-Altman plots of test-retest light and moderate PA intensity for the LTPAI and PAHWI before and after logarithmic transformation. Abbreviation: LTPAI+PAHWI, LTPAI and PAHWI.

Comparison of the International Physical Activity Questionnaire (IPAQ) with a multi-sensor armband accelerometer in women with fibromyalgia: the al-Ándalus project.

Segura-Jiménez V, Munguía-Izquierdo D, Camiletti-Moirón D, Alvarez-Gallardo IC, Ortega FB, Ruiz JR, Delgado-Fernández M.

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Clinical & Experimental Rheumatology

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Comparison of the International Physical Activity Questionnaire (IPAQ) with a multi-sensor armband accelerometer in women with fibromyalgia: the al-Ándalus project

V. Segura-Jiménez[1], D. Munguía-Izquierdo[2], D. Camiletti-Moirón[1,3], I.C. Álvarez-Gallardo[1], F.B. Ortega[1], J.R. Ruiz[1], M. Delgado-Fernández[1]

[1]Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Granada, Spain; [2]Department of Sport and Informatics, Section of Physical Education and Sports, University Pablo de Olavide, Seville, Spain; [3]Department of Physiology and Institute of Nutrition and Food Technology, Faculty of Pharmacy, University of Granada, Granada, Spain.

Víctor Segura-Jiménez, BSc
Diego Munguía-Izquierdo, PhD
Daniel Camiletti-Moirón, BSc
Inmaculada C. Álvarez-Gallardo, BSc
Francisco B. Ortega, PhD
Jonatan R. Ruiz, PhD
Manuel Delgado-Fernández, PhD

Please address correspondence to:
Víctor Segura Jiménez,
Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada,
Carretera de Alfacar, s/n,
18011 Granada, Spain.
E-mail: vsegura@ugr.es

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Key words: accelerometry, physical activity, objective measure, subjective measure, agreement, reliability

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Competing interests: none declared.

ABSTRACT

Objective. *To compare levels of physical activity (PA) assessed by the International Physical Activity Questionnaire (IPAQ) with PA measured with the SenseWear Pro Armband (SWA) in women with fibromyalgia, and to assess the test-retest reliability of the IPAQ.*

Methods. *The study comprised a total of 183 women with fibromyalgia aged 51.1±8.2 years. Participants wore the SWA for 9 consecutive days and filled in the IPAQ twice (separated by a 9-day interval). Total PA, time spent on moderate and vigorous intensity PA, and sitting time assessed by the IPAQ and the SWA (n=123) were compared.*

Results. *Time spent on PA at different intensities (total, moderate and vigorous) was higher and sedentary time was lower when assessed by the IPAQ compared with the SWA (all $p<0.001$). Differences between the IPAQ and the SWA increased as the minutes per day in the IPAQ increased. The Bland-Altman plots showed no agreement between the IPAQ and the SWA. There was no association between the IPAQ and the SWA in any of the variables studied, except for walking domain from the IPAQ and moderate PA from the SWA ($r_p=0.19$, $p=0.03$). Test-retest systematic differences were found for total PA score, moderate and vigorous intensity, working and domestic domains (all $p<0.05$). The ICCs for those domains without systematic differences (sitting, vehicle, walking, active transport time and leisure domains) ranged from 0.52 to 0.71).*

Conclusions. *The IPAQ differs from objectively measured PA and presents limitations to classify different categories of PA based on SWA data. Moreover, the IPAQ is not a reliable tool to assess PA in women with fibromyalgia.*

Introduction

Fibromyalgia is a chronic musculoskeletal condition (1) found primarily in women and characterised by pain disorder and multiple tender points in all body quadrants (2, 3). It is also usually accompanied by other wide variety of symptoms (2, 4, 5) and it commonly accompanies other chronic conditions (6). Different treatments are currently used to improve the symptomatology of the disease (7-9). Several studies have shown the benefits of regular physical activity (PA) on pain, as well as on body composition, physical fitness (10, 11), flexibility (12), psychological outcomes (13) and global well-being (14) in fibromyalgia patients.

Accelerometers are now extensively used in research focused on measuring PA. A wearable body-monitoring device, namely Armband (SWA), has been recently introduced and validated for the measurement of PA in healthy people (15, 16), in several clinical populations (17-19), as well as in people with fibromyalgia (20). This device is portable and provides an objective assessment of PA. The high prices of accelerometers however, do not always allow the possibility to use them in clinical practice. Alternatively, self-report questionnaires are the most commonly used methods to assess PA at population level, because they are inexpensive and easy to administer. The International Physical Activity Questionnaire (IPAQ) was developed to assess health-related PA. The short and long versions of the IPAQ have been tested extensively (21-25) and are now used in international studies with healthy populations (26, 27).

Physical activity is generally difficult to recall, quantify and categorise in healthy adults. Moreover, the cognitive

problems (attention, working memory, long-term verbal memory and spatial memory) (28, 29) and bipolar disorders (30) associated to fibromyalgia can distort or alter the fibromyalgia patients' perception about their PA levels. Even the nature of fibromyalgia symptoms itself (widespread pain, physical function impairments, reduced PA, tiredness, fatigue, depression, etc.) (5, 31) might also alter the own perception of PA levels. Taken together, this may negatively affect the accuracy of self-reported PA. Therefore, whether self-report measures such as IPAQ are adequate to assess PA in fibromyalgia people is uncertain. The aims of the present study were: i) to compare PA assessed by the IPAQ with PA measured by the SWA (objective measure) in Spanish women with fibromyalgia; ii) to study the test-retest reliability of the IPAQ in Spanish women with fibromyalgia.

Materials and methods

Participants

An invitation to participate in this study was sent to all people from two local Associations of fibromyalgia patients from Granada and Seville (Southern Spain). A total of 243 potentially eligible patients were willing to participate in the study and gave their written informed consent after receiving detailed information about the aims and study procedures. Participants were excluded from the analysis if they did not meet the American College of Rheumatology (ACR) criteria: widespread pain for more than 3 months, and pain ≤4 kg/cm^2 of pressure reported for 11 or more of 18 tender points (2); had acute or terminal illness; had severe dementia (Mini-Mental State Examination (MMSE) <10) (32). Fifty-three participants had less than 11 tender points, 1 participant did not fill the IPAQ test, 1 participant did not fill the MMSE and 5 were men. The final study sample included in the statistical analysis consisted of 183 women with fibromyalgia who filled the IPAQ twice (test-retest) and a subset of 123 women who additionally wore the SWA (the quantity of monitors available). The study protocol was reviewed and approved by the Ethics Committee of the *Hospital Virgen de las Nieves* (Granada, Spain).

Procedures

The participants visited the laboratory twice. At the first visit, the tender points count and the weight and height were measured. The MMSE, demographic data and the IPAQ were also completed and the completion time was recorded. Participants were asked to wear a SWA for 9 consecutive days, starting the same day they received the monitor. They were instructed to wear the SWA on their arm attached by an elastic belt during full day as well as sleeping hours. For security reasons, participants were asked to take them off while bathing. Participants had the second visit with 9 days interval for completing the IPAQ (retest) and they also returned the SWAs to the researchers.

Measures

Tender points count. We assessed 18 tender points according to the ACR criteria for classification of fibromyalgia (2) using a standard pressure algometer (FPK 20; Effegi, Alfonsine, Italy). The total count of positive tender points was recorded for each participant.

Fibromyalgia Impact Questionnaire (FIQ) comprises 10 subscales of disabilities and symptoms (physical function, work missed day, job ability, feel good, pain, fatigue, sleep, stiffness, anxiety and depression) and has previously used and validated for Spanish fibromyalgia patients (33). The total score ranges from 0 to 100. A higher score indicates a greater impact on the person's life.

Body Mass Index (BMI). We measured weight (kg) with an eight-polar tactile-electrode impedanciometer (InBody R20; Biospace, Seoul, Korea). Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). BMI was calculated as weight (in kilograms) divided by height (in meters) squared.

Mini-Mental State Examination (32) is a brief cognitive screening test used to assess cognitive capacity and severity of dementia for the exclusion criteria. The MMSE asks questions that assess five areas of cognitive functioning: orientation, immediate memory, attention/concentration, delayed recall and language.

International Physical Activity Questionnaire is used internationally to obtain comparable estimates of PA at population level (21). The original questionnaire was developed for adults aged 18–65 years (21). The long form of the IPAQ includes 27 items that identify the frequency (times per week) and duration (minutes or hours per day) of PA performed in different domains of PA in the last seven days: occupation, transportation, housework, house maintenance and family care, recreation, sport and leisure, and time spent sitting in a weekday and in a weekend day. To adapt the questionnaire to our study population, two items were added about time spent lying as an indicator of sedentary behaviour. Sitting and lying were summed and combined as total sitting time. For all PA domains, participation in vigorous and moderate intensity PA was obtained. Sedentary time was set as sitting plus vehicle transport time. There are no cultural aspects to be acknowledged when using the Spanish version of the IPAQ.

One Metabolic Equivalent (MET) is the amount of oxygen consumed while sitting at rest and is equal to 3.5 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ and 1 $kcal \cdot kg^{-1} \cdot hr^{-1}$ as the caloric equivalent for adults (34). PA intensities were set according to the IPAQ guidelines: moderate intensity as 4 METs, vigorous intensity as 8 METs, and walking as 3.3 METs. Total day PA (MET-min/day) was computed by multiplying METs by minutes of participation in the specific category of PA, and divided by 7 days. Sitting was expressed as min/day. The methods used to score the long-IPAQ can be found on the IPAQ website (www.ipaq.ki.se).

SenseWear Pro Armband

The wearable body-monitoring device (SenseWear Pro$_3$ Armband (Body Media, Pittsburgh, PA)) measures energy expenditure. The SWA has been used recently to compare objective vs. self-reported PA (35) and sedentary time (36) in fibromyalgia patients. The SWA incorporates an ample variety of measured parameter (biaxial accelerometry, heat flux, galvanic skin response, skin

Table I. Clinical and sociodemographic characteristics of fibromyalgia women, n=183.

Variable	n	%
Tender points count, mean (SD)	17.3	(1.6)
FIQ, mean (SD)*	64.6	(18.6)
Body mass index*	28.2	(5.3)
MMSE, mean (SD)	28.2	(1.9)
Age (years)		
≤50	72	39.3
>50	111	60.7
Years since clinical diagnosis*		
≤5 years	82	45.3
>5 years	99	54.7
Marital status		
Married	149	80.9
Unmarried	18	9.8
Separated / Divorced / Widowed	17	9.3
Educational status*		
Unfinished studies	12	6.6
Primary school	88	48.4
Secondary school	47	25.8
University degree	35	19.2
Occupational status*		
Working	62	39.5
Unemployed	64	40.8
Retired	31	19.7

Values are n and % unless otherwise indicated. SD, standard deviation. *Missing data.

temperature, near-body temperature) and demographic characteristics (gender, age, weight, height) into proprietary algorithms to estimate energy expenditure.

Following the manufacturer's recommendations, the SWA was worn on the right upper arm over the triceps muscle at the midpoint between the acromion and olecranon processes. Nine days of consecutive data were collected. Energy expenditure was computed at 1-minute intervals. Data obtained using the SWA were downloaded using software developed by the manufacturer (SenseWear Professional software version 6.1[a]).

The first and last days of recording were not included in the analysis to minimise reactivity. We excluded from the analyses data with less than 7 days of collection and a threshold of 95% "on-body" time was used to include an individual in the data analysis. Sleeping time was removed from analysis. We set the PA levels as follows:

a) total PA, expressed as a measure of overall PA; and time engaged in b) sedentary, c) moderate, and d) vigorous intensity PA based upon the IPAQ cut-off of <3, 3-6, and >6 METs per minute, respectively.

Statistical analysis

The difference between the objective and subjective measures of PA was calculated by means of paired *t*-test. Concordance between the IPAQ and the SWA scores was done using the concordance correlation coefficient (r_c). Pearson correlation coefficient (r_p) was calculated as additional information for the r_c (37). We assessed the agreement between the objective (SWA) and subjective (IPAQ) measures of PA following the Bland-Altman method (38). The association between the mean difference and the magnitude of the measurement (*i.e.* heteroscedasticity) was examined by conducting regression analysis after inverting negative data. We calculated the mean difference, 95% confidence intervals (CIs) of the difference, and the 95% limits of agreement (mean difference ± 1.96 standard deviation (SD) of the differences).

We studied the test-retest reliability of the IPAQ with a paired *t*-test. We also calculated the SD of the mean differences, the 95% CIs for the mean difference, the 2-way mixed average measures intraclass correlation coefficient (ICC) (39), 95% of CIs for ICC, the standard error of the measurement (SEM) (40), and the intra-individual SD (41). The agreement between test and retest was also studied following the Bland-Altman method (38) as described above. All analyses were performed using the Statistical Package for Social Sciences IBM-SPSS, version 20.0 for Windows, and the level of significance was set at $p<0.05$.

Results

The clinical and sociodemographic characteristics of the sample are shown in Table I. The mean time required to complete the IPAQ was 14 minutes in both test and retest.

Table II. Descriptive physical activity (PA) data from the International Physical Activity Questionnaire (IPAQ) and the SenseWear armband (SWA), by sex, age and body mass index (BMI).

	Total PA			Sitting	Sedentary			Moderate	Walking	Moderate + Walking			Vigorous		
	IPAQ min/day	SWA min/day	*p*	IPAQ min/day	IPAQ min/day	SWA[II] min/day	*p*	IPAQ min/day	IPAQ min/day	IPAQ min/day	SWA[II] min/day	*p*	IPAQ min/day	SWA[II] min/day	*p*
All (n=123)	323 (264)	111 (70)	<0.001	319 (171)	359 (195)	907 (136)	<0.001	222 (199)	77 (97)	298 (235)	110 (69)	<0.001	24 (68)	1 (5)	<0.001
	(103; 500)	(64; 146)		(197; 413)	(227; 446)	(817; 973)		(56; 345)	(14; 104)	(97; 467)	(64; 143)		(0; 17)	(0; 1)	
Age (years)															
23-50 (n=53)	268 (231)	135 (80)	<0.001	345 (194)	395 (238)	878 (105)	<0.001	189; 176)	54 (62)	242 (200)	133 (77)	<0.001	25 (82)	3 (7)	0.048
	(52; 431)	(77; 176)		(199; 444)	(228; 482)	(818; 936)		(35; 290)	(11; 73)	(51; 383)	(77; 174)		(0; 7)	(0; 2)	
51-64 (n=70)	364 (281)	93 (57)	<0.001	300 (149)	332 (152)	929 (153)	<0.001	247 (214)	94 (115)	341 (252)	93 (56)	<0.001	23 (56)	0 (1)	0.001
	(154; 538)	(58; 109)		(197; 386)	(223; 425)	(817; 1004)		(69; 370)	(17; 134)	(145; 519)	(58; 109)		(0; 22)	(0; 0)	
BMI ($m \cdot kg^{-1}$)															
<25 (n=36)	207 (197)	142 (85)	0.049	335 (201)	379 (240)	864 (94)	<0.001	135 (139)	68 (87)	203 (198)	139 (83)	0.054	4 (18)	3 (7)	0.491
	(39; 286)	(75; 181)		(198; 401)	(226; 426)	(791; 938)		(22; 220)	(12; 102)	(39; 285)	(73; 175)		(0; 0)	(0; 2)	
25-29.9 (n=49)	422 (292)	115 (63)	<0.001	318 (157)	360 (181)	919 (156)	<0.001	285 (223)	95 (106)	381 (252)	113 (62)	<0.001	41 (97)	1 (4)	0.006
	(174; 582)	(76; 136)		(199; 429)	(225; 461)	(817; 987)		(108; 397)	(29; 149)	(164; 542)	(76; 136)		(0; 34)	(0; 1)	
>30 (n=37)	306 (239)	79 (48)	<0.001	303 (162)	338 (170)	935 (138)	<0.001	221 (192)	63 (95)	284 (215)	79 (47)	<0.001	22 (44)	0 (1)	0.005
	(111; 513)	(46; 105)		(193; 409)	(224; 449)	(859; 1005)		(45; 335)	(13; 54)	(100; 468)	(45; 104)		(0; 17)	(0; 0)	

Values are means (standard deviation), and interquartile ranges. Difference IPAQ – SWA tested for total PA, sedentary time, moderate and vigorous PA intensities using *t*-test. [II]Cut-off values for sedentary, moderate and vigorous were <3, 3-6, and >6 METs*min/day, respectively.

Table III. Concordance correlation coefficient (r_c) and Pearson correlation coefficient (r_p) for total physical activity (PA) and time spent on PA intensities from the International Physical Activity Questionnaire (IPAQ) and the SenseWear armband (SWA), n=123.

IPAQ (min/day)	SWA (min/day)	r_c	r_p	$P_{Pearson}$
Sitting	Sedentary	-0.01	-0.12	0.18
Sitting + Transport	Sedentary	-0.02	-0.11	0.22
Moderate	Moderate	0.03	0.06	0.54
Moderate + Walking	Moderate	0.04	0.13	0.16
Walking	Moderate	0.17	0.19	0.03
Vigorous	Vigorous	0.01	0.04	0.63
Total PA	Total PA	0.04	0.11	0.21

The PA levels for the IPAQ and the SWA by age and BMI are shown in Table II. The IPAQ estimates (min/day) were higher in total PA, moderate and vigorous intensity PA, and lower in sedentary time as compared to the SWA (all p<0.001). Similar results were observed across age and BMI groups (see Table II).

The concordance correlation coefficients between the IPAQ and the SWA ranged from 0.01 to 0.17; whereas the Pearson correlation coefficients ranged from 0.04 to 0.19 (see Table III).

Figure 1 shows the Bland-Altman plot for inter-method agreement between the IPAQ and the SWA. The mean difference (SD) for total PA, vigorous intensity PA, walking time and moderate plus walking time from the IPAQ and SWA was -211 (265), -23 (68), 33 (108) and -188 (237) min/day, respectively (all p<0.001). The differences between the IPAQ and the SWA values were greater as the PA levels increased for total, vigorous, walking and moderate plus walking PA (R^2=0.79; R^2=0.99; R^2=0.41; R^2=0.76, respectively; all p<0.001).

Table IV shows the test-retest mean differences and SDs, 95% CI of the mean differences, the ICCs and 95% CI of ICCs, the SEMs, the intra-individual SDs and the coefficients of repeatabili-

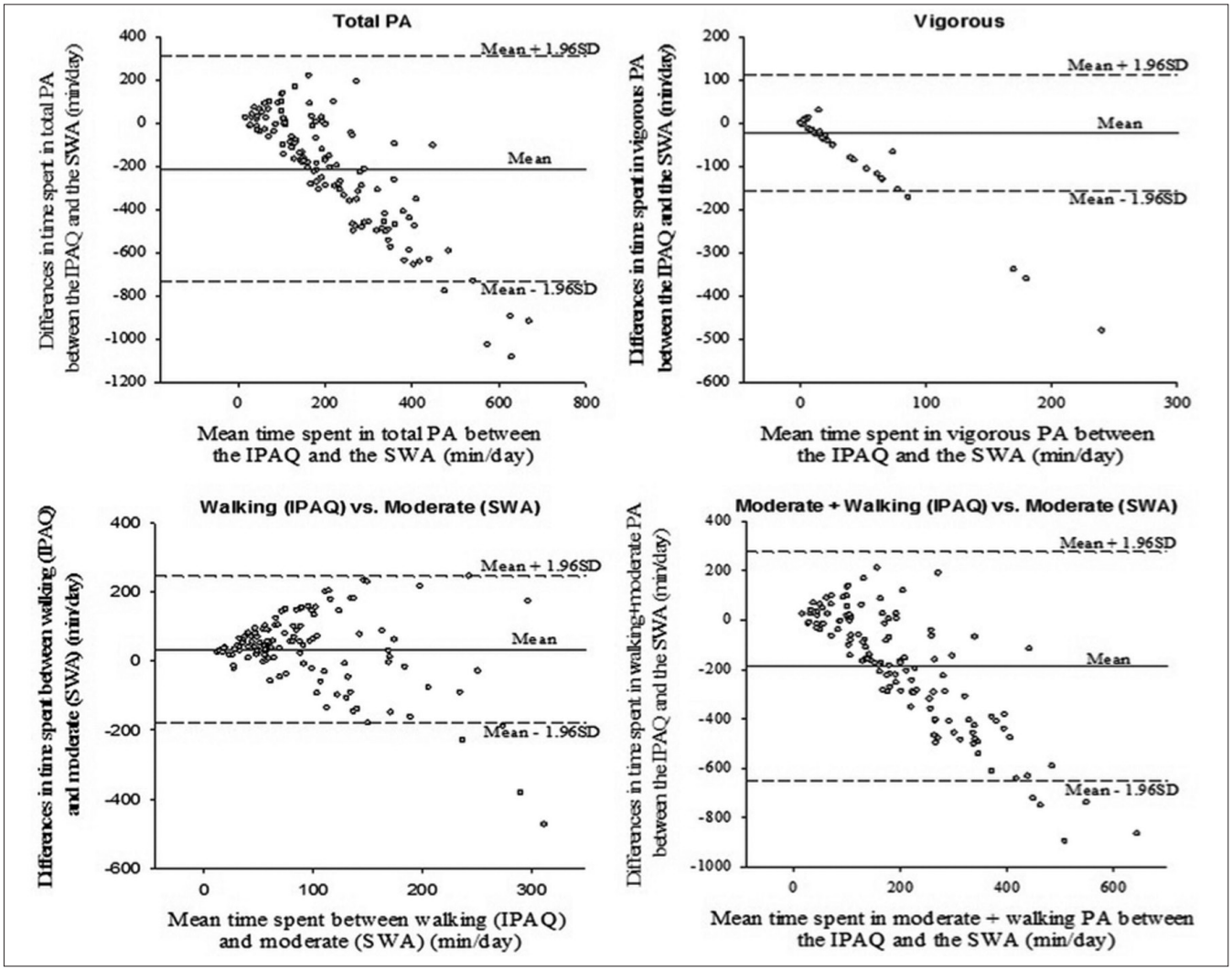

Fig. 1. Bland-Altman plot for inter-method agreement between the International Physical Activity Questionnaire (IPAQ) and the SenseWear armband (SWA).

Table IV. Test-retest agreement and measurement errors for the International Physical Activity Questionnaire (IPAQ), n=183.

	Mean test (SD)	Mean retest (SD)	Mean difference (SD)	95% CI Mean difference	Intra-individual (SD)	SEM	ICC	95% CI ICC	Coefficient of Repeatability
IPAQ, total score (MET/day)	924 (874)	1172 (1198)	-249 (90)***	-380; -117	2378	639	0.77	0.70; 0.83	1299
Sitting (min/day)	318 (174)	314 (167)	4 (167)	-21; 28	35	118	0.68	0.58; 0.76	232
Vehicle (min/day)	45 (64)	43 (67)	2 (75)	-9; 13	19	53	0.52	0.35; 0.64	104
Walking (MET/day)	280 (364)	326 (422)	-46 (374)	-101; 8	441	265	0.71	0.61; 0.78	523
Moderate (MET/day)	500 (439)	634 (621)	-134 (608)**	-222; -45	1277	430	0.53	0.37; 0.65	863
Vigorous (MET/day)	144 (395)	198 (581)	-54 (366)*	-107; 0	513	259	0.84	0.79; 0.88	513
Working (MET/day)	202 (554)	352 (936)	-149 (656)**	-245; -54	1430	464	0.78	0.70; 0.83	932
Active Transport (MET/day)	142 (221)	152 (237)	-11 (256)	-48; 27	103	181	0.55	0.39; 0.66	355
Domestic (MET/day)	415 (353)	483 (484)	-68 (443)*	-132; -3	648	313	0.62	0.50; 0.72	621
Leisure (MET/day)	158 (231)	185 (229)	-27 (256)	-64; 10	257	181	0.55	0.40; 0.67	357

Differences between the test and retest from the IPAQ tested for physical activity using a *t*-test. *p<0.05; **p<0.01; ***p< 0.001. Confidence intervals (CI); intraclass correlation coefficient (ICC); standard deviation (SD); standard error of the measurement (SEM).

ty. No systematic test-retest differences were found for sitting, vehicle, walking, active transport time and leisure domains. Systematic differences were found for total PA score (p<0.001), moderate intensity (p=0.003), vigorous intensity (p=0.049), working (p=0.002), and domestic (p=0.04) domains. The ICCs ranged from 0.52 to 0.84. The ICCs for those domains without systematic differences (sitting, vehicle, walking, active transport time and leisure domains) ranged from 0.52 to 0.71. The SEMs were overall satisfactory for sitting, vehicle, walking, active transport time and leisure domains from IPAQ (see Table IV). Mean differences between test and retest were lower than the SEM for sitting, vehicle, walking, active transport time and leisure domains; ranging from -46 to 4 min/day. The coefficient of repeatability was less than 2 SDs for all the variables studied from the IPAQ.

Figure 2 shows the Bland-Altman graph for the test-retest of the IPAQ. The differences between the test-retest values were greater as time reported in vehicle, walking, active transport, and leisure domains increased (R^2=0.40; R^2=0.47; R^2=0.60, R^2=0.50; respectively, all p<0.001), whereas no positive association was found for sitting domain (R^2=0.01, p=0.153).

Discussion

The present study showed that self-reported IPAQ differed with SWA when assessing PA levels in Spanish women with fibromyalgia. The results also suggested that IPAQ has poor to good test-retest reliability. Taken together, these findings suggest that self-reported IPAQ should not be used to assess PA in Spanish women with fibromyalgia.

A previous study by McLoughlin *et al*. (42) showed that women with fibromyalgia reported significantly higher levels of moderate and vigorous PA with the IPAQ than those measured by the accelerometer. In the present study we also showed significantly greater minutes per day reported with the IPAQ than those measured with the SWA. The study by Kaleth *et al*. (43) in patients with fibromyalgia aged 49.1±9.6 years found no significant relationship between the IPAQ short-version and accelerometry, which concur with other findings (42) when using the IPAQ long-form. These results are in agreement with our findings, yet we used the SWA instead of an Actigraph. Unlike the above mentioned studies in a fibromyalgia population (42, 43), we conducted the Bland-Altman method, since this technique is more adequate and informative when analysing the agreement between different methods (44). In other validation studies with the IPAQ *versus* an accelerometer with Swedish adults (45) and adolescents (46), they found similar results, showing that IPAQ gave significantly higher estimates of PA than the objective measure (Actigraph). They also showed higher differences between both methods when the time spent on PA measured by the accelerometer was higher. These studies however showed a significant poor-to-moderate agreement between the IPAQ and the objective measure (45, 46). Other previous validation studies in healthy people from different countries (23-25, 47, 48) also showed slightly higher correlation coefficients than those obtained in our study. It is noteworthy that the correlation coefficient has previously been criticised in the analysis of measurement method comparison data (44), so previous studies using solely this technique are not appropriate.

The absence of relationship and the observed differences between the IPAQ and an objective measure in the present and previous studies conducted with fibromyalgia population (42, 43) may be due to the inability of the IPAQ for classifying correctly subjects in light or low-moderate intensity PA level. Because this type of activities is the most common in the fibromyalgia population (42), this could result in poor recall, and therefore corroborate the great differences obtained between the results with the IPAQ and the SWA. Our patients underestimated their total sedentary behaviour time and overestimated time spent on PA. This finding has been previously described (49). This may be the result of social desirability bias, whereby the patients underestimate undesirable behaviours and overestimate desirable behaviours. Other reason could be that exercise is perceived as more painful and requiring more effort in this population, as corroborated by Cook *et al*. (50) in patients with chronic fatigue syndrome and co-

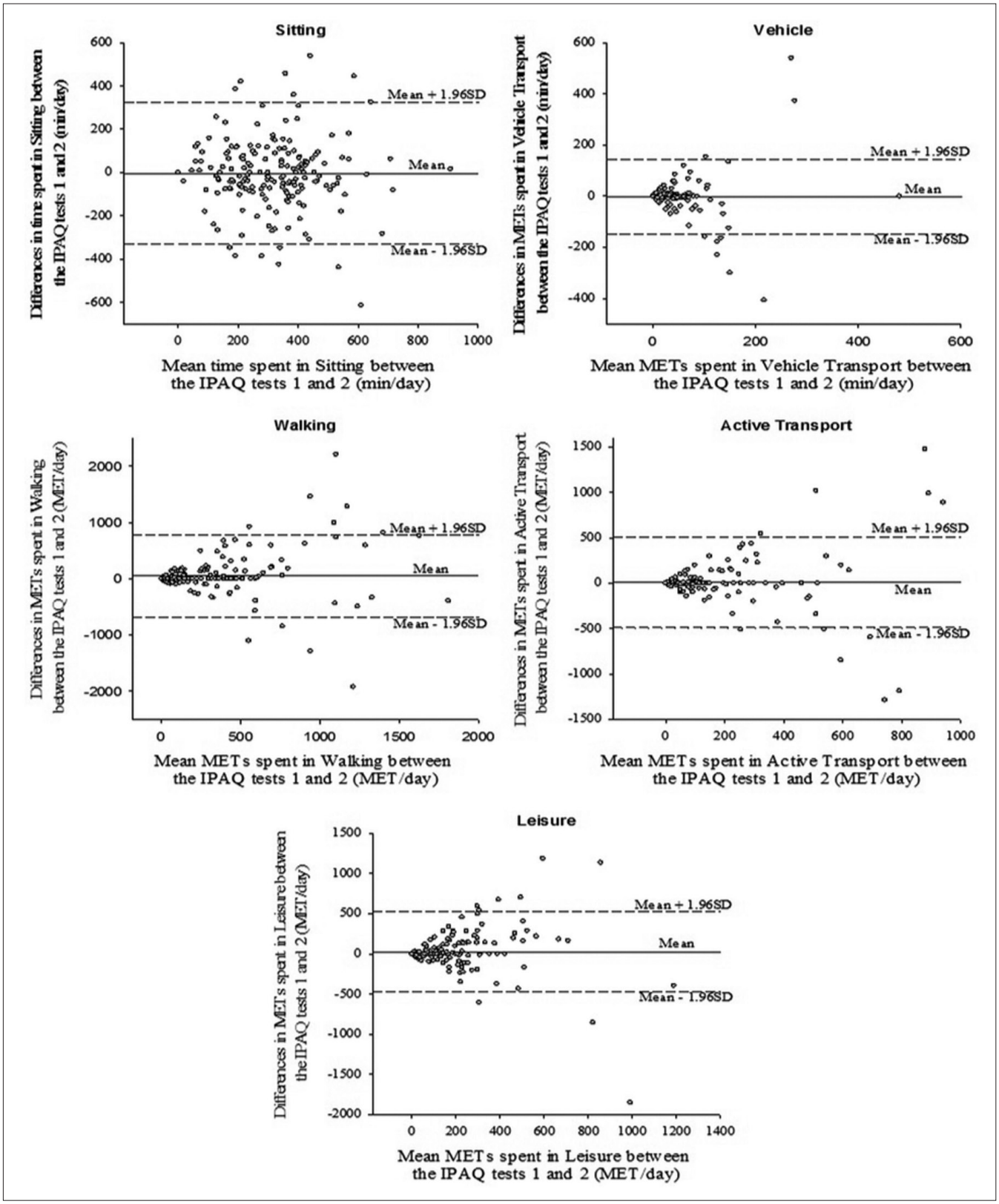

Fig. 2. Bland-Altman plot for test-retest agreement for the International Physical Activity Questionnaire (IPAQ).

morbid fibromyalgia. This perception might manifest in an overestimation of the PA performed (51). Moreover, fibromyalgia patients may also have a greater variability in their manner of self-report than healthy controls (42). Therefore, the absence of a significant relationship between the IPAQ and the SWA in the present study suggests that the IPAQ fail to adequately capture PA behaviours in fibromyalgia patients.

The present study did not show over-

all satisfactory test-retest reliability for the IPAQ domains. The mean difference was low for sitting, vehicle, walking, active transport and leisure activities from the IPAQ. Despite we obtained ICC values from 0.52 to 0.84 in all domains and PA intensities, total, moderate and vigorous PA, and working and domestic domains showed significant test-retest mean differences, so that we did not accept the good reliability of the instrument in these specific PA intensities and domains. Kaleth *et al*. (43) showed low reliability of the IPAQ short-form in a smaller sample (n=28) of patients with fibromyalgia than ours (n=183). Furthermore, they only provided the ICC as a reliability measure, whereas we provided a greater number of reliability measures. Specifically the use of the SEM (together with the ICC) has been highly recommended (40). This measure provides an absolute index of reliability, unlike the ICC which is a relative measure of reliability (40). Other researches with different study populations showed that the IPAQ short-form seems not to be a good indicator of PA behaviour (52-54). Previous studies examining the reliability of IPAQ showed reliability coefficients greater than 0.70 (21, 23, 55-58), whereas other studies showed low reliability coefficients (25, 59, 60). The heteroscedasticity observed in the Bland-Altman plots of the IPAQ test-retest suggested that the reproducibility of the data decreased as the amount of reported time in a specific domain (vehicle, walking, active transport and leisure) increased. This was not the case for sitting domain (heteroscedasticity was not observed). Good levels of repeatability were obtained for the sitting, the vehicle, the walking, the active transport and the leisure activities from the IPAQ, which suggests that the recall was repeatable irrespective of the amount of reported activity.

The present study has some limitations. The absence of a healthy group did not allow direct comparison. The sample is of convenience, which results in some limitations: by lessening representativeness of the Spanish population who have fibromyalgia and unknown levels of sampling error. Otherwise, our sample population was between 23 to 64 years old, which is the same as for whom the IPAQ was designed and which strengthens de validity of our results. The SWA is a valid device to measure PA in people with fibromyalgia (20). General criticisms of belt-mounted PA monitors include the inability to detect arm movements and load work performed by pushing, lifting, or carrying objects. The SWA may solve these issues through heat production measurements and placement on the upper arm. The quality of the SWA data (7 consecutive valid days) was an important strength of our study. The absence of a men sample did not let us know whether these findings apply to men, so future studies should analyse the validity and reliability of the IPAQ in men with fibromyalgia.

In conclusion, the present study showed that the IPAQ is not comparable with a multi-sensor armband accelerometer (SenseWear Pro_3 Armband) and is not a reliable tool to assess PA in women with fibromyalgia. The results suggest that the IPAQ overestimates PA. The instrument reported acceptable test-retest reliability in sitting, vehicle, walking, active transport and leisure activities; but not in the total PA score, moderate and vigorous intensity, as well as working and domestic domains.

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4. EFFECTIVENES OF EXERCISE INTERVENTION PROGRAMS FOR TREATING ACUTE PAIN IN FIBROMYALGIA

(Paper VI and VII)

A warm water pool-based exercise program decreases immediate pain in female fibromyalgia patients: uncontrolled clinical trial.

Segura-Jiménez V, Carbonell-Baeza A, Aparicio VA, Samos B, Femia P, Ruiz JR, Delgado-Fernández M.

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A Warm Water Pool-Based Exercise Program Decreases Immediate Pain in Female Fibromyalgia Patients: Uncontrolled Clinical Trial

Authors

V. Segura-Jiménez[1], A. Carbonell-Baeza[1,2], V. A. Aparicio[1,3], B. Samos[1], P. Femia[5], J. R. Ruiz[1,4], M. Delgado-Fernández[1]

Affiliations

[1] Department of Physical Education and Sports, School of Sport Sciences, University of Granada, Granada, Spain
[2] Department of Physical Education, School of Sciences Education, University of Cádiz, Cádiz, Spain
[3] Department of Physiology, Faculty of Pharmacy, University of Granada, Granada, Spain
[4] Unit for Preventive Nutrition, Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden
[5] Department of Biostatistics, University of Granada, Granada, Spain

Key words
- immediate pain
- fibromyalgia
- women
- exercise therapy
- pool-based
- warm water

Abstract

Fibromyalgia is characterized by chronic and extended musculoskeletal pain. The combination of exercise therapy with the warm water may be an appropriate treatment. However, studies focusing on the analysis of immediate pain during and after an exercise session are rare. This study aimed to determine the immediate changes of a warm water pool-based exercise program (12 weeks) on pain (before vs. after session) in female fibromyalgia patients. 33 Spanish women with fibromyalgia were selected to participate in a 12 weeks (2 sessions/week) low-moderate intensity warm water pool-based program. We assessed pain by means of a Visual Analogue Scale before and after each single session (i.e., 24 sessions). We observed immediate benefits on pain with a mean decrease ~15% in all sessions, except in the fourth one. There was an association of pain difference (pre-post) session with pain pre session ($p=0.005$; $\beta=0.097\pm0.034$) and with age ($p<0.001$; $\beta=0.032\pm0.008$). There were no significant accumulative differences on pain, pre session, post session, and pre-post changes (all $p>0.05$). Therefore this study showed that a warm water pool-based exercise program for 12 weeks (2 times/week) led to a positive immediate decrease in level of pain in female patients with fibromyalgia. Improvements were higher in older women and in those with more intense pain.

Introduction

Fibromyalgia (FM) is a chronic disease characterized by musculoskeletal pain, as well as the presence of multiple locations of tender points (TP) [45,46]. The most prominent symptoms include fatigue, muscle stiffness, sleep disturbances, muscle pain and memory and cognitive difficulties [1,37,46]. Treatment of FM is a complicated and controversial process, but a wide range of effective pharmacological [42], cognitive behavioural [12] and exercise-based interventions [17] are available. Exercise therapy in FM patients has been usually focused on either pool and/or land-based exercises [9,10,18,21,30,36].

There is a mounting evidence of central pain processing abnormalities in almost all FM patients [38,39]. These anomalies include hyperalgesia, allodynia, abnormal temporal summation of second pain, neuroendocrine abnormalities, and abnormal activation of pain-related brain regions [39]. FM syndrome seems to share similar characteristics with neuropathic pain syndromes, including ineffective response to many analgesics [39]. There is an increase of nitric oxide synthesis activity and reduced arginase activity in FM patients, which may be due to increased cyclooxygenase enzyme activity and oxidant/antioxidant imbalance [13]. Nitric oxide is an important transmitter in pain pathways [13]. Pain and fatigue significantly impair health related quality of life [44]. Additionally, pain has been identified as one of the most characteristic symptoms in FM patients [2,4]. Moreover, there is an inverse association between pain and functional capacity levels in this population [11]. Physical activity plays a role in balancing these processes. Physically active FM patients appear to maintain their ability to modulate pain while those who are less active do not [29].

Although FM patients usually associate isometric muscle activity [22] and physical activity with greater pain and fatigue than healthy people [16], there is controversy about the absence [22] or presence [23] of significant changes in pressure pain thresholds before and after the static muscle activity. Some studies showed that pool exercise improves health status and chronic widespread pain in FM patients [27,43]. Hydrotherapy (with

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Correspondence
Víctor Segura-Jiménez, BSc
Department of Physical Activity and Sports
University of Granada
Carretera de Alfacar, s/n.
18011 Granada
Spain
Tel.: +34/958/244 375
Fax: +34/958/244 369
vsegura@ugr.es

or without exercise) has been recommended for the management of FM because of the water's buoyancy and warm temperature [18,30,31]. Balneotherapy sessions appear to reduce pain and increase mobility dynamics in women with FM [5,24]. In addition, the combination of exercise therapy with the warm water reduces pain in this population [32] with greater benefits than exercise by itself [15] and with longer effects on pain management [21]. Indeed, previous studies observed improvements on tender points counts (TPC) [15,31,32], perceived pain [3,15,31,32] or visual analogic scale (VAS) [3,15,19,31] after a pool-based intervention program. Therefore, the physical properties of warm water and the benefits of the adapted exercise [7,8] could collectively promote an analgesic effect and thus reduce pain substantially in women with FM.

Studies focusing on examining the immediate changes of a single water-based exercise session on pain in FM patients are however scarce. It is of relevance to better understand if a single session of warm water-based exercise causes an immediate decrease in pain in female FM patients.

The aim of the present study was to determine the immediate changes in pain in female FM patients through a warm water pool-based exercise program of 12 weeks (2 sessions/week). We also studied the accumulative changes of a warm water pool-based program.

Materials and Methods

Participants

We contacted a total of 44 Spanish female FM patients, from the Granada Fibromyalgia Association (AGRAFIM), who gave their written informed consent after receiving detailed information about the aims of the study and the study procedures. The inclusion criteria were:

1) meeting the American College of Rheumatology criteria: widespread pain for more than 3 months and pain with 4 kg/cm^2 of pressure for 11 or more of 18 Tender Points (TP) [46];
2) no other severe somatic or psychiatric disorders, such as stroke or schizophrenia, chlorine allergy, or other diseases that prevent physical loading;
3) no participation in another type of physical or psychological therapy at the same time.

3 women did not have at least 11 tender points. A total of 41 females were selected and started the program. 4 women discontinued the program due to family commitments, personal and health problems, and another 4 were excluded for attending less than 70% of the program (attendance: 32.4%, 53.1%, 55.9% and 59.4%). A total of 33 (80.5%) participants carried out the intervention program and were included in the final analysis. No differences were observed between the final sample (n=33) and the original sample (n=41) in any demographic and clinical variables (P-value range from 0.35 to 0.99).

Design

The present study was an uncontrolled clinical trial with allocation of participants into one intervention group (n=33). The intervention program comprised of 2 sessions per week for 12 weeks. The 2 sessions (Monday and Wednesday) were performed in a chest-high warm pool (34 °C) each lasting 45 min. The exercise sessions were carefully supervised by a fitness specialist who worked with 4 groups of 7, 8, 9 and 9 women, allocated for convenience to each group. Participants were asked not to change their activity levels and medication during the 12-week intervention period. All water-based sessions were performed in the Virgen de las Nieves Hospital (Granada, Spain). The research protocol was reviewed and approved by the Ethics Committee of the Virgen de las Nieves Hospital (Granada, Spain) and performed in accordance with the ethical standards of the International Journal of Sports Medicine [20]. The study was developed between January 2008 and June 2009, following the ethical guidelines of the Declaration of Helsinki, last modified in 2000.

Exercise intervention

Each exercise session included a 10 min warm-up period with slow walking, mobility and stretching exercises, followed by 25 min of exercise, and finished with a 10 min cool-down period of stretching and relaxation exercises. Monday sessions involved strength exercises developed at a slow pace using water and aquatic materials as a means of resistance including a stepped progression during the program. Wednesday sessions consisted of balance oriented activities: changes of position, monopodal and bipodal stance, walking backwards, coordination by means of exercises with aquatic materials, and dancing aerobic exercises.

Training intensity was controlled by the rate of perceived exertion (RPE) based on Borg's conventional (6–20 point) scale [6]. The intervention medium values of RPE were 12±2 points on both Monday and Wednesday. These RPE values correspond to a subjective perceived exertion of 'fairly light exertion and somewhat hard exertion', that is, low-moderate intensity.

Outcome measures

Tender points

We assessed 18 TP according to the American College of Rheumatology criteria for classification of FM using a standard pressure algometer (EFFEGI, FPK 20, Italy). The mean of 2 successive measurements at each tender point was used for the analysis. Tender point scored as positive when the patient noted pain at a pressure of 4 kg/cm^2 or less. The total count of such positive TP was recorded for each participant.

Body composition

We performed a bioelectrical impedance analysis with an 8-polar tactile-electrode impedanciometer (InBody 720, Biospace). We measured weight (kg) and body fat percentage, and skeletal muscle mass (kg) was estimated. Validity of this instrument was reported elsewhere [25,26]. Height (cm) was measured using a stadiometer (Seca 22, Hamburg, Germany). Body mass index (BMI) was calculated (kg/m^2).

Immediate pain

Patients reported their pain immediately before (pre) and after (post) each session by means of the VAS. The VAS has previously been validated [35] and highly recommended to measure pain in FM patients [40]. The VAS ranges from 0 (no pain) to 10 (severe pain).

Statistical analyses

Demographic and clinical variables were analyzed by comparing the results from the 4 intervention groups with the Kruskal-Wallis test.

Pain pre vs. post session differences were analyzed using the non-parametric Wilcoxon test. Multiple comparisons were

Table 1 Sociodemographic characteristics of women with fibromyalgia.

Variable	Training group (n = 33)	Dropouts (n = 8)
tender points count	17.1 (1.5)	17.1 (1.2)
age (years)	50.0 (7.3)	50.4 (6.9)
weight (kg)	71.1 (12.4)	84.0 (14.4)
body mass index	28.4 (4.7)*	34.8 (5.6)
body fat percentage (kg/m^2)	38.9 (7.1)*	45.6 (4.0)
muscle mass (kg)	23.1 (2.4)*	24.4 (3.7)
years since clinical diagnosis, n (%)		
≤ 5 years	17 (51.5)	5 (62.5)
> 5 years	16 (48.5)	3 (37.5)
marital status, n (%)		
married	25 (75.8)	5 (62.5)
unmarried	2 (6.1)	1 (12.5)
separated/divorced/widowed	6 (18.2)	2 (25.0)
educational status, n (%)		
unfinished studies	1 (3.0)	1 (12.5)
primary school	17 (51.5)	4 (50.0)
secondary school	7 (21.2)	1 (12.5)
university degree	8 (24.2)	2 (25.0)
occupational status, n (%)*		
housewife	18 (54.5)	5 (71.4)
student	1 (3.0)	0
working	11 (33.3)	2 (28.6)
unemployed	2 (6.1)	0
retired	1 (3.0)	0
income, n (%)		
< 1200,00 €	14 (42.4)	3 (37.5)
1201,00–1800,00 €	5 (15.2)	2 (25)
> 1800,00 €	14 (42.4)	3 (37.5)

Values are the mean (standard deviation) unless otherwise indicated
*One missing data

Table 2 Changes of 12-week intervention on perceived acute pain in women with fibromyalgia.

Sessions	Pre	Post	P-value
session 1*			
session 2	6.5 (1.81)	5.87 (2.10)	0.010
session 3	6.68 (1.55)	6.06 (1.98)	0.040
session 4	6.6 (1.94)	6.25 (2.01)	0.158
session 5	6.8 (1.64)	5.93 (2.20)	0.022
session 6	7.22 (1.9)	5.55 (2.17)	<0.001
session 7	6.96 (1.9)	6.16 (2.18)	0.003
session 8	7.07 (1.64)	5.76 (1.78)	<0.001
session 9	6.96 (1.81)	6.34 (2.02)	0.013
session 10	7.3 (1.72)	6.20 (2.04)	<0.001
session 11	7.16 (1.8)	6.38 (1.96)	0.040
session 12	6.66 (2.07)	6.07 (2.01)	0.018
session 13	7.03 (1.42)	5.84 (2.16)	0.001
session 14	7.25 (1.48)	6.33 (2.22)	0.007
session 15	7.25 (2.20)	6.28 (2.67)	0.006
session 16	7.71 (1.41)	6.7 (2.15)	0.002
session 17	7.46 (1.4)	6.57 (1.75)	0.002
session 18	7.34 (1.58)	6.37 (1.97)	<0.001
session 19	7.41 (1.61)	6.35 (2.18)	0.001
session 20	7.1 (1.93)	6.13 (2.23)	0.001
session 21	6.87 (1.93)	6.12 (2.29)	0.001
session 22	6.96 (1.89)	5.76 (2.14)	<0.001
session 23	7.29 (1.23)	6.34 (1.58)	0.004
session 24	6.88 (1.96)	5.88 (2.10)	0.001

Values are the mean (standard deviation). *Values pre session were missing.
Using Bonferroni correction, the significance level was set at p ≤ 0.002

adjusted by Bonferroni. We conducted linear regression analysis to examine the association between pain pre session and pre-post session changes controlling for age. To study the accumulative changes on pain pre, post, and pre vs. post changes we conducted linear mixed models adjusting for age, attendance (number of real sessions) and baseline pain (first session). The level of statistical significance was set at p ≤ 0.05. Analyses were performed using the Statistical Package for Social Sciences (SPSS, v. 16.0 for WINDOWS; SPSS Inc, Chicago).

Results

During the study period, no participant reported an exacerbation of FM symptoms beyond normal flares, and there were no serious adverse events. Patient's adherence to the intervention was 84.4% (range 70–96.9%). No significant differences in baseline subjects' characteristics (age, VAS, TPC and BMI) between the various exercise groups were found (all p > 0.05).

The demographic characteristics of the final study sample and the dropouts are shown in **Table 1**. We observed a ~15% decrease of immediate pain intensity in the comparison of VAS values before and after each session with a decrease mean of 0.93 ± 0.059. In all sessions, the group showed significant immediate changes (p-values from 0.04 to 0.0001 (CI, 0.82, 1.05)), except in the fourth session (p = 0.158) (**Table 2**). We repeated the analysis including all the participants and observed a ~15% decrease of immediate pain intensity in the comparison of VAS values before and after each session with a decrease mean of 1.04 ± 0.06. No significant differences (P-value from 0.51 to 1.0) between the final sample (n = 33) and the original sample (n = 41) were found.

There was an association of pain pre-post session with pain pre session (p = 0.005; β = 0.097 ± 0.034) and with age (p < 0.001; β = 0.032 ± 0.008) (**Fig. 1**). There were no significant accumulative differences in pain, pre session, post session, and pre-post changes (all p > 0.05) (**Fig. 2**). No significant differences (p > 0.05) between the final sample and the original sample were found.

Discussion

The present study showed a positive (beneficial) immediate decrease in pain using a warm water pool-based exercise program in female FM patients. However, no significant accumulative changes in pain were observed. Noteworthy is that the intervention was well tolerated by the patients, and did not have any detrimental effects on patients' health. These findings are clinically relevant and highlight the benefits of a single exercise bout on pain in women with FM.

We used the mean VAS to assess pain before and after each session, and we observed that the mean VAS decreased after each session except after the fourth one. We used the same environmental conditions and water temperature in all the sessions. In addition we carried out all the sessions with the same procedures and characteristics, so we cannot foresee the reason for the non-significant results observed in the fourth session. By using the Bonferroni correction, we obtained a satisfactorily significant difference in 12 sessions, which further strengthen the study's findings. We observed that one exercise session in warm water alone can be effective in improving the perception of

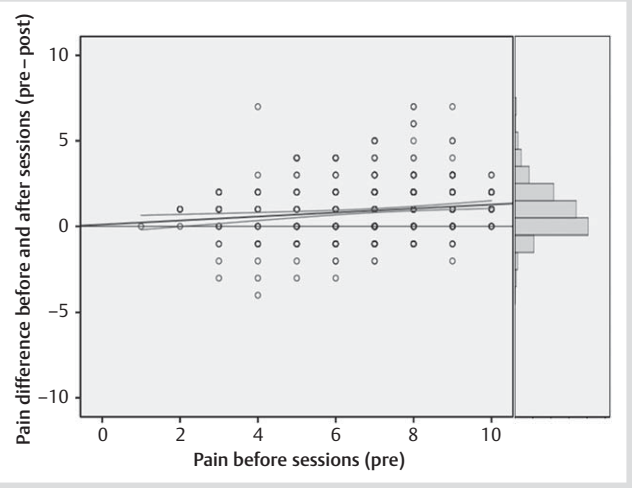

Fig. 1 Relation between pain difference before and after sessions (pre minus post) and pain before sessions (pre) in women with fibromyalgia. Diagram represents the linear least square and confidence bands for average pre-post difference (95 % CI). There was an association of pain pre-post session with pain pre session ($p = 0.005$; $\beta = 0.097 \pm 0.034$) and with age ($p < 0.001$; $\beta = 0.032 \pm 0.008$). Histogram shows frequency distribution of the variable (asymmetry suggests that there are more benefitted subjects). β value is the coefficient ± standard error.

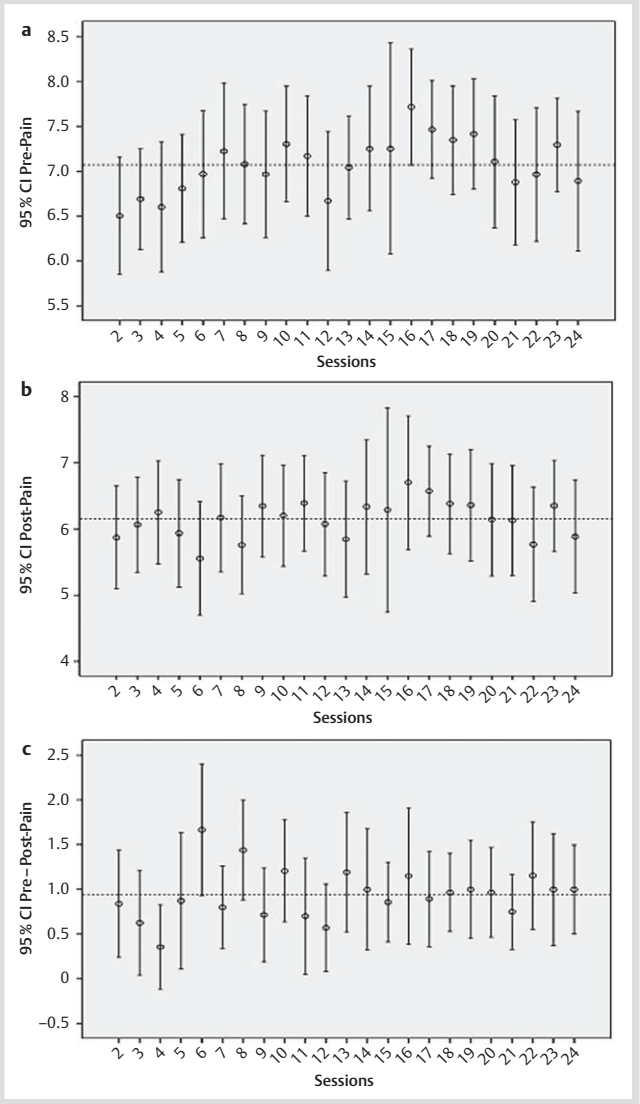

Fig. 2 Changes of 12-week intervention over time on pain in women with fibromyalgia. No significant changes ($p > 0.05$). **a** Changes in pre-values over time, $F = 5.247$ (CI, 0.002, 0.030). **b** Changes in post-values over time, $F = 2.871$ (CI, −0.001, 0.026). **c** Changes in pre – post values over time $F = 0.077$ (CI, −0.010, 0.013).

immediate pain and thus promoting an analgesic effect. These findings concur with those observed by Berger et al. [5] in elderly subjects (11 female and 1 male), but they only compared pain before and after the first and last session, gaining significance in both. Noteworthy is that the conditions were similar to ours: all sessions took place in a swimming pool (1.3 meters in depth) filled with water of 34 °C and water exercise sessions lasted 45 minutes [5]. A recent review points to a dysfunction of endogeneous analgesia during muscle activity and aerobic exercise, resulting in increased generalized pain sensitivity in FM patients [33]. It is remarkable that those studies address acute bouts of exercise (i.e., unilateral contractions and submaximal cycle exercise), whereas we conducted an adapted exercise program [33]. These findings do not contradict the clinical evidence favouring the use of tailored and graded exercise as an intervention for chronic pain. The combination of warm water and the adapted exercise for this population (i.e., aerobic, funny, non-painful, at a slow pace, exercise in group…) might be decisive in the results obtained. These data show that exercise in warm water has an immediate short-term usefulness and should be considered as an option for treating FM pain.

The significant association between pre-post/pre-pain and age indicates that women with higher pain pre-session were also those who benefit the most, so that for every point increased in pain pre session, the pre-post change in pain increased by 0.097 points. Similarly, older women experienced higher pain decrease post-session, so that for every point increased in pain pre session, the pre-post change in pain increased by 0.032 points.

Accumulative changes in pain indicate that intervention is effective over time and patients have less pain as the program progresses, yet this was not the case in our study. Our results did not confirm previous research that found changes over time [3,19]. Although it is important to note that they used other assessment tools (Fibromialgia Impact Questionnaire (FIQ) pain [3] and EuroQol-5D (EQ-5D) [19]) than ours (VAS pain). Moreover, most of previous studies measured pain intensity just before and after the treatment, and did not include measurements during the treatment [15,27,32]. Other methodological differences should be emphasized. We performed a 3 months intervention but some of these studies carried out programs of longer duration (4 months [31,32] or 6 months [28]), and performed a parallel education program [28,34]. Suman et al. [41] showed a VAS decrease after the treatment, yet their intensive program (5 hours a day from Monday to Friday) included educational sessions, physical exercise and a cognitive behavioural approach. De Andrade et al. [14] conducted a 12 weeks (3 sessions/week) program establishing one pool group and one sea group. Both groups improved pain (assessed by VAS and TPC) over time. The fact that we observed immediate decrease in pain but not over time could be partially explained by the fact that we did not apply an appropiate frequency program. Pain relief is related to a higher length and frequency of warm-water based exercise sessions per week [19]. To note is that studies with significant accumulative changes used at least a 3 sessions/week intervention [14,31,32]. Future studies should asssess pain with more objective tools, such as algometry.

Pain is a multifactorial symptomatology. We found that exercise yielded a decrease in immediate pain levels, other factors such as sleep disturbances, fatigue and muscle stiffness could also potentially affect pain. This may partially explain why we observed no accumulative changes. Others used FIQ-pain to assess pain before and after the intervention [27,32]. The FIQ-pain indicates the pain over the previous week, whereas in the present study we asked for the current state of pain. To our knowledge, there are no studies examining the immediate and accumulative changes of a warm water pool-based program on pain by means of VAS in each of the sessions, which hampers further comparisons.

We did not recollect data in the 24–48 h post-exercise, and it would be interesting to study this in future research in order to assess how long decreased pain remains active. We do not know whether these results could be applied to men, and future studies should analyse the immediate and accumulative changes of a warm water pool-based program in pain in male FM patients. Moreover, further research is needed in order to determine whether programs of longer duration (>3 months), higher frequency (>2 sessions/week) or higher intensity (>13 RPE) induce major improvements in pain in female FM patients. It would be also interesting to compare land-based and water-based exercise, to find out which environment produces better benefits.

Conclusions

In summary, the present study showed that a warm water pool-based exercise program for 12 weeks (2 times/week) led to a positive immediate decrease in levels of pain in female FM patients. Improvements were greater in women of a greater age and who suffered more intense pain. These immediate changes in pain did not persist over time. It is strongly recommended that FM patients take part in therapeutic programs.

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Effectiveness of tai-chi for decreasing acute pain in fibromyalgia patients.

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VII

Effectiveness of Tai-Chi for Decreasing Acute Pain in Fibromyalgia Patients

Authors
V. Segura-Jiménez[1], A. Romero-Zurita[1], A. Carbonell-Baeza[1,2], V. A. Aparicio[3], J. R. Ruiz[1], M. Delgado-Fernández[1]

Affiliations
[1] Department of Physical Education and Sports, School of Sport Sciences, University of Granada, Spain
[2] Department of Physical Education, School of Sciences Education, University of Cádiz, Spain
[3] Department of Physiology and Institute of Nutrition and Food Technology, Faculty of Pharmacy and School of Sports Sciences, University of Granada, Spain

Key words
- immediate pain
- cumulative pain
- low-moderate intensity
- visual analogue scale
- alternative therapy
- exercise

Abstract

Tai-Chi has shown benefits in physical and psychological outcomes in diverse populations. We aimed to determine the changes elicited by a Tai-Chi program (12 and 24 weeks) in acute pain (before vs. after session) in fibromyalgia patients. We also assessed the cumulative changes in pain brought about by a Tai-Chi program. Thirty-six patients (29 women) with fibromyalgia participated in a low-moderate intensity Tai-Chi program for 12 weeks (3 sessions/week). Twenty-eight patients (27 women) continued the program for an additional 12 weeks (i.e., 24 weeks). We assessed pain by means of a Visual Analogue Scale (VAS) before and after each single session (i.e., 72 sessions). We observed significant immediate changes (P-values from 0.037 to 0.0001) with an approximately 12% mean decrease of acute pain in the comparison of VAS-values before and after each session (72 sessions in total), with the exception of 4 sessions. We observed significant changes in cumulative pain pre-session (95% CI = −0.019; −0.014; P < 0.001) and cumulative pain post-session (95% CI = −0.021; −0.015; P < 0.001) along the 24-week intervention only. In conclusion, a low-moderate intensity Tai-Chi program for 12 weeks (3 times/week) decreased levels of acute pain in fibromyalgia patients. A longer period is necessary (e.g. 24 weeks) for observing cumulative changes in pain.

Introduction

Pain has been identified as the most relevant symptom in fibromyalgia [1,30]. There is an inverse association between pain and functional capacity levels in these patients [8], and there is evidence that pain and fatigue significantly impair health-related quality of life [34]. This body of literature highlights the importance of treating pain in the fibromyalgia population. The Ottawa Panel recommended the use of regular physical exercise in order to manage fibromyalgia symptoms [3,4]. Physically active fibromyalgia patients are able to maintain their ability to modulate pain better than those who are less active [12,22]. Therefore, physical exercise plays a role in balancing these processes. Together with the physical exercise, the mind-body exercise (which incorporates human biological and psychological aspects into treatment, with the intent of using the mind to affect physical functioning and promote health [32]) and relaxation therapies can increase pain tolerance in fibromyalgia patients [6,7,11]. New approaches which combine the aspects mentioned above are needed in order to reduce pain, to improve the physical and emotional functioning and to enhance the health-related quality of life in fibromyalgia patients.

Tai-Chi is an ancient form of exercise. This discipline is performed at low speed and can be classified as a low-impact exercise [19] with aerobic nature [37]. Breathing, relaxation and mental concentration are essential while exercising in Tai-Chi discipline [32]. Therefore, Tai-Chi exercises combine aspects of mind-body therapy and physical exercise [32]. Tai-Chi has shown benefits on different physical (balance, gait, muscle strength, flexibility, cardiovascular) and psychological (attentiveness, sleep and anxiety) variables in different study populations and different chronic pain conditions [14]. A recent 28-week Tai-Chi intervention study observed improvements on functional capacity, symptomatology, psychological outcomes and pain in female fibromyalgia patients [27]. Lower body flexibility improvements of a 4-month Tai-Chi intervention has been previously reported in men with fibromyalgia [9]. A multiple-patient case report also showed positive changes in algometer score, aer-

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Correspondence
Víctor Segura-Jiménez
Department of Physical Education and Sports
University of Granada
Carretera de Alfacar, s/n.
Granada 18011
Spain
Tel.: +34/958/244 375
Fax: +34/958/244 369
vsegura@ugr.es

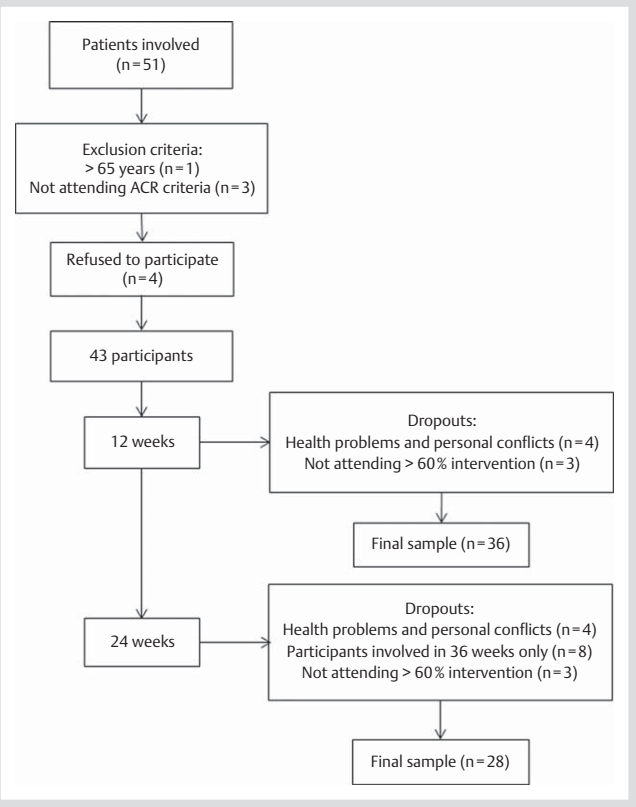

Fig. 1 Flowchart of participants.

obic capacity, agility–dynamic balance, total score of Fibromyalgia Impact Questionnaire (FIQ), and the dimensions of physical function, anxiety and depression in 4 of 6 men [10]. These studies reported improvements in pain by means of the FIQ-pain subscale [17,27,32], the Brief Pain Inventory short form [17], the total number of tender points and algometer score [27] and by the Short Form Health Survey (SF-36) bodily pain subscale [27]. While a positive reduction of pain after a Tai-Chi program in fibromyalgia patients has been described [17,27,32], further research is needed to support evidence-based practice [32].

The warm water pool-based exercise intervention has shown a decrease in acute pain in female fibromyalgia patients [29]. There is a need to better understand whether other physical exercise therapies have the same effect as a warm water pool-based exercise intervention in acute pain in this population. It is of importance to know if a single session of Tai-Chi exercise brings about an immediate decrease in acute pain in fibromyalgia patients, and whether there is a cumulative decrease in pain through a Tai-Chi program. Therefore, the aim of the present study was to ascertain the changes elicited by a Tai-Chi program lasting 12 or 24 weeks (3 sessions/week) in the acute pain experienced by fibromyalgia patients. We also studied the cumulative changes in pain brought about by the Tai-Chi program.

Materials & Methods

Participants

We contacted 2 fibromyalgia associations from Granada and Motril (South of Spain). A total of 51 patients gave their written informed consent after receiving detailed information about the aims and study procedures. The inclusion criteria were: 1) meeting the American College of Rheumatology (ACR) criteria: widespread pain for more than 3 months and pain with 4 kg/cm^2 of pressure for 11 or more of 18 tender points [36]; 2) not having any other severe somatic or psychiatric disorders, such as stroke or schizophrenia, or other diseases that prevent physical loading; 3) not attending another type of physical or psychological therapy at the same time; 4) meeting the age range criteria (35–65 years).

Three patients were excluded from the study because they did not meet the ACR criteria, while 1 patient was excluded for not meeting the age criteria. After the baseline measurements, 4 participants refused to participate due to conflict with their work schedules. Therefore, a sample of 43 fibromyalgia patients took part in the study. Patients were not engaged in regular physical activity >20 min >3 days/week.

The study flowchart for the patients is presented in **Fig. 1**.

Design

While we had an ethical obligation to provide treatment to all patients willing to participate in the study, our limited resources permitted intervention only according to a particular schedule. Patients who could participate in the study were assigned to the intervention group. Only 1 intervention group was established, with intervention being conducted at 2 sites (Granada and Motril). Patients participated in a 12-week Tai-Chi intervention program. Due to the program's success and patients' willingness to continue with the program, we extended the program for a further 12 weeks (72 sessions in total). A quasi-experimental design was applied (lacking a control group). Participant bias was controlled, as the same individual is used at each testing time point. The research protocol was reviewed and approved by the Ethics Committee of the *Virgen de las Nieves Hospital* (Granada, Spain) and followed the ethical standards of the International Journal of Sports Medicine [16]. The studies were carried out between September 2008 and February 2010. The ethical guidelines of the Declaration of Helsinki, last modified in 2000, were followed.

Tai-Chi intervention

The Tai-Chi program was based on the classical Yang Style: extended and natural postures, slow and even motions, light and steady movements, and curved, flowing lines of performance [31]. The Tai-Chi intervention took place 3 times a week for 12 or 24 weeks, with each session lasting 60 min. Each session consisted of the following: 15 min of warm-up with stretching, mobility and breathing techniques; 30 min of Tai-Chi exercises principles and techniques; and 15 min of cool-down (various relaxation methods). The intervention consisted of 8 forms from Yang Style Tai-Chi, with minor modifications that were suitable for patients with fibromyalgia. For example, during the first 2 weeks some exercises were performed with the participants sitting to avoid excessive fatigue. A Tai-Chi master with teaching experience conducted the lessons. The first 2 weeks of the intervention were focused on learning fundamental movement patterns. In subsequent sessions, patients practiced 8-Form, Yang Style Tai-Chi under the master's supervision.

Rate of perceived exertion (RPE) based on Borg's conventional (6–20 point) scale [2] was used to assess training intensity. The RPE intervention mean value was ~11.5 points. This RPE value corresponds to a subjective perceived exertion of 'fairly light exertion and somewhat hard exertion', i.e., low-moderate intensity.

Measures

Tender points

We used a standard pressure algometer (EFFEGI, FPK 20, Italy) to assess the tender points according to the ACR criteria for classification of fibromyalgia [36]. Two successive measurements at each tender point were assessed and the mean value was used for the analysis. A pressure of 4 kg/cm^2 or less was scored as a positive tender point. The total count of positive tender points was recorded for each participant.

Body composition

A bioelectrical impedance analysis with an 8-polar tactile-electrode impedance meter (InBody R20, Biospace, Seoul, Korea) was performed. Weight (kg) was measured, while body fat percentage and skeletal muscle mass (kg) were estimated. This instrument has been previously validated [20]. Waist circumference (cm) was measured by means of a measuring tape (Harpendem anthropometric tape Holtain Ltd.) at the middle point between the ribs and ileac crest, with the participant standing. Height (cm) was measured with a stadiometer (Seca 22, Hamburg, Germany) and body mass index (BMI) was calculated (kg/m^2).

Acute pain

A Visual Analogue Scale (VAS) for pain was administered immediately before (pre) and after (post) each Tai-Chi session. The VAS is a simple assessment tool consisting of a 10 cm line with 0 on one end, representing no pain, and 10 on the other, representing the worst pain ever experienced, which the patients mark to indicate the severity of pain at the present moment. The validity of the VAS has been previously demonstrated [25]. This tool has been highly recommended for measuring pain in fibromyalgia patients [26].

Statistical analyses

Descriptive analysis (i. e., mean, standard deviation and frequency) was used to analyse demographic and clinical (tender points count and body composition parameters) variables. The Kruskal-Wallis test was used to corroborate the equality of baseline characteristics of participants allocated in the different sites. Because pain variables were not normally distributed, nonparametric tests were used. Pain differences (pre vs. post) before and after each session were analysed using the non-parametric Wilcoxon test. To study the cumulative changes in pain pre, post, and pre vs. post changes we created linear mixed models adjusting for age, BMI, attendance (number of real sessions) and baseline pain (first session). The statistical significance level was set at $P \leq 0.05$. The Statistical Package for Social Sciences (IBM-SPSS, v. 20.0 for WINDOWS) was used to perform the analysis.

Results

Four patients discontinued the program due to family commitments, personal and health problems, and 3 were excluded for attending less than 60% of the program (attendance: 22.2%, 33.3% and 52.8%). A total of 36 (83.7%) and 28 (65.1%) participants carried out the 12- and 24-week intervention program, respectively, and were included in the final analysis. There were no differences between the female and male groups in baseline pain ($P=0.41$) or any other socio-demographic and clinical variable, except in the occupational status (housewife 65% vs. 17%, retired 4% vs. 67%; $P=0.005$, respectively) and muscle mass (23.7 ± 3.4 vs. 31.9 ± 2.9; $P=0.001$, respectively). The final 12-week sample ($n=36$) and the original sample ($n=43$) did not show differences in any demographic or clinical variable (P-value ranged from 0.46 to 0.99). The final 24-week sample ($n=28$) and the original sample ($n=43$) did not show differences in any demographic or clinical variable (P-value ranged from 0.30 to 0.99).

No major adverse effects or health problems were detected during the intervention program. Patients' adherence to the 12- and 24-week intervention was 83.6 % (range 61.1–100%) and 79.9% (range 61.1–97.2%), respectively. No significant differences in baseline subjects characteristics (age, VAS, tender points count, waist circumference, body mass percentage, muscle mass and BMI) were observed between the various location groups (all, $P>0.05$).

The demographic characteristics of the final study sample throughout the 12- and 24-week interventions are shown in **Table 1.** In all sessions, the group showed significant immediate changes (P-values from 0.037 to 0.0001), with the exception of 4 sessions (**Table 2**). We observed an approximately 12% decrease in acute pain intensity in the comparison of VAS-values before and after each session with a mean decrease of 0.85 ± 0.04 cm along the 12-week intervention and a mean decrease of 0.67 ± 0.03 cm along the 24-week intervention. We repeated the analysis to include all the participants that started the intervention program and observed an approximately 11% decrease of immediate pain intensity in the comparison of VAS-values before and after each session. No significant differences (P-values from 0.62 to 1.0) were observed between the final sample ($n=36$) and the original sample ($n=43$).

There were no significant cumulative differences in pain pre-session and pain post-session along the 12-week intervention (all $P>0.05$) (**Fig. 2**). A positive (beneficial) significant cumulative change in pain pre-session (95% Confidence Intervals (CI) = −0.019; −0.014; $P<0.001$) and pain post-session (95% CI = −0.021; −0.015; $P<0.001$) along the 24-week intervention was observed (**Fig. 2**). This positive significant cumulative change in pain pre-session (95% CI = −0.011; −0.001; $P=0.03$) was observed from the 46th session onwards. This positive significant cumulative change in pain post-session (95% CI = −0.012; −0.008; $P=0.02$) was observed from the 44th session onwards.

Discussion

The present study showed that a single session of Tai-Chi exercise decreases acute pain in fibromyalgia patients. Moreover, Tai-Chi is a potentially useful therapy at reducing pain in fibromyalgia patients over the long-term, since cumulative positive changes in pain were observed starting with the 16th week of the program. No adverse effects were detected. The intervention was well tolerated by the patients and did not have any detrimental effects on patients' health, suggesting that Tai-Chi is an adequate and safe practice for fibromyalgia participants. These findings highlight the benefit of a single Tai-Chi session on the acute pain experienced by fibromyalgia patients.

To the best of our knowledge only one study reported pre- vs. post-session pain changes by means of the VAS [29]. In that study, researchers carried out a 12-week (2 sessions/week) warm water pool-based exercise intervention and concluded that the program improved levels of acute pain after each session [29]. The results of the current study are consistent with these previous findings, showing that Tai-Chi can be as effective

Table 1 Socio-demographic and clinical variables of the study population.

Variable	12 weeks (n = 36)	24 weeks (n = 28)
	Mean (SD)	Mean (SD)
tender points	17.5 (1.3)	17.8 (0.5)
body mass index (kg/m^2)	28.1 (4.7)	28.4 (5.0)
age (years)	52.0 (6.6)	51.7 (6.4)
body fat percentage* (%)	36.0 (7.9)	37.0 (7.9)
muscle mass* (kg)	25.2 (4.6)	24.2 (3.9)
waist circumference (cm)	91.5 (15.7)	91.9 (16.7)
marital status*, n (%)		
married	31 (88.6)	24 (88.9)
unmarried	2 (5.7)	1 (3.7)
separate/divorced/widowed	2 (5.7)	2 (7.4)
educational status*, n (%)		
unfinished studies	2 (5.7)	2 (7.4)
primary school	23 (65.7)	19 (70.4)
secondary school	8 (22.9)	4 (14.8)
university degree	2 (5.7)	2 (7.4)
occupational status*, n (%)		
housewife	18 (56.3)	17 (68.0)
student	1 (3.1)	1 (4.0)
working	6 (18.8)	3 (12.0)
unemployed	2 (6.3)	3 (12.0)
retired	5 (15.6)	1 (4.0)
years since clinical diagnosis*, n (%)		
≤ 5 years	17 (50.0)	13 (50.0)
> 5 years	17 (50.0)	13 (50.0)
income* (€), n (%)		
< 1 200	16 (57.1)	14 (70.0)
1 201–1 800	5 (17.9)	3 (15.0)
> 1 800	7 (25.0)	3 (15.0)

Values are the mean (standard deviation [SD]) unless otherwise indicated

*Missing data

as a warm water pool-based exercise intervention in decreasing acute VAS-pain after each single session. In the present study we observed that mean VAS-pain decreased after all but four sessions. The same procedures and characteristics were carried out in all the sessions except during the first 2 weeks when patients were sitting to progressively adapt the exercise to their conditions and avoid exacerbating symptoms. Hence, we do not know the reason why no significant reductions were observed in these four sessions. The results of the present study showed that one Tai-Chi session by itself can be effective in improving the perception of acute pain and thus promoting an analgesic effect. A recent review which addressed acute bouts of exercise (i. e., unilateral contractions and submaximal cycle exercise), points to a dysfunction of endogenous analgesia during muscle activity and aerobic exercise in fibromyalgia patients [24]. While these findings do not concur with ours, it is important to note that this previous study addressed only static and extenuating muscular contractions and submaximal cycle exercise [24]. These acute bouts of exercise are characterized by incrementing musculoskeletal pain, stiffness and fatigue in fibromyalgia patients [15,18]. Instead, we performed complete sessions of Tai-Chi exercise, characterized by gentle movements, non-maintained muscle contractions and low-moderate intensity exercise. The multicomponent combination, physical exercise and mind-body practice of Tai-Chi has an immediate short-term usefulness and should be considered as an option for treating acute pain in fibromyalgia. To the best of our knowledge, there are no other studies investigating the immediate changes of a single Tai-Chi session in acute pain that can be used for comparison.

Cumulative changes in pain over time were studied in the present study in order to investigate whether participants decreased their pain levels as the program progressed. We did not observe changes in pain in the first 12 weeks (36 sessions) of interven-

Table 2 Pre- vs. post-pain values of the 24-week Tai-Chi intervention in fibromyalgia patients.

Session	Pre	Post	P	Session	Pre	Post	P	Session	Pre	Post	P
1	6.91 (1.63)	5.85 (1.70)	0.001	25	6.94 (1.55)	6.10 (1.62)	0.002	49	6.24 (1.22)	5.86 (1.20)	0.033
2	6.55 (1.56)	5.94 (1.58)	0.013	26	7.06 (1.81)	6.00 (1.88)	<0.001	50	6.22 (1.35)	5.78 (1.40)	0.112
3	6.52 (1.94)	5.83 (2.00)	0.035	27	7.13 (1.64)	6.09 (1.73)	<0.001	51	5.94 (1.39)	5.53 (1.74)	0.158
4	6.72 (1.53)	6.19 (1.75)	0.034	28	6.61 (1.41)	5.94 (1.57)	0.004	52	5.54 (1.56)	5.08 (1.69)	0.070
5	6.73 (1.96)	6.13 (1.98)	0.009	29	6.77 (1.54)	5.94 (1.69)	0.003	53	5.50 (1.64)	4.70 (1.45)	0.003
6	6.40 (2.13)	5.67 (1.86)	0.006	30	7.13 (1.59)	6.33 (1.69)	0.002	54	5.91 (1.54)	5.09 (1.44)	0.004
7	7.15 (1.10)	5.93 (1.59)	0.001	31	6.93 (1.62)	5.90 (1.76)	<0.001	55	6.10 (1.58)	5.48 (1.60)	0.005
8	7.31 (1.26)	6.58 (1.55)	0.001	32	6.70 (1.51)	5.91 (1.63)	<0.001	56	5.60 (1.64)	5.05 (1.70)	0.009
9	7.32 (1.25)	6.36 (1.52)	<0.001	33	7.16 (1.44)	5.91 (1.75)	<0.001	57	6.05 (1.73)	5.27 (1.61)	0.002
10	6.55 (1.54)	5.97 (1.59)	0.028	34	6.77 (1.48)	5.73 (1.69)	0.001	58	6.82 (1.24)	6.00 (1.06)	0.013
11	6.77 (1.57)	6.00 (1.58)	0.001	35	6.91 (1.40)	6.13 (1.54)	0.006	59	6.08 (1.61)	5.46 (1.67)	0.002
12	7.00 (1.34)	6.30 (1.66)	0.011	36	6.48 (1.62)	5.76 (1.77)	<0.001	60	5.72 (1.72)	4.92 (1.68)	0.001
13	7.47 (1.07)	6.18 (1.33)	0.001	37	6.84 (1.57)	6.05 (1.75)	0.009	61	5.96 (1.63)	5.08 (1.44)	0.001
14	7.00 (1.44)	6.29 (1.71)	0.037	38	6.50 (1.96)	5.85 (1.81)	0.017	62	6.17 (1.86)	5.39 (1.75)	0.004
15	7.50 (1.21)	6.58 (1.84)	0.001	39	6.36 (1.39)	5.93 (1.44)	0.015	63	6.20 (1.54)	5.50 (1.54)	0.001
16	7.32 (1.14)	6.29 (1.70)	0.003	40	6.13 (1.52)	5.35 (1.50)	0.004	64	5.70 (1.87)	5.10 (1.68)	0.003
17	7.52 (1.41)	6.48 (1.38)	0.001	41	6.40 (1.14)	5.65 (1.35)	0.006	65	5.92 (1.85)	5.16 (1.70)	0.001
18	7.07 (1.70)	6.21 (1.95)	0.002	42	6.18 (1.14)	5.36 (1.29)	0.001	66	6.31 (1.30)	5.63 (1.09)	0.013
19	6.81 (1.73)	6.04 (2.01)	0.006	43	6.26 (1.18)	5.65 (1.40)	0.001	67	5.94 (1.89)	5.22 (1.66)	0.016
20	6.93 (1.49)	6.04 (1.82)	0.001	44	6.22 (1.34)	5.63 (1.42)	0.002	68	6.58 (1.57)	5.63 (1.30)	0.002
21	7.19 (1.75)	6.31 (2.01)	0.001	45	6.25 (1.41)	5.70 (1.56)	0.008	69	6.35 (1.57)	5.55 (1.47)	0.003
22	7.03 (1.77)	6.34 (1.70)	0.004	46	6.19 (1.21)	5.86 (1.28)	0.154	70	5.83 (1.38)	4.89 (1.18)	0.002
23	6.67 (1.59)	5.91 (1.67)	0.005	47	6.33 (1.20)	5.76 (1.45)	0.003	71	5.58 (1.54)	4.79 (1.44)	0.002
24	7.13 (1.88)	6.26 (1.83)	0.003	48	6.29 (1.82)	5.57 (1.95)	0.014	72	5.83 (1.86)	5.06 (1.80)	0.001

Values are mean (standard deviation)

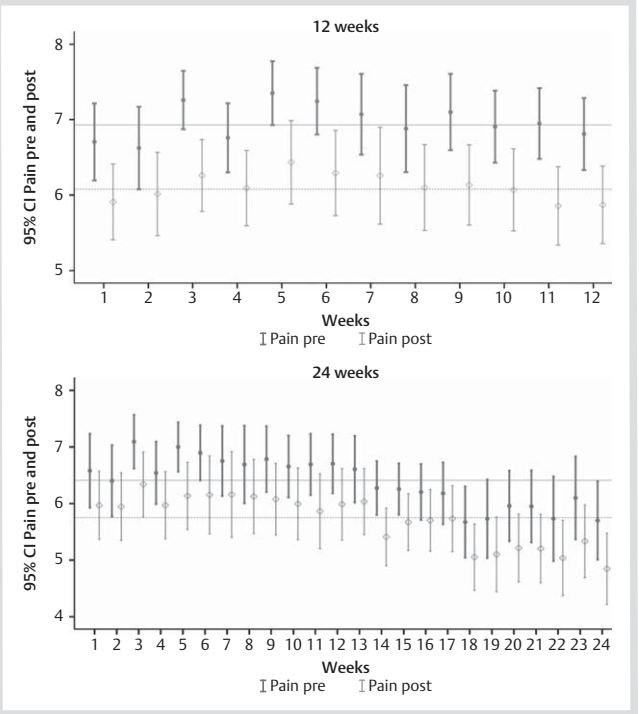

Fig. 2 Changes elicited by 12-week (36 sessions) and 24-week (72 sessions) Tai-Chi intervention over time in pain in fibromyalgia patients. Bold lines represent the pain pre-session, while clear lines represent the pain post-session. The continuous horizontal line represents the mean value of pain pre-session, while the dotted horizontal line represents the mean value of pain post-session.

tion. These results are consistent with previous findings of our group, which showed a warm water pool-based exercise intervention to elicit no cumulative changes in pain in female fibromyalgia patients over a 12-week (2 sessions/week) intervention program [29]. Apart from the intervention treatment (Tai-Chi vs. warm water pool-based exercise), we showed that the weekly frequency (3 sessions/week) of the program does not appear to be effective at increasing the efficacy of the program in treating cumulative pain, since both studies observed the same results. However, different results were obtained when the Tai-Chi intervention was continued for a further 12 weeks (72 sessions in total). In this case, a significant day-by-day decrease in pain pre-session and pain post-session was observed. This means that as intervention progresses, the participants experience a decrease in total pain levels. Therefore, under our experimental conditions, a Tai-Chi intervention longer than 12 weeks (3 sessions/week) is necessary to observe cumulative changes in pain, at least as measured by means of a VAS. Our significant long-term results might be not clinically relevant due to the low levels of VAS-pain decrease. But these slight changes in pain may otherwise be enough to increase the quality of life in fibromyalgia individuals. Furthermore, our findings highlight the need for maintaining physical exercise over time in order to obtain greater benefits.

Only one previous study observed benefits after a 12-week Tai-Chi intervention program (twice/week) in global pain as measured by means of a VAS in fibromyalgia patients [35]. It must be noted that the researchers of that study measured pain just before and after the treatment [35]. Other 6-, 12- and 28-week Tai-Chi intervention studies on fibromyalgia patients used the FIQ-pain subscale to assess pain before and after the intervention [17,27,32]. However, the FIQ-pain indicates the pain over the previous week, whereas in the present study we inquired about the current state of pain. The Brief Pain Inventory has also shown pain improvements after a 12-week Tai-Chi intervention [17] in fibromyalgia patients. Pain decreases as assessed by means of the algometer score item have also been observed previously in male [10] and female [27] fibromyalgia patients. The methodological differences among these previous studies and ours do not allow a direct comparison of results. However the body of literature suggests a decrease in pain levels following a Tai-Chi intervention [17,27,32,35].

Generally, physical exercise has proven to be effective in the management of fibromyalgia [3–5]. Moreover, fibromyalgia patients who are more physically active exhibit lower levels of pain perception [21]. Exercise therapies are relatively economical, easily accessible and widely used in clinical practice as a strategy for pain management [3,4]. Aerobic exercise [5,33], aquatic exercise [23,29] and multidisciplinary programs [7] have exhibited benefits in pain and symptomatology in fibromyalgia patients. Recently, there has been an increase in new exercise interventions being applied for managing fibromyalgia (some examples include: Tai-Chi, Biodanza, Yoga, breathing exercises) [5]. These therapies have accordingly exhibited great benefits for the fibromyalgia population [6,11,27,35]. The findings of the present study incorporate a better understanding of the field of active approaches in fibromyalgia, demonstrating the effectiveness of Tai-Chi for treating acute and long-term pain.

A limitation of the current study is that we did not collect data on the next day or on the first two consecutive days after the session. This is important for knowing how long the decrease in pain lasts. A minimally important clinical change of ~15% in VAS-pain has been reported by a previous study in chronic musculoskeletal pain, which concurs with our study results in acute pain [28]. Because, however, a change of 30% has been considered to be a "much better" improvement [13,28], our results might not be considered clinically relevant. Nevertheless, the pain reduction demonstrated in the present study supports the effectiveness of Tai-Chi treating the fibromyalgia pain symptom. We were unable to perform separate analyses for women and men due to the limited sample of men. Future studies should be conducted using a greater sample of men to demonstrate whether men and women exhibit the same trends or whether there are gender differences in acute pain perception. Further research is needed to verify the present findings. Finally, to compare land- and water-based exercise would aid in determining which environment induces greater benefits for fibromyalgia patients.

Conclusions

In summary, the present study showed that a 12 or 24-week (3 times/week) low-moderate Tai-Chi program decreases acute pain in fibromyalgia patients. Moreover, sustained, cumulative positive changes in pain were observed when the program reached 16 weeks, suggesting that Tai-Chi is an adequate and potential therapy for reducing acute and cumulative (long-term) pain in fibromyalgia patients.

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CONCLUSIONES

- La fibromialgia debe ser entendida como un trastorno dimensional complejo, y no sólo como una condición de dolor crónico generalizado. Además, la fibromialgia parece tener un mayor impacto en la dimensión física que en la dimensión psicológica, aunque ambas se ven afectadas en gran medida.

- Los criterios modificados de 2010 del ACR son una herramienta válida para el diagnóstico de la fibromialgia en España. Además, se recomienda la combinación de los criterios de 1990 y los criterios modificados de 2010 del ACR, ya que presenta las mejores características de diagnóstico de la enfermedad.

- Los tests curl de bíceps, 30 segundos de sentarse y levantarse y fuerza de prensión manual discriminan de forma evidente a las mujeres con fibromialgia de aquellas que no la tienen.

- Los instrumentos auto-administrados de registro de la actividad física analizados en la presente Tesis Doctoral (IPAQ y LTPAI-PAHWI) parecen no ser apropiados para medir la actividad física en pacientes con fibromialgia, ya que difieren consistentemente con los registros de acelerometría.

- Un programa de ejercicio en piscina de agua caliente de 3 meses de duración y un programa de Tai-Chi de 6 meses de duración reducen el dolor agudo en mujeres con fibromialgia. El efecto es más elevado en las mujeres de mayor edad y en aquellas con dolor más intenso. Parece que es necesario un período superior a 3 meses de duración para observar cambios en el dolor a largo plazo.

Conclusión general:

Los resultados de la presente memoria de Tesis Doctoral ponen de manifiesto la utilidad de los nuevos criterios preliminares de diagnóstico de la fibromialgia y de los test de condición física como herramienta de ayuda al diagnóstico y seguimiento de la fibromialgia. Los cuestionarios de actividad física son de dudosa utilidad en esta

población y se desaconseja su uso. Se recomienda el ejercicio físico como tratamiento de la enfermedad por su efecto positivo sobre el dolor agudo y acumulado.

CONCLUSIONS

- Fibromyalgia must be understood as a complex dimensional disorder beyond chronic widespread pain condition. Furthermore, fibromyalgia seems to have a greater impact on physical outcomes than on psychological outcomes, though both are largely affected.

- The modified 2010 ACR criteria are a valid tool for the diagnosis of fibromyalgia in Spain. Furthermore, the combination of the 1990 and the modified 2010 ACR criteria is recommended, since this approach presents the best diagnostic characteristics.

- The arm curl, 30-s chair stand, and handgrip strength tests powerfully discriminate women with fibromyalgia from those without fibromyalgia.

- The self-reported PA instruments used in the present Doctoral Thesis (IPAQ and LTPAI-PAHWI) show questionable usefulness to assess PA in fibromyalgia patients, since they differ from accelerometry data.

- A 3-month warm water pool-based exercise program and a 6-month Tai-Chi program reduce acute pain in fibromyalgia women. Improvements are higher in older women and in those with more intense pain. It seems that longer than 3-month period is necessary for observing cumulative changes in pain.

Overall conclusion:

The results of the current Doctoral Thesis underline the usefulness of the new preliminary diagnostic criteria for fibromyalgia and fitness testing as a complementary tool for the diagnosis and monitoring of the disease. Physical activity questionnaires seem useless in this population and its use is discouraged. Physical exercise is recommended as a treatment of the disease due to its positive effect on acute and cumulative pain.

CURRICULUM VIATE RESUMIDO [SHORT CV]

Víctor Segura Jiménez

Fecha de nacimiento: **10 de junio de 1985**

Correo electrónico: **vsegura@ugr.es**

Actividad Académica

- Diplomado en Magisterio Especialidad de Educación Física. Facultad de Ciencias de la Educación. Universidad de Granada.
  Fecha: 2005 – 2008

- Licenciado en Ciencias de la Actividad Física y el Deporte. Facultad de Ciencias de la Actividad Física y el Deporte. Universidad de Granada.
  Fecha: 2008 – 2010

- Máster Oficial de Investigación en Ciencias de la Actividad Física y el Deporte. Facultad de Ciencias de la Actividad Física y el Deporte. Universidad de Granada.
  Fecha: 2010 – 2011

- Doctorado en el programa Oficial de Biomedicina, con mención de calidad. Departamento de Educación Física y Deportiva. Facultad de Ciencias del Deporte. Universidad de Granada.
  Fecha: 2011-2014

- Estancia de Investigación en el Departamento de Didáctica de la Educación Física, Plástica y Musical. Facultad de Ciencias de la Educación. Universidad de Cádiz.
  Fecha: abril 2013 – mayo 2013 (1 mes y 15 días)

- Estancia de Investigación en el Institute of Metabolic Science. MRC Epidemiology Unit. University of Cambridge.
  Fecha: junio 2013 – septiembre 2013 (3 meses)

- Estancia de Investigación en el Departamento de Didáctica de la Educación Física, Plástica y Musical. Facultad de Ciencias de la Educación. Universidad de Cádiz.
  Fecha: junio 2014 – julio 2014 (1 mes y 16 días)

- Estancia de Investigación en el Research Centre for Physical Activity, Health and Leisure. Faculty of Sport Sciences and Physical Eduction. University of Porto.
  Fecha: septiembre 2014 – diciembre 2014 (3 meses)

- Docencia oficial en el Departamento de Educación Física y Deportiva. Facultad de Ciencias del Deporte. Universidad de Grada. Curso 2013 – 2014.
  - Actividad Física y Salud (5º curso): 3 créditos prácticos.
  - Prácticum Gestión y Recreación (5º curso): 1,5 créditos prácticos.
  - Prácticum Entrenamiento Deportivo (5º curso): 1,5 créditos prácticos.

- Profesor invitado en el Máster Oficial Universitario en Rendimiento Deportivo y Salud. Universidad de Miguel Hernández de Elche.
  Fecha: junio 2014

Participación en proyectos de investigación

- Intervención para la mejora de la calidad de vida relacionada con la salud. Financiado por la Asociación Granadina de Fibromialgia (AGRAFIM).
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- Mejora de la calidad de vida en personas con fibromialgia a través de programas de actividad física y multidisciplinares. Centro de Iniciativas de Cooperación al Desarrollo. Universidad de Granada.
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Máxima gratificación por Publicación de Trabajo Científico en revista de alto impacto, dentro de la Beca de Iniciación a la Investigación. Cuantía: 800€. 13 de julio de 2011.

Otras actividades relevantes

Participación como revisor en las revistas citadas a continuación:

1. Arthritis Care & Research
2. BMC Public Health
3. Clinical Interventions in Aging
4. International Journal of Environmental Research and Public Health
5. International Journal of Sports Medicine
6. Journal of Sports Sciences
7. PlosOne

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Una vez llegado a este momento es cuando uno entiende la gran cantidad de personas que confluyen en tu vida y te ayudan a recorrer el arduo camino. Sinceramente, esta tesis no solo ha sido posible al trabajo de los últimos años de mi vida dedicados a la investigación, sino que hay toda una vida detrás en la que muchas personas han sido partícipes de mi crecimiento humano. Intentaré dar rienda suelta a mis recuerdos, dejando en este caso que sea el corazón quien moldee las palabras que escribo a continuación.

Hasta donde alcanzan mis recuerdos, mi niñez se podría caracterizar por una etapa de inmensa felicidad. Siempre que recuerdo sucesos de mi infancia y adolescencia no puedo evitar que una sonrisa se esboce en mis labios. Hijo de un sastre y una costurera con cuatro descendientes, nuestra familia nunca se distinguió por su poder adquisitivo. Mas no por ello ninguno nos hemos sentido faltos de compañía, amistad, educación, cariño y amor. Siempre se nos ha permitido hacer aquello que nos gustaba, ya que se nos inculcó desde pequeños que si uno tiene un sueño sólo tiene que proponerse perseguirlo para cumplirlo. Me pasé gran parte de mi infancia jugando en la calle y practicando una gran diversidad de deportes. Mis padres, **Manuel** y **Rosi**, siempre me dieron libertad para escoger mi camino, no por ello obviando una continua y esmerada educación. Y por ello siempre les estaré eternamente agradecido. Gracias por todos y cada uno de los momentos en los que habéis estado ahí. "*¡No podríais haberlo hecho mejor!".* Ahora recuerdo con cariño incluso cuando mi madre nos lanzaba la zapatilla a mi hermano y a mí cuando nuestro comportamiento no era el más adecuado. También he tenido la inmensa suerte de contar con dos hermanos y una hermana mayor, que me han cuidado, protegido y educado con paciencia. Mi hermano **Jose**, el primogénito, siempre alardeaba ante sus amigos del hermano pequeño que tenía, lo cual siempre me ha hecho sentir en parte especial, porque sé que aunque le cueste decirlo, me tiene un gran aprecio, del mismo modo que yo le tengo a él. Mi hermana **Silvia** me cuidó desde recién nacido. Con sólo 9 años ya se ocupaba de mí mientras mis padres trabajaban para poder sacar a la familia adelante. "*Siempre te estaré agradecido desde lo más profundo*

de mi ser". Mi hermano **Ale** siempre fue mi ejemplo a seguir. Con él tuve una mayor cercanía por la menor diferencia de edad con respecto a mis otros hermanos. Aunque refrescando la memoria recuerdo que siempre solíamos terminar con peleas, cogotazos y riñas (por supuesto, siempre ganaba él). Aunque en el fondo sé (o quiero creer) que lo hacía sin maldad ninguna, y esto ayudó a reforzar nuestra relación. Estoy convencido de que la influencia de todos y cada uno de ellos ha conformado la persona que soy hoy en día y no existen palabras para agradecer todo lo que han hecho por mí. También quiero agradecer la cercanía y cariño del resto de mis familiares, abuelos, tíos, primos y sobrinos, y en especial a mi tía **Ani** que siempre me inculcó desde pequeño un interés especial por aprender.

A veces el destino se empeña en endulzarnos la vida. Y como agua de mayo, **Elena** pasó a formar parte de la mía. Dulce, cariñosa, simpática, alegre, extrovertida, son algunos adjetivos que apenas si describen su hermosa personalidad. Su amor desinteresado y su afán de ayudar siempre al prójimo son cualidades innatas que la hacen ser fácilmente querida por los demás. Ella ha sufrido más que ninguna otra persona mi período investigador, soportando con paciencia la alterada vida que todo doctorando parece llevar. Me ha enseñado a respirar profundo, a no mantener la mente siempre ocupada, a no darle importancia al pasado y entender la vida como una calle con un único sentido. *"¡Gracias por sacar lo mejor de mí!"*.

"*Al final, lo importante no son los años de la vida, sino la vida de los años.*"
Abraham Lincoln.

No concibo un mejor director de tesis que **Manuel**. Él fue quien me permitió iniciarme en el mundo de la investigación. Cuando otros me cerraron las puertas, él me tendió su mano con decisión, y en un abrir y cerrar de ojos pasé a formar parte de su grupo de investigación. Es todo un ejemplo a seguir como profesional y como persona. A pesar de su inmensa sabiduría, no sólo en el ámbito de la actividad física y el deporte, se muestra como una persona sencilla, noble, bondadosa y generosa. Todos aquellos que hayan trabajado con Manuel sabrán muy bien a lo que me refiero. No es que siempre esté disponible para ayudarte, sino que además disfruta haciéndolo. No puedo sentir más

orgullo de haber tenido cuan admirable mentor. Recuerdo el día que Manuel me firmó mi solicitud de beca de iniciación a la investigación, cuando yo sólo era un estudiante de licenciatura de 4º curso. Allí estaba **Ana**, junto a él, y recuerdo que me dijo: "*¡qué bien!, ¿tú eres el que va a solicitar la beca de iniciación a la investigación? Pues prepárate que aquí tenemos trabajo de sobra*". Y era verdad, hoy en día todavía me sigue dando trabajo, *"ya está bien, ¿no Ana?".* Ella estuvo junto a mí desde el primer momento, introduciéndome paso a paso en el ámbito de la investigación. Con ella aprendí a medir las pruebas de condición física, a picar datos (lo cual no es un recuerdo muy agradable) y me enseñó a escribir mi primer artículo. Todavía recuerdo con angustia el borrador de vuestra revisión de mi primer artículo, en el que sólo se apreciaban correcciones en rojo por todas partes. Espero que todo el esfuerzo que empleasteis en mí se haya visto en parte recompensado con el paso del tiempo.

Aunque las circunstancias no hayan permitido que su nombre esté junto al de Manuel y Ana, él bien sabe que es también DIRECTOR de esta tesis doctoral. **Jonatan** ha sido el continuo flujo de energía y pasión de esta tesis. Junto a él he aprendido más de lo que podría haber llegado a imaginar jamás. Supo darme ánimos cuando más lo necesitaba. Además inculcó su capacidad de trabajo y amor por la ciencia en mí, puliéndome poco a poco, día tras día, como si de un diamante en bruto se tratara y quisiera sacar lo mejor de mí. Él ha sabido encender dentro de mí esa *chispa adecuada* como diría Bunbury. "*Como ya te dije, siempre estaré en deuda contigo y sólo espero poder seguir aprendiendo a tu lado*". Ahora puedo decir que tengo el "*Jonatan style*" dentro de mí.

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Y por último y no por ello menos importante, me gustaría dedicar esta tesis a las/los pacientes de fibromialgia de todas y cada una de las provincias andaluzas en las que hemos trabajado durante estos años. Sin ellas/ellos este trabajo no habría visto la luz sin duda alguna. Recordad que nuestra relación es una auténtica simbiosis, en la que vuestra valiosa participación nos ayuda a avanzar en el conocimiento, pero a su vez este progreso permite que podáis comprender mejor la enfermedad y conocer las posibles herramientas para paliar sus síntomas. Sinceramente, espero que todo el esfuerzo sea en pro de vuestra prosperidad.

"A veces sentimos que lo que hacemos es tan solo una gota en el mar, pero el mar sería menos si le faltara una gota."

Madre Teresa de Calcuta.

UTILIDAD DE CRITERIOS DIAGNÓSTICOS, CONDICIÓN FÍSICA, CUESTIONARIOS DE ACTIVIDAD FÍSICA Y EJERCICIO FÍSICO EN FIBROMIALGIA

USEFULNESS OF DIAGNOSTIC CRITERIA, PHYSICAL FITNESS, PHYSICAL ACTIVITY QUESTIONNAIRES AND PHYSICAL EXERCISE IN FIBROMYALGIA

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