Efficacy of motor activity in the quality of life in fibromyalgia patients: meta-analysis of clinical trials

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Summary

Introduction: Physical activity is effective in reducing fatigue, anxiety and depression in patients with fibromyalgia, and to improve the quality of life.
Objective: To evaluate the efficacy of physical activity in improving the quality of life of people with fibromyalgia, 2004-2014.
Methods: Meta-analysis of controlled clinical trials evaluating the efficacy of physical activity on the FIQ (Fibromyalgia Impact Questionnaire) and MOSSF-36 (Medical Outcome Study Short Form) scores, with 18 search strategies in four multidisciplinary databases. A protocol that containing criteria for inclusion, exclusion, assessment of methodological quality and extraction of information, were applied by two researchers to ensure reproducibility. Random effects meta-analysis, sensitivity analysis, DerSimonian-Lairds heterogeneity and publication bias with Begg test was performed.
Results: 10 studies were included, the most in Spain and Brazil; 203 patients with intervention and 238 in the control group. The meta-analysis showed homogeneity in the FIQ and MOSSF-36 scores between groups, prior to the implementation of the intervention; after the application of intervention were identified difference of 14.9 points (95% CI 10.3; 19.5) in the FIQ and 2.0 on the MOSSF-36, was best in the group that received exercise therapy.
Conclusion: The major efficacy of regular physical exercise is evident, compared with conventional treatment, to improve the quality of life of patients with fibromyalgia. Measuring the quality of life as a primary outcome in clinical trials should be performed with the FIQ.

Key words:
Fibromyalgia. Quality of fife. Health status. Motor activity. Controlled clinical trials as topic. Meta-analyses.

Eficacia del ejercicio físico sobre la calidad de vida en fibromialgia: meta-análisis de ensayos clínicos

Resumen

Introducción: La actividad física es eficaz para disminuir fatiga, ansiedad y depresión en pacientes con fibromialgia, esto redunda en un mejoramiento de su calidad de vida.
Objetivo: Evaluar la eficacia de la actividad física en el mejoramiento de la calidad de vida de personas con fibromialgia, 2004-2014.
Métodos: Meta-análisis de ensayos clínicos que evaluaron la eficacia de la actividad física sobre los puntajes del FIQ *(Fibromyalgia Impact Questionaire)* y MOSSF-36 *(Medical Outcome Study Short Form),* con 18 estrategias de búsqueda en cinco bases de datos multidisciplinarias. Se aplicó un protocolo que, a priori, contenía criterios de inclusión, exclusión, evaluación de la calidad metodológica y extracción de la información, aplicado por dos investigadores para garantizar reproducibilidad. Se realizó meta-análisis de efectos aleatorios, análisis de sensibilidad, heterogeneidad con DerSimonian-Lairds y sesgo de publicación con estadístico de Begg.
Resultados: Se incluyeron 10 estudios, la mayoría desarrollados en España y Brasil; se aplicó la intervención a 203 pacientes y el control a 238. El meta-análisis demostró homogeneidad en los puntajes del FIQ y MOSSF-36 entre los grupos de estudio previo a la aplicación de la intervención; posterior a ella la diferencia en el FIQ fue de 14,9 puntos (IC 95% 10,3; 19,5) a favor del grupo que recibió la terapia con ejercicio físico; mientras que en los componentes del MOSSF-36 fue de 2,0.
Conclusión: se evidencia la mayor eficacia del ejercicio físico regular, en comparación con el tratamiento convencional, para mejorar la calidad de vida de pacientes con fibromialgia. La medición de la calidad de vida como desenlace primario en estudios clínicos debe realizarse con el FIQ.

Palabras clave:
Fibromialgia. Calidad de vida. Estado de salud. Actividad física. Ensayos clínicos como asunto. Meta-análisis.

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Introduction

Fibromyalgia is a chronic illness of unknown aetiology, characterised by the presence of generalised pain that may become incapacitating for the patient; it affects the patient's biological, psychological and social spheres, generating difficulties at work, sleep pattern alterations, and a reduction in the performance of everyday activities[1]. Furthermore, it is associated with fatigue, tiredness, depression, anxiety, headaches and paraesthesia in the extremities[2,3]. Its diagnosis is carried out following the criteria of the American College of Rheumatology, which include widespread pain lasting over three months, muscular-skeletal pain and pain upon palpating at least 11 of 18 painful points[2,4,5]. This illness represents a worldwide health problem due to its high prevalence, morbidity rate and high consumption of health resources[1]. Added to this, it greatly affects the patient's quality of life, including development in the workplace, home life and social sphere[5].

To improve the pain and quality of life of these patients, pharmacological and non-pharmacological treatments are undertaken; the non-pharmacological treatments include exercise programmes, relaxation, physiotherapy and psychological or psychiatric support[5]. With reference to physical activity, previous studies have revealed their efficiency in reducing the impact of the illness by improving symptoms, including low levels of fatigue, anxiety, depression, and in general an improvement to the health-related quality of life (HRQL) and the overall state of health[6-7].

The assessment of health-related quality of life in this illness has been performed using specific and generic instruments, including in particular the *Fibromyalgia Impact Questionnaire* (FIQ) and the *Medical Outcome Study Short Form* (MOSSF-36), which both enable clinical monitoring, help guide decision making for health providers, obtain clinical outcome measures and perform cost-effectiveness or cost-usefulness analyses[1,8].

In view of the aforementioned, various controlled clinical trials about the effectiveness of physical activity in improving health-related quality of life and the state of health of people with fibromyalgia have been carried out. Despite this, there are no clear conclusions, with powerful and solid statistics, which is why a systematic review must be performed to meta-analyse the evidence from previous articles and to give greater external validation to the outcomes and conclusions. With this objective, in 2008 a meta-analysis was published with controlled clinical trials that collected research carried out up to 2005[9]; however, this information requires updating, as systematic reviews on this issue have revealed that the most research has been concentrated over the past two three-year periods, meaning that it is possible that the effects of physical activity on the quality of life of fibromyalgia patients have changed over these past 6 years with the diversification of exercise programmes[8]. Added to this, this meta-analysis concentrated the results on a specific scale (FIQ), leaving aside the generic MOSSF-36 scale that may be more sensitive to clinical changes[10].

In accordance with the aforementioned, this study was designed with the aim of assessing the effectiveness of physical activity on improving the health-related quality of life and overall state of health of fibromyalgia sufferers, based on articles published between 2004 and 2014.

Material and methods

Type of study

Meta-analysis of clinical trials.

PICO: Population Intervention Comparison Outcome

Population. Patients diagnosed with Fibromyalgia according to the criteria established by the American College of Rheumatology[11].

Intervention. Physical activity for at least 3 weeks, by which physical activity is understood to mean aerobic exercise in which the heart rate is maintained at over 50% of the maximum frequency, flexibility exercises, stretching, strengthening or a mixture of these according to the *American College of Sports Medicine guidelines for exercise testing and prescription*[12].

Comparison. Patients with fibromyalgia that do not perform physical activity or that do so with less intensity than that established in the intervention. This group includes conventional education or guidance interventions about lifestyle provided by the rheumatologist; pharmacological treatment prescribed by the doctor and light physical activity such as stretching or routines that do not exceed 30 minutes per session or three days per week.

Outcome. Quality of life score obtained using the FIQ or MOS-SF36 scales, or both, for the study group as well as the control group, before and after the intervention. Note that this review was not restricted to studies that simultaneously applied both scales, given that the index generated by the FIQ is independent from the physical and mental components of the MOSSF-36, meaning that this restriction would reduce the exhaustive nature of this study.

Measuring health-related quality of life

The FIQ is a specific instrument to measure the impact of fibromyalgia in functional capacity and the quality of life of the people affected. It is composed of 10 dimensions that evaluate physical capacity, habitual work, impact on paid labour activity, pain, fatigue, feeling of tiredness, stiffness, feeling of well-being, anxiety and depression; the domains generate a score between 0 and 100, with 0 being the best result in HRQL, or the least impact caused by the fibromyalgia[13].

The MOSSF-36 is a generic HRQL questionnaire composed of 36 items that generate an 8-dimension profile: body pain, physical performance, physical function and overall health that is summarised in a

physical component, emotional performance, social function, mental health and vitality that conform to the mental component. The instrument generates a score that can vary from 0 to 100 points; the higher the score, the better the HRQL, and the reference value established in a healthy population is 50±10 points[14].

Research Protocol according to PRISMA phases (Preferred Reporting Items for Systematic reviews and Meta-Analyses)[15]

Article identification or search. A sensitivity search was carried out in the literature related to quality of life in fibromyalgia from the Pubmed database, Science Direct, Lilacs and Scielo; using the following search strategies: *"Calidad de vida & Fibromialgia", "Calidad de vida relacionada con la salud & Fibromialgia", "Calidad de vida & FIQ", "Calidad de vida & SF-36", "Calidad de vida relacionada con la salud & FIQ", "Calidad de vida relacionada con la salud & SF-36"* and their counterparts in English and Portuguese. As well as this, a search was performed of clinical trials in the Cochrane Library with the terms *"physical activity in the quality of life in fibromyalgia" and "motor activity in the quality of life in fibromyalgia".*

Screening or applying the inclusion criteria

- Contain search terms in the title or abstract,
- research studies published between 2004 and September 2014,
- original articles and
- being a controlled clinical trial.

Some syntax used were:

- *(quality of life [Title/Abstract]) AND fibromyalgia [Title/Abstract];*
- *(health related quality of life[Title/Abstract]) AND fibromyalgia impact questionnaire [Title/Abstract];*
- *TITLE-ABSTR-KEY (health related quality of life) and TITLE-ABSTR-KEY (fibromyalgia impact questionnaire);*
- *pub-date > 2003 y iv) TITLE-ABSTR-KEY (quality of life) and TITLE-ABSTR-KEY (fibromyalgia).*

Selecting or applying the exclusion criteria

- Publications with interventions different to physical activity or multi-disciplinary interventions (educational, pharmacological, physiotherapeutic, psychological);
- articles with internal validation problems due to the failure to control bias or confusing variables;
- articles that do not explicitly mention the quality of life scores before and after the intervention in each of the compared groups.

To assess the methodological quality of the studies, the following criteria were applied: randomisation, concealment, calculation of the sample size, analysis by treatment intentions, safety report and homogeneity analysis. A form was made categorising the study with 1 if it contained the criteria, and with 0 for those that did not apply. With these a total was reached, taking scores equal or greater than 4 as good quality. Given that in the studies included the majority had a similar character (between 2 and 4 points), a meta-regression was not carried out for this variable.

Gathering the information

Two researchers applied the research protocol independently to ensure the ability to reproduce the review; discrepancies were resolved by consensus or through reference to a third party. The articles obtained were exported to an Endnote Web programme to eliminate duplicates. Once this stage was finished, the classification process of the studies began by carefully reading the abstracts and by creating a data extraction format stored in an Excel-designed database. Extracting the information was performed independently by two researchers with the aim of ensuring the inter-observer reproducible nature, in which the kappa coefficient of 1.00 for the year and place of study variables was obtained; and Intraclass Correlation Coefficient (CCI) of 1.0 for quality of life scores.

Analysing the information

The studies were characterised according to the place and year of performance. The standard deviation of the overall scores of each of the MOSSF-36 and FIQ dimensions was established based on the variation coefficient calculated in the individual studies.

To ensure the homogeneity of the groups, a meta-analysis was performed for average differences with the quality of life scores at the start of the study. The aforementioned was carried out given that in the studies this analysis was not performed, nor was a health-related quality of life score defined as inclusion criteria.

The efficacy of physical activity on the quality of life of fibromyalgia patients was assessed using a meta-analysis for average differences of scores after the intervention in both the treated and control group. With the aim of equalling out the direction of the FIQ and MOSSF-36 scales, the following formula was applied: "101- FIQ score".

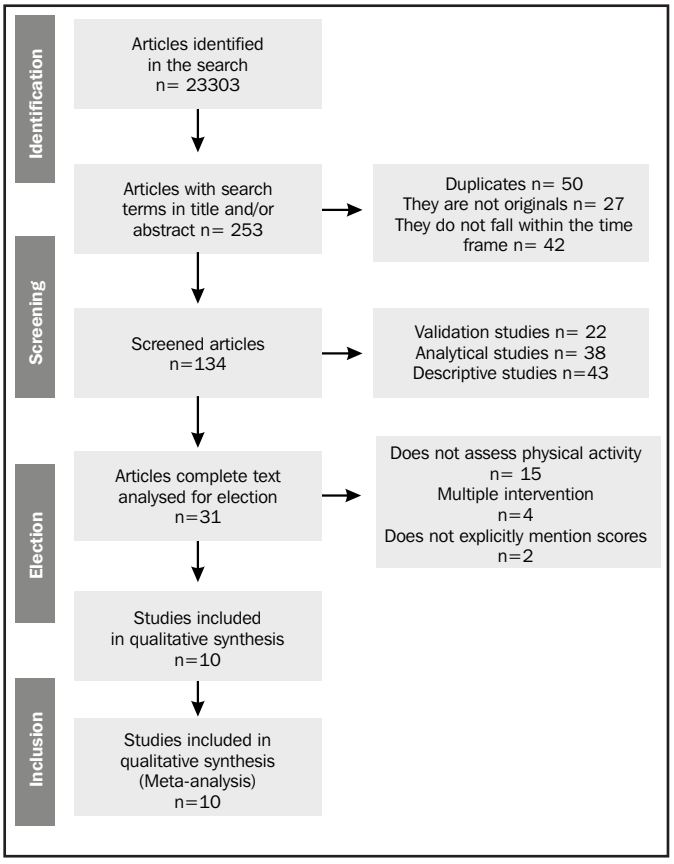
The heterogeneity was assessed with the Q statistic of the DerSimonian and Lairds test, the publication bias using the Funnel Plot, and the Begg's test statistic and a sensitivity analysis was carried out to explore the influence of each study on the size of the overall effect.

For the analyses, the Excel and Programme for Epidemiological Analysis of Tabulated Data from the Pan American Health Organisation (EPIDAT) version 3.0 was used.

Results

In the initial search, 31 articles were identified that complied with the inclusion criteria, of which 21 were eliminated for not assessing the effect of the physical activity in fibromyalgia symptoms (n=15), for using multiple treatment simultaneously, such as sociotherapy, physiotherapy, psychotherapy and art-therapy (n=4) and for not explicitly mentioning the changes in the FIQ or MOSSF-36 scores before and after the intervention (Figure 1). Based on the Cochrane search with the *"motor activity quality of life fibromyalgia, in Title, Abstract, Keywords in Trials"* strategy, six results of 893,010 articles were found that contained one or more of the search terms, and all focused on pain as the central link; with the

Figure 1. Algorithm of the article selection.



"physical activity quality of life fibromyalgia, in Title, Abstract, Keywords in Trials" strategy, 28 results were obtained, from which only two complied with the protocol and were duplicated in the findings on Pubmed.

In the studies included in the quantitative synthesis (n = 10), the majority were published between 2012 and 2014, mainly in Spain and Brazil and all included women with fibromyalgia, apart from the study by Elijk-Hustings, which included one male in the control group (n = 48). The physical intervention was performed with aerobic exercises, hydrotherapy, bio-dance and strengthening. The frequency was between 2 and 3 times a week and the total duration of the intervention was between 3 and 24 weeks. With regards to the characteristics of the people included, there was an intra-study homogeneity for the variables of age and years with the illness; however, there was inter-study variability regarding the same variable in that the average age fluctuated between 42 and 59 years. The same occurred with the average duration of the symptoms of the illness, which oscillated between 4 and 26 years (Table 1). It should be specified that the majority of the studies did not reveal other variables in the analyses of homogeneity and in the inclusion criteria the majority circumscribe to the diagnostic criteria of the illness and the type of institutions where the patients were found; this prevents further research into potential variables for a meta-regression.

All the test groups applied interventions in which they reached a minimum of 50% of their maximum heart rate, though in some studies this intensity was higher with increases between 55-64%[16], 60-85%[18], 50-69%[23] or 60-70%[25] according to ACSM recommendations.

Table 1. Description of the articles included in the quantitative synthesis.

Author	Year	Country	Group	n	Age	Years with the illness	Treatment
Eijk-Hustings[16]	2013	Netherlands	EG	19	43.9±7.6	6.2±7	Aerobic exercises
			CG	48	42.9±11	7.1 ± 6.4	Conventional treatment
Fernandes de Melo[17]	2006	Brazil	EG	24	48.9±9.2	---	Hydrotherapy
			CG	23	46.6±8.4	---	Conventional physiotherapy
García-Martínez[18]	2012	Spain	EG	12	59.3±4.8	9.9±3.8	Physical exercise
			CG	13	58.6±7.8	10.6 ±4.1	Conventional treatment
Latorre[19]	2013	Spain	EG	42	50.9±7.7	9.1 ± 3.8	Physical exercise
			CG	30	52.4±8	9.0±4.8	Conventional treatment
López-Rodríguez[20]	2012	Spain	EG	19	55.5±7.7	12.5±7.4	Aquatic bio-dance
			CG	20	55.3±7.5	14.3±8.3	*Stretching*
Martín-Nogueras[21]	2012	Spain	EG	15	52.6±8.4	4.6±3.2	Physiotherapy and aerobics
			CG	13	48.1±6.9	6.4±6	Conventional treatment
Oliveira[22]	2014	Brazil	EG	35	44.3±7.9	---	*Strengthening*
			CG	31	48.6±7.6	---	FLEX
Sañudo[23]	2007	Spain	EG	14	57.9±6.2	---	Physical exercise and vibration training
			CG	12	60.1±9.4	---	Physical exercise
Tomas-Carus[24]			EG	17	51±10	24±9	Aquatic exercise
			CG	17	51±9	27±4	Conventional treatment
Vinícius letieri[25]	2013	Brazil	EG	33	58.2±10.6	---	Hydro-kinesiotherapy (PSE)
			CG	31	59.6±9.4	---	Conventional treatment

Group EG: Experimental group; CG: Control group.

All the studies applied the intervention with a duration of one hour per session, with the exception of two studies which lasted 45 minutes[22,25], each session included between 5-10 minutes of warming up, 30-40 minutes of physical aerobic exercise and/or strengthening, with 5-10 minutes of stretching and relaxing. The intervention time varied with six[23], twelve[16-18,20,21], fifteen[25], 1622 or 24 weeks[19]; in half of the studies 2 sessions per week were applied[16,21,22,23,25] and in the rest, three.

Regarding the instruments to assess the effect of physical activity on the quality of life, 4 used both the FIQ and the MOSSF-36, 4 studies only applied the FIQ and 2 only applied the MOSSF-36. Before starting the intervention, the FIQ scores in the test group and the control group fluctuated between 22.5 ± 11.1 and 52.1 ± 12.1 points; the same procedure was performed after the intervention and in this case the test group scores were between 44 ± 16 and 57.2 ± 12.3 and for the control group between 22.0 ± 10 and 51.2 ± 14.9. With regards to the HRQL according to the MOSSF-36 in the physical component prior to treatment, scores were obtained between 9.7 ± 26.4 and 44.6 ±12.7; following intervention the test group displayed scores between 33.6 ± 35.8 and 75.6 ± 14.2. Mental health was also assessed before treatment in both groups with results between 38.4 ± 17.0 and 58.0 ± 16.5 points and after the intervention the scores in the treated group were between 50.1 ± 25.0 and 69.3 ± 20.9 (Table 2).

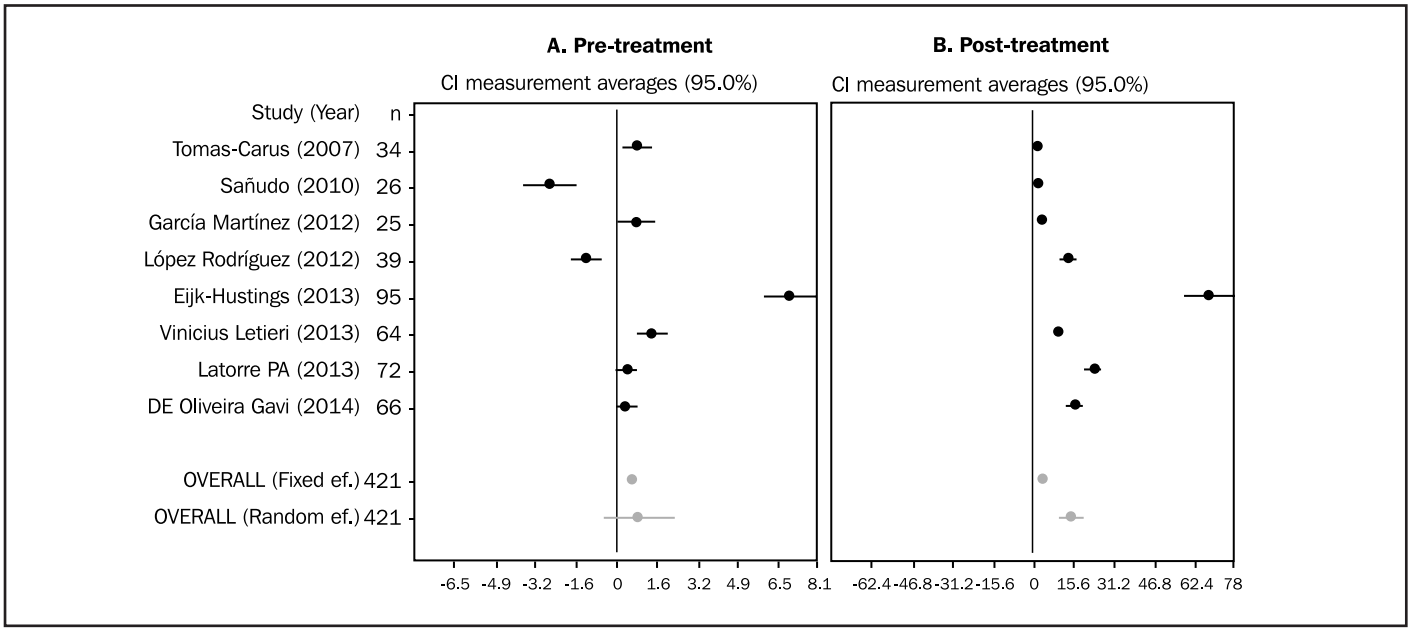
Upon performing the meta-analysis of the FIQ scores before and after the intervention, both the treated and control groups revealed heterogeneity in the studies included (Statistic Q Vp 0.000), lack of publication bias (Begg Test 0.915) and good robustness of the combined

Table 2. Description of the FIQ scores and the SF-36 pre and post treatment in the experimental and control groups.

Author	Group	FIQ score X±DS		36 Score Physical X±DS		36 Score Mental X±DS	
		Pre*	Post**	Pre*	Post**	Pre*	Post**
García-Martínez	EG	28.9±13.1	50.8±12.9	33.9±18.5	50.6±27.4	46.6±18.2	61.7±18.5
	CG	32±12.5	36.2±16.7	39.6±17.5	35.4±17.2	48.0±21.3	41.5±20.3
Latorre	EG	35.5±13.5	47.7±16.3	38.7±16.2	41.5±21.3	43.1±13.4	52.7±17.4
	CG	36.2±11.6	35.3±11.8	34±17.0	34.3±16.6	48.0±18.1	39.7±17.4
Oliveira	EG	33.2±15.4	49.9±18.4	12.1±24.5	33.6±35.8	39.0±21.5	50.1±25.0
	CG	34.2±17.2	49.9±18.4	9.7±26.4	28.2±38.6	45.9±24.5	61.0±24.5
Tomas-Carus	EG	38.0±20	44.0±16	36.0±23	48.0±21	48.0±20	62.0±27
	CG	42.0±16	41.0±17	33.0±19	37.0±17	51.0±24	50.0±20
Fernandes de Melo	EG	---	---	35.5±20.1	75.6±14.2	42.4±19.4	69.3±20.9
	CG	---	---	35.5±15.0	67.7±23.5	38.4±17.0	66.8±23.9
Martín-Nogueras	EG	---	---	39.7±13.3	55.3±12.9	52.5±15.3	62.9±20.7
	CG	---	---	44.6±12.7	40.0±14.9	58.0±16.5	54.0±23.8
Eijk-Hustings	EG	41.0±2.1	49.0±3.2	---	---	---	---
	CG	45.6±2.3	44.8±2.9	---	---	---	---
López-Rodríguez	EG	33.9±10.5	48.8±16.2	---	---	---	---
	CG	31.5±13.0	31.8±12.9	---	---	---	---
Sañudo	EG	52.1±12.1	57.2±12.3	---	---	---	---
	CG	44.1±11.6	51.2±14.9	---	---	---	---
Vinicius Letieri	EG	22.5±11.1	48.5±15.6	---	---	---	---
	CG	25.3±10.3	22.0±10	---	---	---	---

Group EG: Experimental group; CG: Control group; *Pre: Pre-treatment; **Post: Post-treatment.

Figure 2. ***Forest Plot*** **for the difference in averages of the FIQ scores in the test and control groups.**



measures, given that in the sensitivity analysis the exclusion of each of the studies did not affect the overall result. In the *Funnel Plot* of random effects, no significant differences were found in the FIQ scores before starting the intervention 0.90 (CI 95% -0.39; 0.89) between the treated and control group; on the other hand, after intervention the difference in the average FIQ score was 14.9 points (CI 95% 10.3; 19.5) in favour of the group that received the therapy with physical exercise, proving the effectiveness of the intervention (Figure 2).

In the domain of physical health of the MOSSF-36, heterogeneity in the studies was observed (Statistic Q Vp 0.0002), lack of publication bias (Begg Test Vp 0.1329), equality in the test and control group scores prior to the intervention 0.20 (CI 95% -0.36; 0.76) and difference in favour of the group with physical activity of 2.06 points (CI 95% 1.18; 2.95) following intervention.

In the domain of mental health, the heterogeneity is maintained (Statistic Q Vp 0.000), the lack of publication bias (Begg Test Vo 0.7071), equality in the test and control groups before initiating treatment 0.07 (CI 95% -0.56; 0.71) and the difference in favour of the group that received the physical therapy, in this case of 1.86 points (CI 95% 0.30; 3.40) (Figure 3).

Discussion

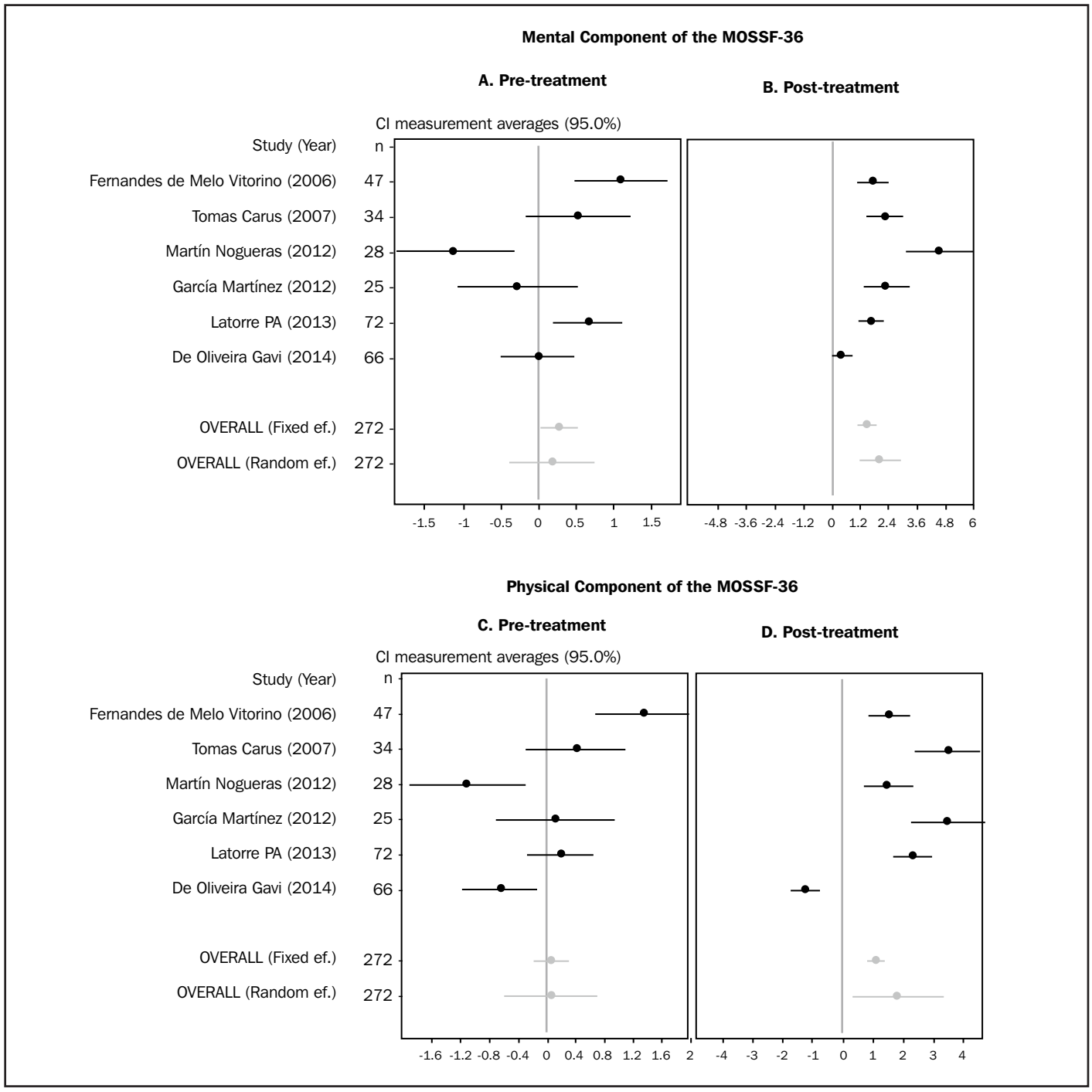
Fibromyalgia strongly affects the quality of life of sufferers, especially in the physical and mental domain. The physical alterations are revealed as chronic pain, disability to perform everyday activities and the ongoing use of medication. The psychological and mental limitations are characterised by stress, depression and anxiety. Previous studies have described the impact of the illness on the physical and mental domain on the quality of life of patients, using instruments such as the FIQ and the MOSSF-36. The latter reveals scores below 50 which is the benchmark for healthy populations[10], which is in keeping with this research in that the pretreatment scores were lower than 50 points.

Among the therapeutic options to treat the illness and reduce the impact on the patient's quality of life, performing regular physical exercise has been established as one of the main non-pharmacological strategies to control the symptoms. Despite this, there are still discrepancies regarding the muscular and physical capacity of these patients to take on an exercise programme, as well as the physiological mechanism by which these types of therapy generate a reduction in symptoms[26].

Discrepancies regarding the capacity of the patients to perform exercise arise because they can perceive a greater effort during physical activity; however, previous studies have revealed that muscular strength and resistance in patients with fibromyalgia are similar to those in healthy control subjects. Furthermore, in patients that undergo physical activity therapy, the beneficial effects are evident, such as reduced pain, increased strength, improved sleep quality, less fatigue and an improved psychological state[27].

In keeping with the above, in this study it was clear that the patients with physical activity experienced improvements to their HRQL by the end of the treatment, proven by the increase in the FIQ and MOSSF-36 scores. The FIQ scores of the treated group increased by 14.9 points whilst in the physical and mental domain of MOSSF-36 the increase was 2.06 and 1.86 respectively. The difference in the score of both treatments could be attributed to the nature of the scales, as the FIQ is a specific scale for fibromyalgia patients, making it more sensitive to detecting

Figure 3. ***Forest Plot*** **for the difference in averages of the Mental and Physical scores of the MOSSF-36 in the test and control groups.**



changes associated to the illness in aspects such as stiffness, morning tiredness, pain, depression and anxiety; on the other hand, MOSSF-36 is a generic measurement, in that its sensitivity is greater when it comes to detecting unforeseen effects of the illness via the domains of physical function, the physical role, body pain, general health, vitality, social role, emotional role and mental health[28].

In allusion to the mechanism that explains the beneficial effects of exercise in fibromyalgia patients, some studies have described a clear reduction in the levels of the systemic inflammatory markers such as the IL-8, and of stress such as the noradrenaline and extra-cellular heat shock proteins 72 kDa (eHsp72), which are usually increased in patients with the illness and its regulation would in part explain the reduction

of the symptoms and the increase in the HRQL. Despite this, there is no consensus on this matter; furthermore physical activity should be regulated because acute exercise, with no physiological adaptation or training, could exacerbate, rather than improve, the systemic state of stress or inflammation in women with fibromyalgia[29].

Research studies into the effectiveness of physical activity in improving the symptoms of fibromyalgia and its impact on FIQ and MOSSF-36 scores, are summarised in this meta-analysis, and in this respect it provides useful information for orientating later studies and consolidating causal hypotheses, as it includes an exhaustive literary search, groups the results of various research studies into one sole measurement, gives a more precise estimation of the effect, and improves the statistical power by increasing the sample size[30].

It is important to highlight that the methodological quality of the articles included in the quantitative synthesis of this research were conditioned by aspects such as the calculation of the sample size, blinding, the analysis of the results with the treatment intentions and the analysis of the safety of the intervention. The analysis with treatment intentions implies including all the patients in the analysis, regardless of whether or not they received the whole treatment or if the originally established protocol was removed. Omitting this analysis influences the results, as the motives of the lack of adherence may be related to the prognostic or effectiveness of the treatment[31]. Blinding refers to the fact that the participants and researchers did not know which group received the intervention, reducing the bias in the physiological or physical response motivated by the type of intervention received. This is particularly important in studies in which the result measurements are far from objective, such as pain or quality of life. However, the majority of the patients involved in this meta-analysis could not be blinded regarding the treatment, as in general terms one group received physical therapy whilst the other did not, impeding blinding for obvious reasons[32]. Safety refers to the protection of patients faced with adverse and secondary effects of the intervention, in the studies included in this analysis, no long-term analysis was performed on the safety of physical activity; however, it is clearly better than the effects of pharmacological treatments with anti-depressives and anticonvulsants[33].

Among the limitations of this study, which at the same time constitute suggestions for later research that aims to assess the effect of physical activity on the HRQL of patients with fibromyalgia, is the diversity of physical interventions included, which highlight the need for experts in the field to unify criteria such as intensity, duration, frequency, and even the design of the exercise regime prescribed, particularly when dealing with an intervention to assess in a clinical trial. Furthermore, it should be noted that the Begg statistic provides good statistical power for meta-analyses with 75 or more studies, and moderate power for analyses with 25, meaning that in meta-analyses with few research studies the publication bias should be interpreted with caution. However, the number of studies included should not be taken categorically, as there are other parameters that affect the power of this statistic, even more importantly than the number of studies, such as the research selection criteria, the variations in the size of the effect and global effect. In addition, it should not be forgotten that this statistic is exploratory, and is performed as a formal procedure to complement the *Funnel_plot*[34].

Conclusion

This exercise highlights that practising regular physical activity is statistically better than conventional treatment in improving the quality of life of fibromyalgia patients, though the quality of the recommendation is low due to the limitations of the studies included, the variability in defining the test group and the low number of analysed research studies. However, the hypothesis is consolidated regarding the benefits of physical activity on this illness, as a base for the design of posterior random controlled clinical trials, and it is recommended that the measurement of quality of life as a primary outcome in clinical studies should be performed with the FIQ.

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