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REVIEW ARTICLES

The effects of physical exercise on axial spondyloarthritis – a systematic review

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ABSTRACT

Aim: To collect and summarize the available scientific evidence that evaluates the effects of physical exercise interventions on axial spondyloarthritis (axSpA).

Methods: A systematic review was conducted in accordance to the guidance of Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) to collect randomized controlled trials on the PubMed, Embase and Web of Science Core Collection databases. The search strategy included terms regarding physical exercise interventions targeted to axSpA participants and all of its variants in multiple combinations adapted to each one of the databases regarding its own special requirements. Several outcomes were defined: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), ASDAS (Ankylosing Spondylitis Disease Activity Score), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), the 36-item short form health survey (SF-36) and the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL). Two independent researchers screened the titles and abstracts followed by full-text analysis when suitable, using EndnoteTM online. Selected articles, according to exclusion/inclusion criteria defined, were submitted to data extraction and bias assessment was performed for each study's outcomes using the Cochrane risk-of-bias tool for randomized trials.

Results: A total of 2063 articles were identified through the electronic databases search. After removal of duplicates, 1435 were eligible for screening, of which 45 articles went through full text evaluation. Only 24 articles met the inclusion/exclusion criteria. Physical exercise contributes for a statistically significant improvement of BASDAI in 13 studies, BASFI in 10, BASMI in 6, ASDAS in 3, CRP in 2, ESR in 1, SF-36 in 2 and ASQoL in 3.No major adverse effects were reported and an overall benefit was noted with the implementation of physical exercise as a treatment modality for axSpA.

Conclusion: Physical exercise seems to be an effective non-pharmacological therapy for axSpA, with positive effects in disease activity, physical function, and quality of life.

Keywords: Spondyloarthropathies (including psoriatic arthritis); Systematic review; Spondylarthritis; Patient attitude to health; Complementary therapies; Education (patients).

KEY MESSAGES

- Physical exercise is a reliable non-pharmacological treatment option for axSpA
- Physical exercise has positive effects on disease activity, physical function, mobility and quality of life
- Physical exercise seems to be safe for axSpA patients, even high-intensity modalities

INTRODUCTION

Axial spondyloarthritis (axSpA), with a prevalence up to 1,6%[1], is a chronic inflammatory disease that mainly compromises the axial skeleton. However, peripheral joints, entheses and systemic manifestations are also common[2,3]. The diagnosis is challenging but the Assessment of SpondyloArthritis international Society (ASAS) criteria, a combination of clinical, laboratory (HLA-B27 positivity and inflammatory markers) and imaging (sac-

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roiliitis identification trough radiography[4] or magnetic resonance imaging[5]) features contributes to axSpA patients' recognition. Ankylosis results from progressive vertebral fusion due to disease progression, eliciting marked stiffness, impaired mobility and loss of physical function. These changes culminate in work incapacity, decreased quality of life and high consumption of healthcare resources. Early diagnosis and treatment are key to decreasing the disease burden to patients and society[6]. Physical exercise (PE) has been increasingly used to treat and manage inflammatory rheumatic diseases and has also been positive in different aspects of axSpA. Nevertheless, most physicians (and patients) still have concerns regarding the frequency, duration and intensity of PE that should be prescribed, due to concerns of disease flaring and/or other side effects. Adherence to PE programs is also a major concern. There is increasing evidence suggesting that behavioral changing techniques should be added to PE in order to increase long-term adherence[9]. Most evidence of the benefits of PE arrives from studies of patients with rheumatoid arthritis. This systematic literature review was designed to fully appreciate the effects of physical exercise on axSpA in order to more clearly evaluate its effects on axSpA, in contrast to other recommentions that encompass the full spectrum of treatment for this disease. To strengthen the positive effects of PE on axSpA and help to determine the best strategies and modalities, we performed a systematic review encompassing randomized controlled trials evaluating the efficacy of PE in axSpA, in terms of disease activity, function, mobility and heath-related QoL.

METHODS

This study was performed in accordance with the guidance of Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA)10 (Supplementary file 1). A systematic literature research of the PubMed, Web of Science and Embase Core Collection databases was performed to identify articles published from January 2000 to December 2021. The PICO model (Population, Intervention, Comparison, Outcomes) was used to formulate the search terms. The search strategy included the following terms and all of its variants in multiple combinations adapted to each one of the databases regarding its own special requirements: spondylitis, ankylosing; spondyloarthritis; physical activity; exercise; exercise therapy; exercise movement techniques; circuit-based exercise; plyometric exercise; resistance training; muscle stretching exercises; high-intensity interval training; sports; physical exertion; physical education and training; physical endurance; hydrotherapy; fitness; mind-body therapies (Supplementary file 2). Established inclusion criteria were: 1. Randomized controlled trials articles; 2. Articles published in English, Portuguese, Spanish or French languages; 3. axSpA (both radiographic and non-radiographic), according to the modified New York criteria or the ASAS criteria; 4. Physical exercise programs with no restrictions regarding the duration, modality, intensity and frequency, having as comparators no intervention, usual treatment or comparative programs of physical exercise; 5. Higher than 18 age years old participants; and exclusion criteria were: 1. Studies involving patients with different diseases in which axSpA patients might not be identified; 2. Combined interventions studying effects of non-physical exercise related components; 3. Studies not reporting outcomes' group comparison; 4. Articles in languages other than English, Portuguese, Spanish or French (to minimize translation biases); 5. RCTs presented only in an abstract form. The following outcomes were selected: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), ASDAS (Ankylosing Spondylitis Disease Activity Score), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), the 36-item short form health survey (SF-36) and the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL). After identifying the database articles and removing duplicates, three researchers (NPG, MSA, MES) independently screened all selected articles through their titles and abstracts (full texts were analysed when suitable). A fourth independent researcher (EBC) resolved disagreements regarding the inclusion/exclusion of studies. To implement this strategy, EndnoteTM online was utilized. Selected articles were submitted to data extraction regarding the lead author and study date, study duration, type of exercise intervention, frequency of PE, control activity, outcomes specified for each study and pre and post-intervention group comparison, follow-up timings, sample size, participants age, gender and pharmacological therapies, axSpA classification criteria, and outcomes' group (control *vs* intervention) comparisons. For the qualitative analysis, bias assessment was performed for each study's outcomes using the Cochrane risk-of-bias tool for randomized trials (RoB2)11, by two independent researchers (NPG, MES), with disagreement solved by another independent researcher (EBC).

A meta-analysis was not performed due to studies heterogeneity related to the type of intervention, study design and outcomes studied.

RESULTS

A total of 2063 articles were identified through the search of the electronic databases, with one additional article

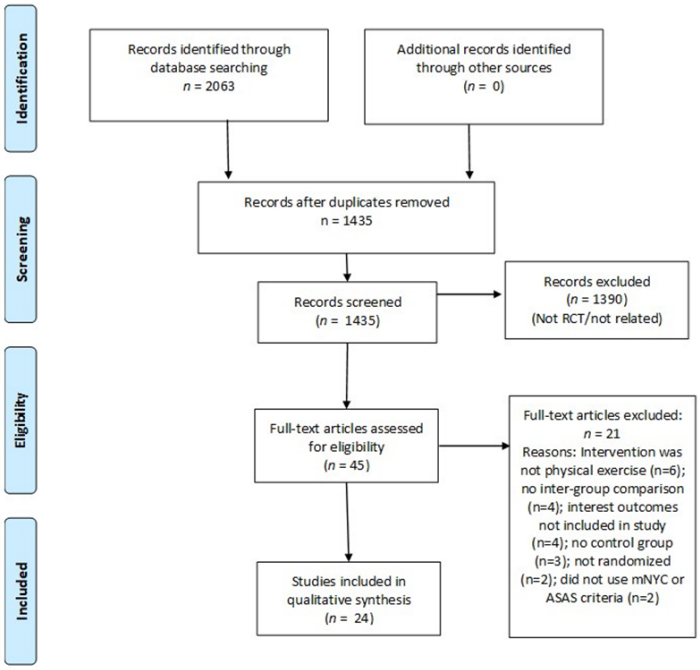

Figure 1. Flow of trials through the review.
RCT: randomized controlled trial; ASAS: Assessment of SpondyloArthritis international Society; mNYC: modified New York Criteria

identified through the reference list of the included articles. After removing duplicates, 1435 were eligible for screening, in which 45 articles were selected for full text evaluation. A sum of 24 articles met the inclusion/exclusion criteria for qualitative analysis. Figure 1 illustrates the PRISMA flow-chart, with the reasons for the articles' exclusion. The extracted data from the articles is shown in Table I. Studies involved 1916 participants, with 952 participants in the intervention groups and 964 participants as controls. The smallest sample size was 19 participants[12] (9 *vs* 10 controls) while the biggest sample size comprised 756 participants[13] (381 *vs* 375 controls). Most studies used the modified New York criteria for the classification of axSpA; only three used the ASAS criteria[14-16]. Six studies did not report the pharmacological therapy allowed during the trial[17-22]. Participants' age was not mentioned in one study[21]. While two studies did not provide information regarding the gender of participants[18,19], all remaining studies include both female and male participants, with female participants being the majority in three studies[15,23,24]. Only six studies[17,18,20,25-27] had intervention groups with a single exercise modality; the others used a combination of different PE modalities. Just two studies applied education-behavioral programmes[13,28]. All but seven studies had a supervised intervention[12,13,16,21,29-31] (either full or partial supervision). Unsupervised studies had an initial training session with a physiotherapist or rheumatologist to ensure the exercises were performed correctly and compliance was monitored through participant logs or telephone communication. Adherence to the PE programs was not incorporated as an exclusion/inclusion criteria and no references were made about this topic in nine of the studies. In the others fifteen studies, 1 made a reference to adherence criteria to inclusion the patients, but not specified the criteria; 4 presented specific inclusion criteria relatively to adherence of the PE programs; 1 referred to that was made an assessment of the compliance, but then not presented the results. In 7 studies, the intervention group presented an adherence ≥75% to the PE program.

Exercise programs took place in varied settings, such as homes, hospitals, swimming pools or unspecified fitness locations. The shortest PE intervention period was three weeks[20], with the longest being 12 months[28,32,33]. However, one of the studies maintained the follow-up until 12 months after the end of PE programs[32] (the longest follow-up time). There were no reports of adherence below 75% to any of the applied interventions. Exercise frequency and duration ranged from 60 minutes one time per week[33] to 150 minutes five times per week[19]. Aerobic exercise intensity was reported in four studies: two applied high-intensity training up to 95% maximal heart rate[14,15]; one used a treadmill for walking/running up to 80% of peak oxygen uptake ($V\dot{O}_2$ peak)[12]; another one an intensity up to 80% maximal heart rate[23]; while other an intensity of 75% maximal heart rate[22]. Tai chi was the intervention in three studies[16,17,27], pilates in other three studies[18,22,29], while one article studied the benefits of Baduanjin

TABLE I: Clinical trials of physical exercise effects on axial spondyloarthritis

Study Authors/Year	Therapy	Participants Age (C/I)*	n (CG/IG)	Female-CG/ Female-IG	Intervention Duration
Fernández-de-las-Peñas et al/2005	NSAIDs	46 (8)/45 (9)**	20/20	4/5	4M
Fernández-de-las-Peñas et al/2006	NSAIDs	46 (8)/45 (9)**	20/20	4/5	4M
Lee et al/2007	N/A	34.9±12.9/ 35.2±11.5	17/13	2/3	8W
Altan et al/2010	N/A	43.6 (10.1)/ 46.5 (11.2)	24/29	N/A	12W
Masiero et al/2013	bDMARDs	46.15 (10.3)/ 49.11 (11.8)	21/21	5/4	12M
Niederman et al/2013	bDMARDs	47.6± 12.4/ 50.1 ± 11.9	53/53	19/19	12W
Rodríguez-Lozano et al/2013	NSAIDs, Corticosteroids, csDMARDs, bDMARDs	46 ± 11/ 45 ± 12	375/381	101/110	24W
Roȕ et al/2013	NSAIDs, bDMARDs	24.98 (3.83)/ 25.33 (3.77)	48/48	8/9	48W
Dundar et al/2014	NSAIDs, Corticosteroids, csDMARDs, bDMARDs	43.1 ± 11.7/ 42.3 ± 11.3	34/35	6/5	4W
Hsieh et al/2014	NSAIDs, csDMARDs	42.1 ± 8.8/ 36.2 ± 11.7	10/9	3/3	12W
Sveaas et al/2014	NSAIDs, bDMARDs	49.9 (11.1)/ 46.6 (13.6)	14/10	4/8	12W
Jennings et al/2015	NSAIDs, Corticosteroids, csDMARDs, bDMARDs	40.2 (9.3)/ 42.9 (9.9)	35/35	12/9	12W

Control	Intervention	Frequency of IG	Outcomes	Follow-up	Adherence to the PE program
Conventional physical therapy (20 exercises, supervised)	Supervised strengthening and flexibility exercises (Global Posture Reeducation method)	1h, 1x/week	BASDAI; BASFI; BASMI	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Conventional physical therapy (20 exercises, supervised)	Supervised strengthening and flexibility exercises (Global Posture Reeducation method)	1h, 1x/week	BASDAI; BASFI; BASMI	PT, 12M	Minimum of 3x/month of PE programs to be included – 80% performed PE program every week
Usual treatment	Supervised tai chi (21 movements)	45 min, 2x/week	BASDAI	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Usual treatment	Supervised Pilates exercise program	1h, 3x/week	BASDAI; BASFI; BASMI; ASQoL	PT, 3M	Not included as exclusion/ inclusion criteria and no data about compliance
Standard biological therapy	Educational-behavioral programme + Supervised training and home exercises (Stretching, strengthening, aerobic and flexibility)	1h, 2x/week (6 weeks) followed by 3x/week	BASDAI; BASFI; BASMI; CRP; ESR	PT, 12M	Compliance assessed, but not included as exclusion criteria and no data about it
Attention control intervention	Supervised Nordic walking + Standard flexibility exercise + 1 session/week of unsupervised endurance exercise	30min, 2x/week (Nordic movement) + 1x/week (flexibility)	BASDAI; BASFI; BASMI; CRP; ESR	PT	74.6% IG and only 25% performed at least 3 training units per week
Usual treatment	Education programme + 30 home exercises (+ 10 water exercises (unsupervised) (stretching, deep breathing, spinal extension, and range of motion exercises)	1h, 2x/week	BASDAI; BASFI; ASQoL	PT	54.6% of adherence to the whole programme
Multimodal exercise (step-aerobic + stretching + pulmonary exercise)	Unsupervised multimodal exercise program combining Pilates, McKenzie and Heckscher techniques	50 min, 3x/week	BASDAI; BASFI; BASMI	PT	Only the subjects attending the kinetic program on a regular basis were accepted for the final evaluation (all accepted) – not defined
Home-based exercise (muscle relaxation + flexibility, range of motion, strength, respiratory and posture exercises)	Supervised Aquatic exercise program	1h, 5x/week	BASDAI; BASFI; BASMI; SF-36	PT, 3M	Not included as exclusion/ inclusion criteria and no data about compliance
Unsupervised Range of motion exercises	Unsupervised range-of-motion exercise + strengthening of the muscles of the major muscles + aerobic exercise	Strengthening exercise 2x/week (10 repetitions) + 45min aerobic exercise 3x/ week	BASDAI; BASFI; CRP; ESR	PT	Mean compliance to PE program: 48% COMB group; 54% ROM group
Usual treatment	Supervised endurance (high intensity interval training) and strength exercise (external load for major muscle groups) (American College of Sports Medicine recommendations)	40–60 min, 3x/week	BASDAI; BASFI; BASMI; ASDAS	PT	To fulfill the PE protocol attend at least 80% of the sessions (accomplished by all selected participants)
Stretching exercises	Unsupervised aerobic exercise (walking) + stretching exercises	80min, 3x/week (50min walking + 30 min stretching)	BASDAI; BASFI; BASMI; ASDAS; CRP;ESR; SF-36	PT, 3M	> 80% of frequency to training (2 patients with poor adherence not excluded)

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TABLE I. Clinical trials of physical exercise effects on axial spondyloarthritis

Study Authors/Year	Therapy	Participants Age (C/I)*	n (CG/IG)	Female-CG/ Female-IG	Intervention Duration
Wook So et al/2015	bDMARDs	38.0 ± 9.1/ 34.6 ± 5.9	23/23	1/1	16W
Fang et al/2016	NSAIDs, Corticosterioids, csDMARDs, bDMARDs	26.46 (6.78)/ 26.62 (4.72)	13/21	0/4	6M
de Souza et al/2016	NSAIDs, Corticosteroids, csDMARDs, bDMARDs	43.8 (10.2)/ 45 (9.8)	30/30	9/7	16W
Gunay et al/2018	N/A	44.5±12.58/ 40±11.40	10/11	N/A	3W
Calik et al/2018	NSAIDs, bDMARDs	39.12±12.26/ 35.62±8.18	16/16	9/9	8W
Ma et al/2019	NSAIDs	36.58±5.2/ 35.67±5.2	42/42	12/13	12W
Sveaas et al/2019	NSAIDs, bDMARDs	47.2/45.1***	49/48	28/25	3M
Xie et al/2019	N/A	N/A	23/23	5/6	12W
Cetin et al/2020	bDMARDs	44.66±8.02/ 46.88±10.46	18/18	10/9	10W
Calik et al/2020	NSAIDs, Corticosteroids, csDMARDs, bDMARDs	46.58±11.94/ 42.85±11.07	14/17	9/9	12W
Nolte K et al/2021	N/A	39±12.8/ 39.44±14.8	13/16	7/7	6M
Oksüz S et al/2021	N/A	41.7 ± 12.5/ 46.2 ± 11.6	13/13	2/6	8W

CG: control group; IG: intervention group; PT: post-treatment; M: month; W: week; N/A: not available; PE: Physical Exercise
*Mean±SD; **: Median (interquartile rage); ***: no SD available on original paper. C: Controls; I: Intervention; CG: control group; IG: intervention Group. PT: post-treatment; 3M- three m
protein; ESR: erythrocyte sedimentation rate. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index ;BASMI: Bath Ankylosing Spondylitis Metrological Index ; BASFI: Bath Ankylosin
Form Health Survey ; ASQoL Ankylosing Spondylitis Quality of Life. NSAIDs: Nonsteroidal anti-inflammatory drugs ; csDMARDs: Conventional synthetic disease modifying antirheumatic

Control	Intervention	Frequency of IG	Outcomes	Follow-up	Adherence to the PE program
20 Conventional exercises	Unsupervised incentive spirometer exercise (ISE) + 20 conventional exercises	30min/day ISE + 30min/day conventional exercises	BASDAI; BASFI	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Conventional drugs + disease education + guidance of home-based exercise training	Supervised home-based flexibility exercises + exercise therapy (recommendations from American College of Sports Medicine)	1h, 3x/week	BASDAI; BASFI; BASMI; SF-36	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Usual treatment	Supervised group resistance exercises on a Swiss ball	3 sets of 10 repetitions, 2x/week	BASDAI; BASFI; BASMI; ASDAS; CRP; ESR; SF-36	PT	> 80% attendance at the training sessions
Transcutaneous electrical nerve stimulation (20 min)+ Supervised Spa/land-based physiotherapy (30 min)	Supervised Balance and postural stability exercises (60 min) + transcutaneous electrical nerve stimulation (20 min) + spa/land-based physiotherapy (90 min)	150 min, 5 days/week	BASDAI; BASFI; BASMI, ASQoL	PT	Exclusion if not participate in more than 2 intervention sessions (in 1 of 35 patients).
Exercise regimen of 20 exercises	Inspiratory muscle training+ Exercise regimen of 20 exercises (supervised)	3 sessions/day, 5 days/ week	BASDAI; BASFI; BASMI	PT	Exclusion if "no regular attendance" (not defined)
Celecoxib + standard exercise therapy (stretching, flexibility, strengthening)	Celecoxib + standard exercise therapy (stretching, flexibility, strengthening) + Tai Chi spinal exercise (unsupervised)	30-40min, 3x/week	BASDAI; BASFI; ASDAS; CRP; ESR	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Usual treatment	Supervised cardiorespiratory and muscular strength exercises at high intensity (American College of Sports Medicine recommendations)	40 min, 3x/week (2 supervised), 1 unsupervised)	BASDAI; BASFI; BASMI; ASDAS; CRP; ESR	PT	8% discontinued the PE after having attended just a few sessions; 76% in IG followed ≥80% of the PE protocol (≥29 of 36 sessions)
Usual treatment	Baduanjin qigong – 10 postures (4 weeks supervised + 8 weeks unsupervised)	2x/week (4 weeks) + 3x/week (8 weeks)	BASDAI; BASFI; BASMI	PT	Not included as exclusion/ inclusion criteria and no data about compliance
Home exercise (20 exercises)	10 basic Tai Chi forms (supervised)	1 h, 2 days/week	BASDAI; BASFI; BASMI; CRP, ESR; ASQoL	PT	Participation rates: 97.2 % IG; 99.4 % CG
Spinal mobility exercises (supervised)	Aerobic exercise sessions + spinal mobility exercises (supervised)	40 min, 3x/week	BASDAI; BASFI; BASMI	PT; 3M	Compliance <75% as exclusion criteria
Usual treatment	Unsupervised swimming + land-based exercises (postural correction, strengthening, stretching, breathing)	Land exercises + 12 min swimming 3x/week	BASDAI; BASFI; BASMI; CRP; ESR	PT	Compliance 66.85%
Aerobic Training	Clinical Pilates + Aerobic exercise (supervised)	Pilates programme + 30min aerobic 3x/week	BASDAI; BASFI; BASMI; ASQoL	PT	Not included as exclusion/ inclusion criteria and no data about compliance

nonths follow-up; 12M- twelve months follow-up; NA: Not available (information not provided by study authors); CRP: C-reactive
g Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short
drugs ;bDMARDs: Biologic disease-modifying anti-rheumatic drugs

qigong[20] and one studied an aquatic exercise program[25]. All studies reported BASDAI measurements. Only one study did not measure the BASFI17 and five did not measure the BASMI[12,13,16,17,31]. The ASDAS was measured in six studies[14-16,26,30,34], CRP in nine[12,14-16,21,26,28,30,34], ESR in eight[12,14-16,21,26,28,30], ASQoL in five[13,18,19,22,27] and SF-36 in four[25,26,30,35]. All studies reported pre and post-treatment measures and group outcomes comparison (table II). Comparison of baseline and post-treatment values for each outcome is shown in table III.

Out of the 24 selected studies, BASDAI showed a statistically significant improvement favoring the intervention group in thirteen studies[13-18,21-23,27-29,33], BASFI in ten studies[12-16,21,27,28,33] and BASMI in six studies[15,18,21,27-29]. Two studies[32,33] did not report a BASMI total score group comparison, but in some of the parameters of this score evaluated, there was a significant improvement favoring the intervention groups. When compared to control groups, ASDAS significantly improved in three studies[14,15], CRP in two[15,16], ESR in one study[16], SF-36 in two studies[25,35] and ASQoL in three studies[13,22,27].

A total of six studies measured these outcomes after a follow-up period. The intervention group had a sustained benefit for the BASFI and BASMI scores at three months in one study[18] (intervention: Pilates exercise program of 1 hour given by a certified trainer 3 times a week for 12 weeks) and for the SF-36 at 3 months in another study25 (intervention: 20 sessions of aquatic exercise program, 5 times per week for 4 weeks in a swimming pool at 32–33 °C, in groups of 8–9 patients for 60 min). The BASDAI, BASFI and BASMI at 12 months had a sustained significant improvement in one study[28]. A study that made a follow-up 12 months after intervention[32] found that, after the post-treatment evaluation, there was no improvement in all outcomes except for the BASDAI. A total of seven studies reported no benefits in the intervention´s variables when compared to the control group,[20,24,26,30,31,36].

Reported adverse outcomes were: re-admission of two participants due to disease flare[17]; pain exacerbation in one patient and calcaneus tendon rupture in another patient[26]; chest pain in one participant (that was able to conclude the study after evaluation by the cardiologist) and two participants with persistent pain during the exercises (although the authors note that exercise safety was proven by the group-effect improvement on disease activity)[15]; increased back pain in one participant[18]; increase in the ASDAS score after exercise intervention, although with no reported adverse outcomes[14]; worsening of disease activity[30]; pain and stiffness of the lower back and buttocks, although with significant improvement in all outcomes[25]; worsening of knee pain in one participant[20]. One study[30] excluded three participants after the initial ergometric testing revealed changes suggestive of myocardial ischemia.

Regarding qualitative analysis, 98 outcomes were submitted to bias assessment (Figures 2-5). Most outcomes were classified as having a "high-risk" of bias (*n*= 64), mostly corresponding to patient-reported outcomes (e.g. BASDAI). "Some-concerns" were found in 33 studies, while only one outcome (BASMI) had a "low-risk" bias assessment[15]. The most common methodological limitations were related to the randomization process (main lack of allocation concealment), deviations from intended interventions and outcome measurements (mainly due to lack of blinding of participants). Other frequent study biases were related to deviations from intended intervention (e.g. inability to control physical exercise practice outside study design) and failure to include data from more than 95% of participants (in two studies[17,26] there were "some-concerns" bias assessment due to missing data being related to health concerns of excluded participants: one participant re-admitted due to disease flare[17] and pain exacerbation and one rupture of calcaneus tendon[26]). All studies showed no statistically significant differences between participants and controls at baseline for either the sociodemographic characteristics or established outcomes.

DISCUSSION

In general, our study confirms a positive effect of PE on axSpA disease activity, physical function and quality of life, without major safety concerns. These benefits were observed both during the PE programs and after their completion[18,28]. This may suggest that PE programs should be maintained, either intermittently or continuously, in order to maintain or amplify the positive effects in axSpA patients. However, it was not possible to determine the minimum period of PE programs to obtain these longstanding benefits. Additional studies are needed to provide more information regarding the long-term effects of PE and define PE implementation strategies. Furthermore, just seven studies presented specific results about the adherence to the PE programs, which data that is really important to interpretate the results of efficacy of the implemented exercise modalities and lacking in most studies.

It is worth noting that only six studies[17,18,20,25-27] presented results of a single PE modality intervention, which compromised the possibility to stablish the isolated effect of each type of exercise.

Nevertheless, through these studies, it was possible to obtain some conclusions regarding aerobic/

TABLE II. Effects of different exercise programs on axial spondyloarthritis (studies' inter-group comparisons - control vs intervention)

Study Authors/ Year	BASDAI PT	BASFI PT	BASMI PT	ASDAS PT	CRP PT	ESR PT	SF-36- PT	ASQoL PT	BASDAI 3M	BASFI 3M	BASMI 3M	ASDAS 3M	CRP 3M	ESR 3M	SF-36- 3M	ASQoL 3M	BASDAI 12M	BASFI 12M	BASMI 12M
Fernández-de-las-Peñas et al/2005	NS	**0.04**	**NA#**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fernández-de-las-Peñas et al/2006	**0.04**	NS	**NA#**	-	-	-	-	-	-	-	-	-	-	-	-	-	NS	**0.008**	**NA##**
Lee et al/2007	**<0.05**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Altan et al/2010	**0.003**	0.059	**0.304**	-	-	-	-	0.620	0.106	**0.023**	**0.013**	-	-	-	-	0.808	-	-	-
Masiero et al/2013	**0.035**	**0.01**	**0.001**	-	NA	NA	-	-	-	-	-	-	-	-	-	-	**0.012**	**0.05**	**0.01**
Niederman et al/2013	0.31	0.63	0.46	0.38	0.12	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rodríguez-Lozano et al/2013	**0.005**	**0.002**	-	-	-	-	-	**0.009**	-	-	-	-	-	-	-	-	-	-	-
Roú et al/2013	**0.001**	**0.001**	**0.001**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dundar et al/2014	>0.05	>0.05	>0.05	-	-	-	**<0.001***	-	>0.05	>0.05	>0.05	-	-	-	**<0.001***	-	-	-	-
Hsieh et al/2014	0.414	**0.041**	-	-	1.000	0.743	-	-	-	-	-	-	-	-	-	-	-	-	-
Sveaas et al/2014	**0.02**	**0.02**	0.32	**0.07**	0.89	0.40	-	-	-	-	-	-	-	-	-	-	-	-	-
Fang et al/2015	0.325	0.162	0.346	-	-	-	**<0.05**	-	-	-	-	-	-	-	-	-	-	-	-
Jennings et al/2015	NS	NS	NS	NS	NS	NS	NS	-	NS	NS	NS	NS	NS	NS	NS	-	-	-	-
Wook So et al/2015	NS	NS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
de Souza et al/2016	0.885	0.386	0.344	NS	NS	NS	NS	-	-	-	-	-	-	-	-	-	-	-	-
Gunay et al/2018	0.50	0.78	0.17	-	-	-	-	0.14	-	-	-	-	-	-	-	-	-	-	-
Calik et al/2018	0.910	0.895	0.875	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-
Ma et al/2019	**0.040**	**0.037**	-	**0.038**	**0.021**	**0.003**	-	-	-	-	-	-	-	-	-	-	-	-	-
Sveaas et al/2019	**<0.001**	**<0.001**	**0.016**	**<0.001**	**0.041**	0.066	-	-	-	-	-	-	-	-	-	-	-	-	-
Xie et al/2019	0.39	0.74	0.83	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cetin et al/2020	**0.00**	**0.05**	0.76	-	-	-	-	**0.00**	-	-	-	-	-	-	-	-	-	-	-
Calik et al/2021	**0.032**	0.544	0.279	-	-	-	-	-	NA	NA	NA	-	-	-	-	-	-	-	-
Nolte K et al/2021	**0.002**	**0.007**	**0.003**	-	0.350	0.562	-	-	-	-	-	-	-	-	-	-	-	-	-
Oksüz S et al/2021	**0.001**	0.209	**0.034**	-	-	-	-	**0.039**	-	-	-	-	-	-	-	-	-	-	-

Table expresses p-values, since most studies did not provide confidence intervals. Bold values express significant values favoring intervention.
#Total score not available. Authors decomposed BASMI score: a statistical significance was achieved in all parameters (favoring intervention) except for the "tragus to wall" parameter.
Total score not available. Authors decomposed BASMI score: a statistical significance was achieved in all parameters (favoring intervention) except for the "tragus to wall" and "cervical rotation" parameters.
* Significant in 6 domains of SF-36: bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, general mental health
PT: post-treatment; 3M- three months follow-up; 12M- twelve months follow-up; NS: not significant (inter-group comparison p-value not provided by study authors); NA: Not available (information not provided by study authors); CRP: C-reactive protein; ESR: erythrocyte sedimentation rate
BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index ; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short Form Health Survey ; ASQoL Ankylosing Spondylitis Quality of Life

Table III: Baseline and Post intervention differences of the outcomes' values between control and intervention groups (

Study Authors/ Year	BASDAI (Baseline/Post-treatment)		BASFI (Baseline/Post-treatment)		BASMI (Baseline/Post-treatment)	
	C	I	C	I	C	I
Fernández-de-las-Peñas et al 2005	2.3 (5, -0.4)*#	1.6 (4.3, -1.1)*#	0.5 (4.5, -3.5)*#	6.1 (9.8, 2.4)*#	NA	NA
Fernández-de-las-Peñas et al 2006	2.3 (5, -0.4)*#	1.6 (4.3, -1.1)*#	0.5 (4.5, -3.5)*#	6.1 (9.8, 2.4)*#	NA	NA
Lee et al 2007	0.35±6.77*	-7.38±13.02*	-	-	-	-
Altan et al 2010	2.6±1.8/ 3.1±2.0	2.8±1.7/ 2.4±1.7	2.2±1.6/ 2.3±2.1	2.4±1.6/ 1.7±1.6	8.9±1.7/ 9.1±1.7	8.8±1.8/ 8.4±1.8
Masiero et al 2013	3.1±1.7/ 3.0±2.1	3.8±1.6/ 2.7±1.6	2.9±1.7/ 3.0±2.0	3.0±1.5/ 2.1±1.2	4.0±1.3/ 3.9±1.5	4.7±1.1/ 3.7±1.1
Niederman et al 2013	3.6±2.1/ 3.15±0.23	3.3±1.9/ 2.84±0.24	2.4±2.1/ 2.40±0.20	2.4±1.9/ 2.53±0.21	2.8±1.9/ 2.66±0.28	2.9±2.1/ 2.40±0.28
Rodríguez-Lozano et al 2013	-0.37 (-0.55;-0.19)*#	-0.65 (-0.82;-0.47)*#	-0.21(-0.36;-0.007)*#	-0.54 (-0.68;-0.40)*#	-	-
Roû et al 2013	5.29±1.96/ 4.13±1.66	5.14±1.95/ 2.10±0.82	3.42±1.94/ 2.76±1.56	3.56±1.83/ 1.50±1.11	3.3±0.45/ 3.02±0.44	3.73±0.45/ 1.19±0.84
Dundar et al 2014	4.0 ± 2.3/ 2.8 ± 2.5	3.9 ± 1.9/ 2.7 ± 1.7	3.6 ± 2.8/ 2.6 ± 2.3	3.5 ± 2.9/ 2.6 ± 2.4	5.2 ± 3.1/ 4.0 ± 2.7	5.3 ± 2.7/ 4.1 ± 2.6
Hsieh et al 2014	4.5±2.1/ 4.5±3.0	4.2±1.9/ 3.7±1.8	3.5±2.9/ 3.5±3.1	3.7±3.3/ 1.9±2.3	-	-
Sveaas et al 2014	5.3±1.3/ 5.2±2.0	5.3±1.4/ 3.3±2.0	3.1±1.6/ 3.1±1.4	2.6±2.2/ 1.5±1.5	3.0±1.8/ 2.9±1.8	2.3±1.5/ 2.0±1.6
Fang et al 2015	3.19±1.29/ 2.00±1.64	2.66±1.69/ 1.21±1.54	2.05±2.26/ 1.63±2.24	1.35±1.74/ 0.24±0.75	2.31±2.06/ 2.00±1.87	1.62±1.941.19±1.66
Jennings et al 2015	3.46±2.39/ 2.87±1.97	3.62±2.06/ 3.27±2.07	4.27±2.32±3.73±2.19	4.28±2.78/ 3.47±2.48	4.79±2.22/ 4.61±2.24	5.15±1.95/ 4.95±2.03
Wook So et al 2015	2.75 ± 1.15/ 2.58 ± 1.65	2.37 ± 1.09/ 1.97 ± 1.54	1.72 ± 1.73/ 1.26 ± 1.56	0.98 ± 1.23/ 0.75 ± 1.17	-	-
de Souza et al 2016	2.34±2.26/ 2.12±2.4	2.52±1.65/ 2.08±1.84	4.09±2.40/ 3.90±2.6	4.62±2.49/ 3.36±2.16	5.19±2.04/ 5.37±2.2	4.94±2.09/ 4.69±1.94
Gunay et al 2018	4.09±2.37/ 2.69±2.22	3.80/ 1.64	3.41±2.56/ 2.18±2.28	2.35±1.19/ 1.25±1.08	4.06±1.78/ 2.98±1.87	3.44±1.21/ 2.04±1.35
Calik et al 2018	4.48 ± 3.17/ 3.25 ± 2.34	4.52 ± 2.75/ 3.57 ± 2.77	3.13 ± 2.98/ 2.61 ± 2.25	3.17 ± 2.13/ 2.88 ± 2.28	2.93 ± 1.48/ 2.43 ± 0.96	3.37 ± 1.40/ 2.81 ± 1.64
Ma et al 2019	4.35±2.90/ 3.05±1.71	4.23±2.86/ 2.30±1.58	2.50±1.60/ 1.84±1.27	2.44±1.57/ 1.30±1.06	-	-
Sveaas et al 2019	5.3±1.5/ 4.8±1.5	4.9±1.6/ 3.3±1.6	3.6±2.1/ 3.2±2.0	2.9±1.8/ 1.8±1.4	2.6±1.3/ 2.5±1.4	2.9±1.3/ 2.5±1.2
Xie et al 2019	2.70±1.15/ 2.55±1.19	2.87±1.09/ 2.28±1.09	1.05±1.02/ 1.17±1.10	1.40±1.10/ 1.28±1.02	1.02±1.01/ 3.15±1.21	2.97±1.36/ 2.84±1.27
Cetin et al 2020	4.30±1.98 / 3.85±1.79	4.57±1.80 / 1.98±0.85	3.71±1.98 / 1.55±0.96	2.97±2.02 / 1.66±1.25	2.92±1.37 / 1.87±0.95	2.58±1.22 / 1.61±1.18
Calik et al 2021	4.22±2.15 / 3.81±1.60	4.52±1.50 / 2.21±1.44	3.03±2.63 / 2.56±2.30	3.19±2.40 / 2.15±1.84	2.88±1.08 / 2.74±1.01	3.32±1.49 / 2.90±1.42
Nolte K et al 2021	5.89/ 5.15**	4.04/ 1.56**	4.18/ 4.7**	2.48/ 0.95**	1.5/ 1.9**	1.8/ 0.70**
Oksüz S et al 2021	3.3 ± 1.80/ 2.5 ± 2.0	4.4 ± 1.9/ 1.8 ± 1.4	3.1 ± 2.7/ 2.6 ± 2.6	3.4 ± 2.3/ 1.5 ± 1.5	4.4 ± 2.2/ 4.0 ± 2.5	4.1 ± 2.0/ 3.3 ± 1.9

*Authors only provided Intergroup comparison of improvement (Prepost scores); #: 95% confidence interval **: no standard deviation was provided by the authors BASDAI: Bath Ankylosin Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; ASQoL Ankylosing Spondylitis Quality of Life; C: Control; I: Intervention. No values were provided by th

values are shown as mean with standard deviation unless stated otherwise)

ASDAS (Baseline/Post-treatment)		CRP (Baseline/Post-treatment)		ESR (Baseline/Post-treatment)		ASQoL (Baseline/Post-treatment)	
C	I	C	I	C	I	C	I
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	3.5±3.3/ 3.0±3.4	3.7±4.6/ 4.0±4.8
-	-	-	-	-	-	-	-
2.3±1.0/ 2.23±0.18	2.2±0.8/ 2.43±0.17	6.4±8.7/ 4.93±1.30	7.5±9.8/ 7.49±1.22	-	-	-	-
-	-	-	-	-	-	-0.23 (-0.54;0.07)*#	-0.98 (-1.29;-0.68)*#
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	1.07±1.24/ 0.9±0.99	1.27±1.10/ 0.79±0.56	24.7±23.1/ 25.0±28.3	36.8±28.6/ 24.8±12.0	-	-
2.7±0.8/ 2.6±0.8	2.3±0.6/ 1.8±0.9	2(1,23)/ 3(1,13)#	1(1,9)/ 1(1,12)	6(1,24)/ 7(1,46)	10(2,41)/ 9(5,26)	-	-
-	-	-	-	-	-	-	-
2.24±0.91/ 2.24±0.89	2.44±1.07/ 2.10±0.92	6.01±7.33/ 7.84±11.59	10.49±11.90/ 6.53±6.01	17.1±13.6/ 14.7±9.7	18.5±12.5/ 20.5±15.2	-	-
-	-	-	-	-	-	-	-
1.89±1.00/ 1.86±1.10	2.20±0.91/ 1.93±0.84	4.70±5.96/ 4.51±6.75	6.53±6.00/ 9.27±13.50	18.00±12.27/ 18.71±14.33	18.10±13.23/ 13.31±9.01	-	-
-	-	-	-	-	-	8.60±5.15/ 4.70±3.94	5.73±2.65/ 3.45±1.97
-	-	-	-	-	-	-	-
3.42±2.37/ 1.78±1.29	3.48±2.38/ 1.24±1.04	14.38±10.70/ 10.23±8.18	14.54±10.83/ 6.54±6.03	20.69±16.40/ 14.58±11.66	21.05±16.84/ 8.25±6.87	-	-
2.7±0.6/ 2.6±0.7	2.6±0.8/ 1.9±0.7	NA	NA	NA	NA	-	-
-	-	-	-	-	-	-	-
-	-	5.31±6.01/ 4.98±5.00	11.35±14.24/ 6.25±9.04	18.72±7.05/ 17.50±9.14	31.00±24.59/ 23.11±17.75	7.16±4.73/ 5.88±3.78	7.38±4.77/ 2.66±2.91
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	7.6 ± 5.7/ 5.9 ± 5.6	8.5 ± 5.4/ 3.9 ± 2.9

ng Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index ; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis
he authors regarding the : 36-Item Short Form Health Survey

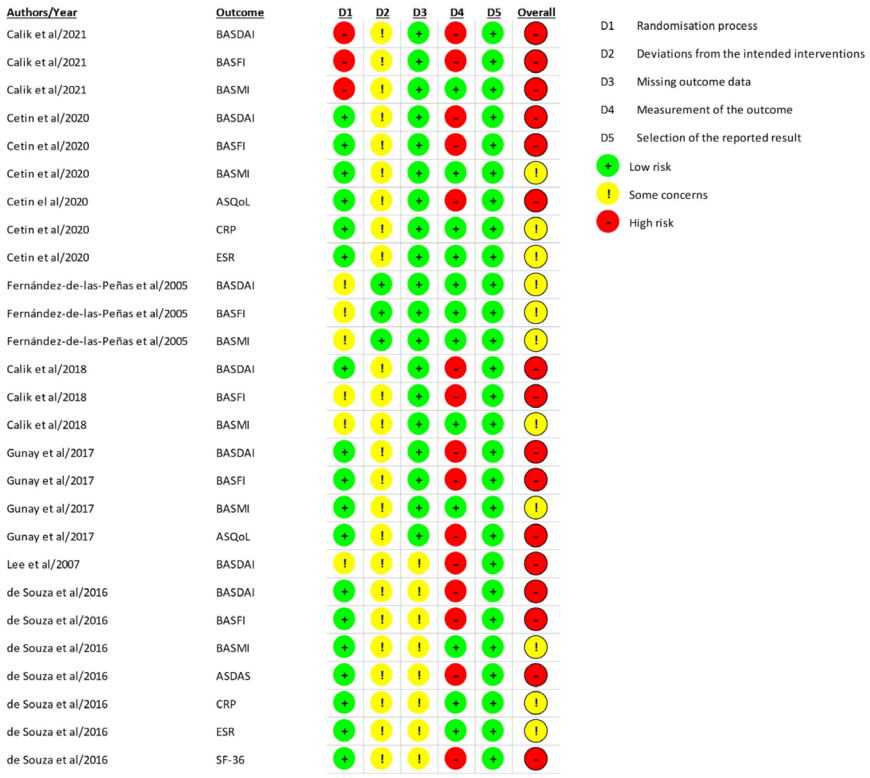

Figure 2a. Risk of bias for each article outcomes using the Cochrane Risk of Bias Tool - BASDAI: Bath Ankylosing Spondylitis Disease Activity Index ;BASMI: Bath Ankylosing Spondylitis Metrological Index ; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short Form Health Survey ; ASQoL Ankylosing Spondylitis Quality of Life

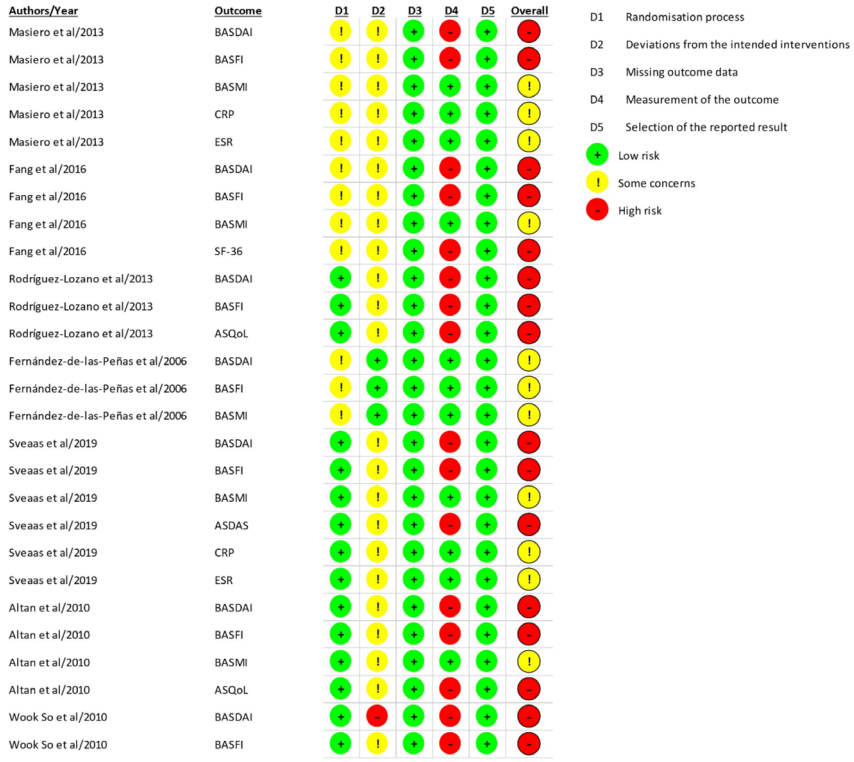

Figure 2b. Risk of bias for each article outcomes using the Cochrane Risk of Bias Tool (continued) - BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short Form Health Survey; ASQoL Ankylosing Spondylitis Quality of Life

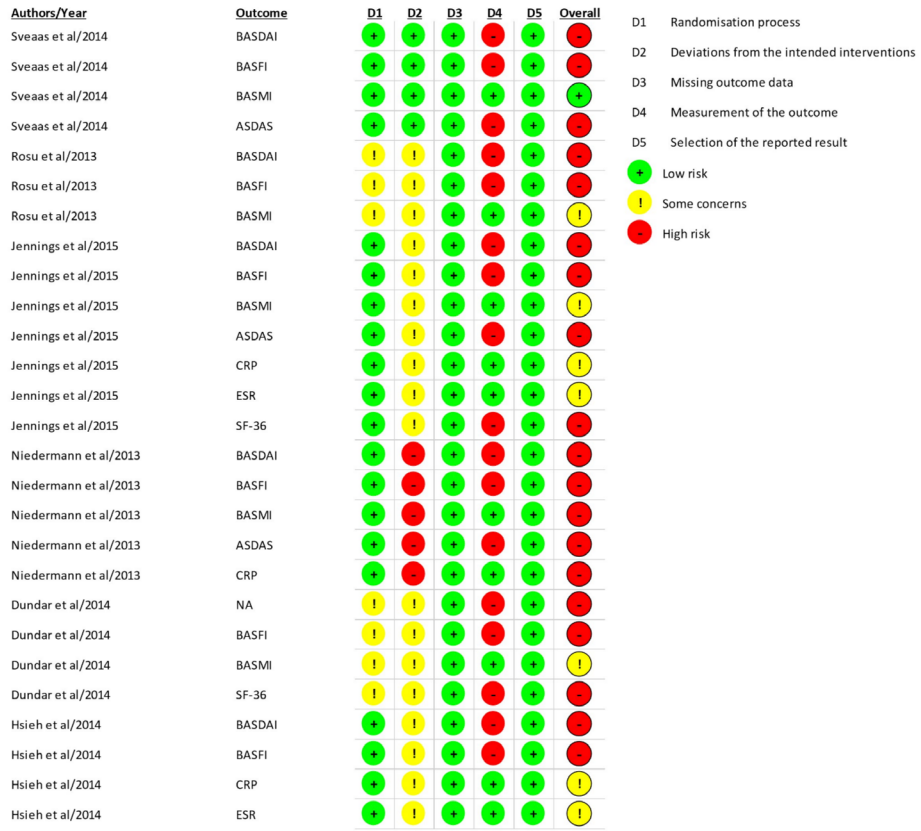

Figure 2c. Risk of bias for each article outcomes using the Cochrane Risk of Bias Tool (continued) - BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index ; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short Form Health Survey; ASQoL Ankylosing Spondylitis Quality of Life

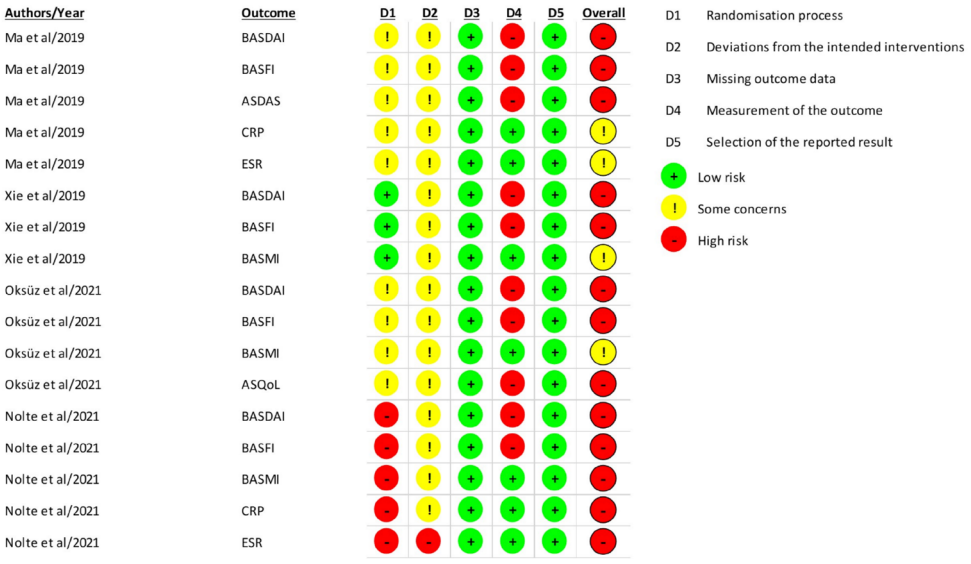

Figure 2d. Risk of bias for each article outcomes using the Cochrane Risk of Bias Tool(continued) - BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrological Index; BASFI: Bath Ankylosing Spondylitis Metrological Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: c-reactive protein; ESR: Erythrocyte sedimentation rate; SF-36: 36-Item Short Form Health Survey; ASQoL Ankylosing Spondylitis Quality of Life

cardiovascular, strength and flexibility PE programs.

Aerobic exercise (even of high intensity) was proven to have positive effects both on disease activity and in managing classic cardiovascular risks and, whereby should be considered as a non-pharmacological treatment option for axSpA[36].

On the other hand, both strength and flexibility PE programs seems to contribute for an increase in physical function and joint mobility. However, these benefits did not result in a consistent improvement of BASFI and BASMI scores. This lack of correlation can be associated to the pre-existing functional/mobility irreversible limitations. Furthermore, combined interventions may be more efficacious than single flexibility interventions[23]. This is according to existing international recommendations that propose a combination of aerobic exercise (moderate to high intensity) and strength/mobility/flexibility exercises to decrease cardiovascular morbidity and mortality in the healthy population[37,38] and people with inflammatory rheumatic diseases[7].

There were two particular combined PE modalities that showed consistent results. Tai Chi (combining cardiovascular and flexibility exercises), showed positive effects on disease activity, functional and mobility indexes (particularly in cervical spine) and in levels of inflammation markers[17,27]. These benefits translate into better quality of life indexes[27]. Pilates had similar results[18,29], particularly if performed for longer periods (a minimum of 24 weeks)18.

Regarding the safety of the implemented PE modalities, as already noticed, no major adverse outcomes were reported regarding the safety of implemented PE modalities. Cardiovascular disease represents a significant concern in this group of patients[2], however, this review has shown that even high-intensity aerobic PE programs were safe. Only one study[15] reported a participant with chest pain, ultimately able to continue the exercise program after approval by a cardiologist (although at moderate intensity). One study[30] found three participants with signs of myocardial ischemia during initial screening, reinforcing the importance of cardiovascular screening before prescribing physical exercise.

Concerning to minor adverse events, the increased pain intensity after different PE interventions was the most common adverse effect reported, even in healthy people[39]. However, it would have been helpful to analyze the comorbidities of these patients to understand if there were other factors that could have influenced the increase of pain. Beyond this, no information was given regarding the follow-up of these participants, in particular concerning the duration and evolution of this adverse event to understand its real impact on daily life of these patients.

One of the main concerns is the long-term adherence to PE programs. As most studies considered a compliance below 75% as exclusion criteria, it is not possible to have a precise estimate regarding the compliance to PE programs. Nevertheless, some studies presented several effective strategies to improve PE adherence, namely strategies aimed at changing behavior (educational programs)[9], patient communication and feedback and monitoring unsupervised interventions. Unfortunately, only two studies applied and evaluated these techniques with a positive effect. More studies focused on adherence outcomes are needed to have statistically relevant results to define future recommendations concerning these topics, additionally to the PE programs.

The relevance of this study is the strong demonstration of consistent results of efficacy and safety of PE in all domains of daily life of axSpA patients, supported by the most recent RCTs. It demonstrates the importance of including structured PE programs in the non-pharmacological management of these patients. However, the diversity of the included studies and their exercise modalities, hinder the authors from making specific recommendations, but rather more general ones. A continued effort should be made regarding study design to allow homogenous PE interventions and adherence analysis.

Despite the already highlighted relevance of this review, there are some limitations that should be mentioned, namely: research and selection of the articles (to facilitate the studies analyze after their selection, we restricted their language possibilities, which can have led to the exclusion of articles with relevant interventions; however, this strategy avoid other bias, namely translation bias); the diversity of the PE interventions made it difficult to define the most effective therapy strategies; absence of a measure of the magnitude of the PE program's effect of the analyzed outcomes, in order to facilitate the comparison between them; some studies considered level of compliance as exclusion criteria, which may lead to biased results; and bias of information, resultant of the study design (e.g. non-blinded studies may lead to a biased patient-reported outcomes which can directly affect some of the evaluated scores). This last limitation may justify the fact of the majority studies resulted in the "some concerns" classification, since the chosen tool to evaluate the bias of the selected studies has a designated category regarding the probability of bias due to knowledge of the assigned intervention, and since most studies failed to address the allocation concealment adequately and used patient-reported outcomes. However, we cannot ignore the difficulty of designing an RCT with blind groups when the main outcome is to evaluate the effectiveness of PE programs.

In conclusion, physical exercise is a reliable non-pharmacological treatment option for axSpA, since it has positive effects on disease activity, physical function, mobility and quality of life. It also seems to be safe although a cardiovascular screening may be

appropriate before exercise initiation, particularly if high-intensity modalities are chosen.

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SUPPLEMENTARY FILE

Supplementary File 1. PRISMA 2020 Check-list

Section and Topic	Item#	Checklist item	Location where item is report
Title			
Title	1	Identify the report as a systematic review.	Page 2
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2, 3
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	N/A
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses	Page 4, 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4, supplementary 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5

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Supplementary File 1. Continuation

Section and Topic	Item#	Checklist item	Location where item is report
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	N/A
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 5, figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	Page 5-7, Table I
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 7, Figures 2-5
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table II
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	Page 7
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 7
	23b	Discuss any limitations of the evidence included in the review.	Page 9
	23c	Discuss any limitations of the review processes used.	Page 9
	23d	Discuss implications of the results for practice, policy, and future research.	Page 9

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Supplementary File 1. Continuation

Section and Topic	Item#	Checklist item	Location where item is report
		Other information	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 9
Competing interests	26	Declare any competing interests of review authors.	Page 9
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Supplementary File 2. Research equations used for each database searching Web of Science

((Exercise OR Exercise Therapy OR Exercise Movement Techniques OR Circuit-Based Exercise OR Plyometric Exercise OR Resistance Training OR Muscle Stretching Exercises OR High-Intensity Interval Training OR Sports OR Physical Exertion OR Physical Education and Training OR Physical Endurance OR Hydrotherapy OR Fitness OR Mind-Body Therapies)) AND : (spondyloarthritis OR spondyloarthropathies OR spondylitis)
Refined by: DOCUMENT TYPES: (ARTICLE OR EARLY ACCESS OR CORRECTION)
Timespan=2000-2020

PubMed

(Exercise OR Exercise Therapy OR Exercise Movement Techniques OR Circuit-Based Exercise OR Plyometric Exercise OR Resistance Training OR Muscle Stretching Exercises OR High-Intensity Interval Training OR Sports OR Physical Exertion OR Physical Education and Training OR Physical Endurance OR Hydrotherapy OR Fitness OR Mind-Body Therapies) OR ("Mind-Body Therapies"[Mesh] OR "Physical Fitness"[Mesh] OR "Exercise"[Mesh] OR "Hydrotherapy"[Mesh] OR "Physical Endurance"[Mesh] OR "Physical Education and Training"[Mesh] OR "Physical Exertion"[Mesh] OR "Sports"[Mesh] OR "High-Intensity Interval Training"[Mesh] OR "Muscle Stretching Exercises"[Mesh) OR "Exercise Therapy"[Mesh) OR "Resistance Training"[Mesh] OR "Plyometric Exercise"[Mesh] OR "Circuit-Based Exercise"[Mesh] OR "Exercise Movement Techniques"[Mesh])
AND
"Spondylitis, Ankylosing"[Mesh] OR Spondylarthritis OR Spondylarthropathies OR Spondylitis
Filters applied: English, French, Portuguese, Spanish, from 2000 - 3000/12/12

Embase:

(('exercise'/exp OR exercise OR 'exercise therapy'/exp OR 'exercise therapy' OR (('exercise'/exp OR exercise) AND ('therapy'/exp OR therapy)) OR 'exercise movement techniques'/exp OR 'exercise movement techniques' OR (('exercise'/exp OR exercise) AND ('movement'/exp OR movement) AND techniques) OR 'circuit-based exercise'/exp OR 'circuit-based exercise' OR ('circuit based' AND ('exercise'/exp OR exercise)) OR 'plyometric exercise'/exp OR 'plyometric exercise' OR (plyometric AND ('exercise'/exp OR exercise)) OR 'resistance training'/exp OR 'resistance training' OR (('resistance'/exp OR resistance) AND ('training'/exp OR training)) OR 'muscle stretching exercises'/exp OR 'muscle stretching exercises' OR (('muscle'/exp OR muscle) AND ('stretching'/exp OR stretching) AND exercises) OR 'high-intensity interval training'/exp OR 'high-intensity interval training' OR ('high intensity' AND interval AND ('training'/exp OR training)) OR 'sports'/exp OR sports OR 'physical exertion'/exp OR 'physical exertion' OR (physical AND ('exertion'/exp OR exertion)) OR 'physical education'/exp OR 'physical education' OR (physical AND ('education'/exp OR education))) AND ('training'/exp OR training) OR 'physical endurance'/exp OR 'physical endurance' OR (physical AND ('endurance'/exp OR endurance)) OR 'hydrotherapy'/exp OR hydrotherapy OR 'fitness'/exp OR fitness OR 'alternative medicine'/exp OR 'alternative medicine') AND ('spondylitis'/exp OR spondylitis OR 'spondyloarthritis'/exp OR spondyloarthritis OR spondyloarthropathies)
OR
'exercise'/exp OR **'kinesiotherapy'**/exp OR **'physical activity, capacity and performance'**/exp OR **'sport'**/exp OR **'hydrotherapy'**/exp OR **'fitness'**/exp
AND
'ankylosing spondylitis'/exp
[2000-2020]/py AND ([english]/lim OR [french]/lim OR [portuguese]/lim OR [spanish]/lim) AND ([article]/lim OR [article in press]/lim OR [data papers]/lim OR [erratum]/lim)