Original Article
Male reproductive health and infertility

pISSN: 2287-4208 / eISSN: 2287-4690
World J Mens Health Published online Jan 2, 2024
https://doi.org/10.5534/wjmh.230106

The World Journal of MEN's HEALTH

Effects of Physical Activity on Fertility Parameters: A Meta-Analysis of Randomized Controlled Trials

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Purpose: Augmented adiposity may negatively impact sexual sphere through its metabolic effects and its detrimental impact on reproductive hormones. Moreover, a dysregulated metabolic pathway may promote apoptosis among spermatogenic cells. Based on these premises, a relation between weights loss and ameliorate semen parameters seems beneficial. To investigate if physical activity may affect semen parameters and fertility rate, a systematic literature search on major dataset has been performed.

Materials and Methods: The search terms included: "Assisted reproduction therapies," "fertility," "semen parameters," "sperm parameters," and "physical activity." This analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and it was registered on PROSPERO (CRD42023384471). A total of 47 studies have been identified; 1 reference has been eliminated after duplication check. After preliminary screening 32 papers have been excluded. Considering the exclusion criteria, 15 full-text articles were evaluated for eligibility. After a full-text review, six studies published during a span of eight years (2014–2022) have been included in the meta-analysis. Semen parameters, pregnancy and birth rates were investigated. The revised Cochrane risk of bias tool (Rob2) has been used to check the risk of bias.

Results: The number of patients enrolled in studies ranges from 17 to 521; in the end, a total of 1,637 patients have been enrolled in the study. Fertility parameters investigated were semen quality parameters and pregnancy rates and live births. A statistically significant relationship between physical exercise and sperm concentration ($p=0.02$), total sperm motility ($p<0.01$), total sperm count ($p<0.01$), normal morphology ($p<0.01$) has been established. Moreover, the study registered a statistically significant association within physical activity and total pregnancy rate ($p<0.01$) and live birth rate ($p<0.01$).

Conclusions: We demonstrated that physical activity is significantly associated with amelioration of semen parameters and may be crucial in improving or even reverting male infertility.

Keywords: Exercise; Fertility; Oligospermia; Reproductive techniques; Semen analysis

Received: Apr 13, 2023 **Revised:** Jul 19, 2023 **Accepted:** Aug 10, 2023 **Published online** Jan 2, 2024
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INTRODUCTION

Physical activity has been shown to have both positive and negative effects on fertility parameters [1] while moderate physical activity has been associated with improved sperm quality, including increased sperm count and motility [2]. In fact, an increase in adiposity may adversely affect male fertility due to its metabolic and hormonal effects [3].

In a recent systematic review and meta-analysis of observational studies, authors reported that sperm count was lower in class II and class III obesity categories (−0.66; p<0.001, and −0.20; p=0.001, respectively) if compared to non-obese patients [1].

Since infertility occurs as a result of different metabolic conditions, the underlying mechanisms could be better investigated from a multidisciplinary perspective. It is important to note that the relationship between physical activity and fertility is complex and it may depend on the individual's exercise habits, overall health, and underlying medical conditions.

In fact, sedentary lifestyle behaviors not only impact general wellness but also fertility parameters by accelerating aging-processes. A study conducted by Sharqawi et al [4] reported that patients with longer telomere length (16/84 *vs.* 7/91; p=0.04) are the ones who train most; contrarily those who practice less physical activity are reported to have shorter telomeres. Consequently, sperm motility was negatively correlated with telomeres length (0.588; p=0.002).

However, evidence about the role of exercise on fertility and sperm parameters have never been summarized due to discordant results and heterogeneity of findings.

Based on these premises, the aim of this paper is to perform a systematic review of randomized clinical trials with metanalysis to assess if physical activity may have a positive impact.

MATERIALS AND METHODS

1. Literature search

This analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines [5] and it was registered on PROSPERO (CRD42023384471). We performed a systematic literature search of PubMed, EMBASE and Scopus using Medical Subject Headings (MeSH) indexes, keyword searches, and publication types. The research was limited to English articles. The search terms included: "Assisted reproduction therapies," "fertility," "semen parameters," "sperm parameters," and "physical activity". Relevant articles identified in the reference lists of the selected manuscripts have been included, too. Eligible studies included published journal articles that provided quantitative data on the association between physical activity and sperm concentration, semen volume, total motility, total sperm count, morphology (normal forms), pregnancies rate and live birth rate.

2. Data extraction

Three reviewers applied eligibility criteria and selected studies for inclusion in this systematic review. Two reviewers (ALG, MGA) independently screened records for inclusion; one reviewer (GIR) checked for final inclusion or exclusion and resolved disagreements. Decisions have been recorded in an excel sheet reporting principal data of the studies included (Authors, year, DOI). A single reviewer (MGA) performed data extraction using an excel sheets master format and a single reviewer (ALG) checked extracted data that are suitable for analysis. A Third reviewer (GIR) checked for final inclusion or exclusion and resolved disagreements. The following data were extracted from selected paper: authors of the study, source, year of publication, type of study design. Moreover, patients from selected studies were divided into expose and control group; for each category sperm concentration at baseline and at follow-up, semen volume at baseline and at follow-up, total motility at baseline and at follow-up, total sperm count at baseline and at follow-up, morphology (percentage of normal sperm morphology) at baseline and at follow-up, total pregnancies rate at follow-up, live birth rate at follow-up were reported. All data will be collected and managed with an excel spreadsheet and the software Review Manager (RevMan, Version 5.4; The Cochrane Collaboration, 2020).

3. Risk of bias assessment

Two reviewers (MGA and ALG) assessed the risk of bias before the outcome's extraction; the following characteristics have been assessed: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcomes assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias). Cochrane risk of bias tool had been applied to accomplish the task. In conclusion, the third reviewer (GIR) solved any disagreement between reviewers' judgements.

4. Data analysis

Semen parameters, sperm concentration, semen volume, total sperm motility, total sperm count, sperm morphology (percentage of normal sperm morphology) had been reported at baseline and follow-up time as mean with standard deviation for both groups. The number of patients in groups have been reported as continuous variable. Data about total pregnancies rate and live birth rate at follow-up have been reported as dichotomous variable of total events within patients' groups. Also in this case, the number of patients belonging to the different groups have been reported as continuous variable. Statistical heterogeneity has been explored using χ^2 test for continuous or dichotomous variable. The outcomes about sperm concentration, semen volume, total sperm motility, total sperm count, morphology (percentage of normal sperm morphology) have been reported as a standard mean difference between the values at follow-up in physical activity and controls group. The outcomes about total pregnancies rate and live birth rate have been reported as a risk difference (RD) between the ratio of total events to total patients in physical activity group and controls group.

RESULTS

1. Characteristics of the studies

A total of 47 studies have been identified; 1 reference has been eliminated after duplication check. After preliminary screening 32 papers have been excluded. Considering the exclusion criteria, 15 full-text articles were evaluated for eligibility. After a full-text review, six studies published during a span of eight years (2014–2022) have been included in the meta-analysis (Supplement Fig. 1) [2,6-10]. Semen parameters, pregnancy and birth rates were investigated. The revised Cochrane risk of bias tool (Rob2) has been used to check the risk of bias (Supplement Fig. 2).

The number of patients enrolled in studies ranges from 17 to 521; in the end, a total of 1,637 patients have been enrolled in the meta-analysis. Parameters investigated were semen quality parameters (*i.e.*, sperm concentration, semen volume, total sperm motility, total sperm count, sperm morphology) and pregnancy and live births rates. In particular, a total of 340 patients have been enrolled in the three studies investigating semen quality [2,6,7] while a total of 1,297 patients have been enrolled in the studies investigating pregnancy rate and live births rate [8-10]. A total of two references that studied sperm concentration parameters in a sample of 280 total patients were included [2,6]; three studies investigated semen volume and total motility parameters among a 340 patients-sample [2,6,7]; two studies enrolling 99 patients assessed total sperm count [2,7]; two more articles investigated normal sperm forms among 323 participants [6,7]; finally, three studies enrolling a total of 1,297 patients investigated pregnancy rate and live births rate [8-10]. Characteristics of the studies included in the meta-analysis are listed in Table 1. The qualities of these studies were all satisfactory according to the previously specified criterion.

2. Analysis

Standard mean difference (SMD) (IV, Fixed, 95% confidence interval [CI]) analysis has been performed to investigate on the association between physical activity and sperm concentration, semen volume, total motility, total sperm count and normal forms. RD (IV, Fixed, 95% CI) analysis has been performed to investigate on the association between physical activity and total pregnancies rate and live birth rate.

We revealed that the association between physical activity and sperm concentration is statistically significant ($Z=2.37$; $p=0.02$) with a SMD of 0.28 (95% CI 0.05–0.52); heterogeneity between studies was 0% ($chi^2=0.16$, $df=1$; $p=0.69$) (Fig. 1).

We also evidenced that the association between physical activity and total motility is statistically significant ($Z=5.62$; $p<0.00001$), with a SMD of 0.63 (95% CI 0.41–0.85); heterogeneity between studies was 60% ($chi^2=4.99$, $df=2$; $p=0.08$) (Fig. 2).

We demonstrated that the association between physical activity and total sperm count is statistically significant ($Z=2.83$; $p<0.005$), with a SMD of 0.62 (95% CI 0.19–1.05); heterogeneity between studies was 0% ($chi^2=0.00$, $df=1$; $p=0.99$) (Fig. 3).

The association between physical activity and normal forms is also statistically significant ($Z=4.93$; $p<0.00001$), with a SMD of 0.56 (95% CI 0.34–0.78); heterogeneity

Table 1. Characteristics of the studies included in the meta-analysis

Id	Authors	Year	Parameter investigated	Type of study	No. of cases	No. of control	No. of patients	Physical activity protocol
1	Andersen et al [2]	2022	Semen quality	RCT	9	8	17	WHO recommendations of 150 min per week of moderate physical activity or 75 minutes per week of vigorous exercise or a combination of both by given the opportunity to participate in two 45 minutes group exercise sessions facilitated and supervised at Hvidovre Hospital (Denmark) and two 30 minutes individually exercise sessions. The aim for each session was an intensity of 80% of the maximum heart rate.
2	Montano et al [6]	2022	Semen quality	RCT	137	126	263	Individualized moderate physical activity plan for 16 weeks, based on a step-by-step achievement of the objectives. Face-to-face meetings and phone checks to verify and update physical activity goals were carried out regularly, every week for the 1st month, every 2 weeks for the 2nd and 3rd months, and once in the 4th month.
3	Rosety-Rodriguez et al [7]	2014	Semen quality	RCT	30	30	60	A 14-week, home-based, treadmill training program, 3 sessions per week, consisting of a warm-up (10–15 min), 40 minutes treadmill exercise at a work intensity of 55%–70% of peak heart rate (increasing by 2.5% each two weeks) measured during a maximal treadmill test, and cooling-down (5–10 min).
4	Maleki and Tartibian [8]	2017	Natural Pregnancy and Live birth	RCT	258	263	521	The training session consisted of a 10-minute warm-up period, which included walking and jogging as well as muscle stretches. This was followed by 30–35 minutes of interchanged walking/running on a treadmill. Then, there were 30–35 minutes of resistance training, which included exercises for all major muscle groups. The exercises to strengthen the upper body included bench press (pectoralis), chest cross (horizontal flexion of the shoulder joint), shoulder press (trapezius and latissimus dorsi), pull-downs (back muscles), biceps curls, triceps extension, upright row, trunk extension, and exercises for abdominal muscles (sit-ups). Lower body exercises included leg press (quadriceps femoris), calf raises, hip extensions (biceps femoris), hamstring curls using quadriceps table, hip abduction, and hip adduction. The exercise training started with 50% of VO2max-1RM (for aerobic and resistance, respectively), and the intensity of the training was increased by 5% after every 3 training sessions (after 3 sessions of aerobic exercise, VO2max was increased by 5% and in the same way 1RM was increased by 5% after every third resistance exercise session), which reached 70% of VO2max-1RM by the end of the fourth week.
5	Hajizadeh Maleki and Tartibian [9]	2017	Natural Pregnancy and Live birth	RCT	188	202	390	Patients performed a 40- to 50-minute treadmill running protocol, three times a week, that consisted of 10 minutes of running at 70% to 75% of their VO2max (the work phase) followed by 3 minutes at 50% to 60% of VO2max (the recovery phase). This cycle was repeated four times within each EX session. During the final 12 weeks, participants performed a 50- to 60-minute treadmill running protocol, three times a week, that consisted of 10 minutes of running at 75% to 85% of their VO2max (the work phase) followed by 3 minutes at 50% to 60% of VO2max (the recovery phase). This cycle was repeated five times within each EX session. All training sessions consisted of 10 to 15 minutes of warm up and cool down.
6	Hajizadeh Maleki and Tartibian [10]	2017	Natural Pregnancy and Live birth	RCT	197	189	386	Moderate aerobic exercise protocol included walking or jogging on a treadmill supervised through certified personal trainers. During the first 12 weeks of the study, the EX groups exercised (25–30 min/day, 3–4 days/week) at 45%–55% of their VO2max and then the volume and the intensity of exercise sessions were increased during the final 12 weeks (40–45 min/day, 4–6 days/week, and 56%–69% of VO2max). Adherence to the exercise was acknowledged via Polar heart rate monitors, and patients received immediate feedback to adjust to the prescribed intensity

RCT: randomized controlled trial, EX: exercise, RM: maximum repetition, VO2max: maximum oxygen consumption.

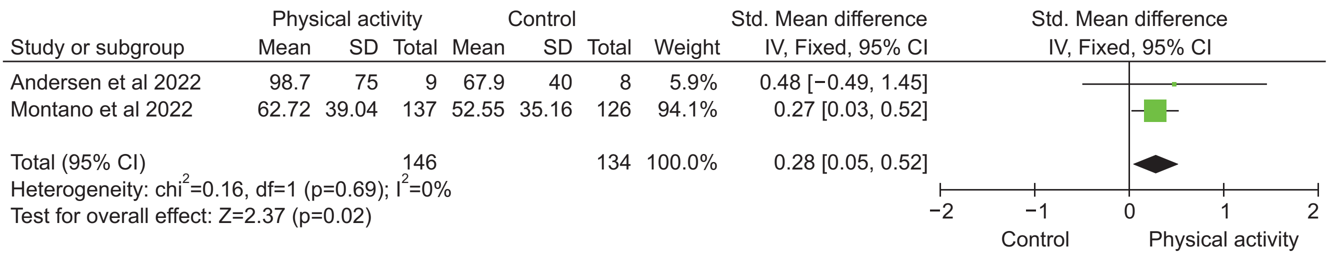

Fig. 1. Forest plot of sperm concentration and physical activity. SD: standard deviation, CI: confidence interval.

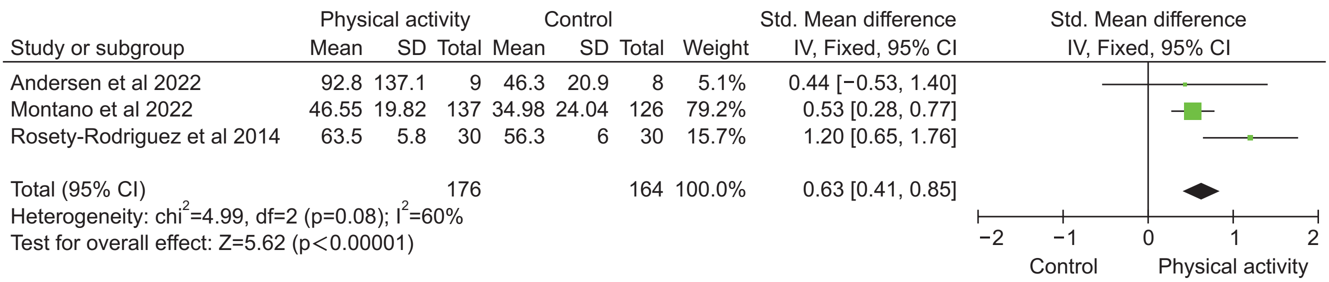

Fig. 2. Forest plot of total motility and physical activity. SD: standard deviation, CI: confidence interval.

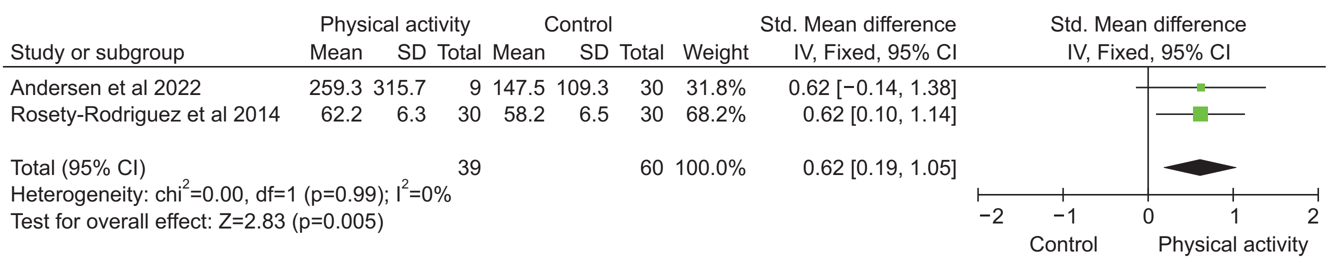

Fig. 3. Forest plot of total sperm count and physical activity. SD: standard deviation, CI: confidence interval.

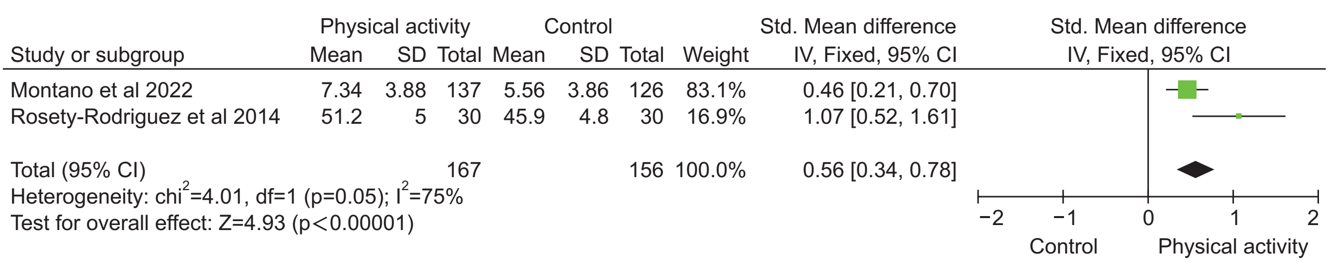

Fig. 4. Forest plot of normal forms and physical activity. SD: standard deviation, CI: confidence interval.

between studies was 75% (chi^2=4.01, df=1; p=0.05) (Fig. 4).

The association between physical activity and semen volume is not statistically significant (Z=1.37; p=0.17), with a SMD of 0.15 (95% CI 0.06–0.36); heterogeneity between studies was 0% (chi^2=1.04, df=2; p=0.60). Regarding physical activity and total pregnancies rate, our results proved that a statistically significant association existed (Z=27.91; p<0.00001), with a RD of 0.50 (95% CI 0.46–0.53); heterogeneity between studies was 99% (chi^2=233.09, df=2; p=0.00001) (Fig. 5).

Moreover, we found that the association between physical activity and live births rate is statistically significant (Z=7.97; p<0.00001), with a RD of 0.71 (95% CI 0.54–0.89); heterogeneity between studies was 75% (chi^2=8.22, df=2; p=0.02) (Fig. 6).

DISCUSSION

Herein our data suggested that physical activity sig-

Study or subgroup	Physical activity Events	Physical activity Total	Control Events	Control Total	Weight	Risk difference IV, Fixed, 95% CI
Maleki and Tartibian 2017	191	258	7	263	37.4%	0.71 [0.66, 0.77]
Hajizadeh Maleki and Tartibian 2017	31	188	6	202	36.1%	0.14 [0.08, 0.19]
Hajizadeh Maleki and Tartibian 2017	139	197	5	189	26.5%	0.68 [0.61, 0.75]
Total (95% CI)		643		654	100.0%	0.50 [0.46, 0.53]
Total events	361		18			

Heterogeneity: chi^2=233.09, df=2 (p<0.00001); I^2=99%
Test for overall effect: Z=27.91 (p<0.00001)

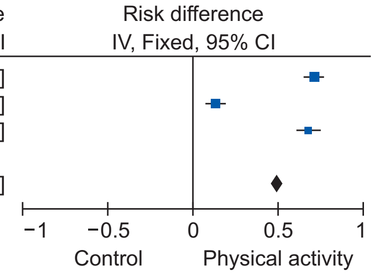

Fig. 5. Forest plot of total pregnancies and physical activity. SD: standard deviation, CI: confidence interval.

Study or subgroup	Physical activity Events	Physical activity Total	Control Events	Control Total	Weight	Risk difference IV, Fixed, 95% CI
Maleki and Tartibian 2017	180	191	3	7	22.8%	0.51 [0.15, 0.88]
Hajizadeh Maleki and Tartibian 2017	24	31	3	6	17.0%	0.27 [−0.15, 0.70]
Hajizadeh Maleki and Tartibian 2017	127	139	0	5	60.3%	0.91 [0.69, 1.14]
Total (95% CI)		361		18	100.0%	0.71 [0.54, 0.89]
Total events	331		6			

Heterogeneity: chi^2=8.22, df=2 (p=0.02); I^2=76%
Test for overall effect: Z=7.97 (p<0.00001)

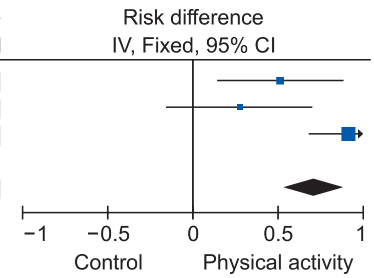

Fig. 6. Forest plot of live birth and physical activity. SD: standard deviation, CI: confidence interval.

nificantly influenced semen parameters and pregnancy outcome in infertile patients. A statistically significant relationship between physical exercise and sperm concentration (p=0.02), total sperm motility (p<0.01), total sperm count (p<0.01), normal morphology (p<0.01) has been established. Moreover, the study registered a statistically significant association within physical activity and total pregnancy rate (p<0.01) and live birth rate (p<0.01). However, no relevant connection between exercise and semen volume has been documented.

Previous studies have reported that obesity has a detrimental impact on male fertility [11,12]. In more details, Salas-Huetos et al [1] reported that overweight and obesity were linked with lower sperm quality like semen volume, sperm count and concentration, sperm vitality, total motility, and normal morphology and underweight was linked with reduced normal sperm morphology.

Augmented adiposity may negatively impact on sexual sphere through its metabolic effects and its detrimental impact on reproductive hormones [3,13]. In fact, disrupted hypothalamic-pituitary-gonadal axis negatively influences spermatogenesis process and, therefore, fertility. Overabundance of adipose tissue impacts on hormonal profile leading to altered testosterone/estrogen ratio and insulin, sex-hormone-binding globulin, leptin, inhibin B level; all these components play a pivotal role on testosterone level and consequent impaired spermatogenesis [14]. In addition, Jia et al [15] revealed the increment of apoptosis of spermatogenic cells in their "obesity group rats". Moreover, according to Garolla et al [16], dysregulated metabolic pathways may promote apoptosis among spermatogenic cells via overexpression and overactivation of pro-apoptotic factors as Bax. Furthermore, a recent study found that apoptosis of testicular spermatogenic cells is one of the major causes of male subfertility [17]. Moreover, obesity and dyslipidemia are reported to challenge sperm function through the activation of oxidative stress and proinflammatory signaling among testicular cells [18]. Based on these premises, a relation between weights loss and improvement of semen quality seems consistent.

According to these findings and due to the multiple influence of different metabolic conditions, a multidisciplinary approach seems the most appropriate to investigate the underlying connections between body weight and semen quality. Focusing on the role of exercise on sperm characteristics, a great heterogeneity of results had been registered.

Literature evidenced that recreational physical activity has a positive or neutral effect on semen quality while highly intense training may lead to worsen parameters [19]. Several studies reported that relevant modification of semen parameters may occur according to the type, duration and intensity of the training performed.

In an animal study conducted by Silva et al [20], the impact of physical exercise on testicular function and antioxidant capacity were evaluated. Testicular mitochondrial adaptation has also been investigated in animal model performing intense training. Authors demonstrated that higher level of serum testosterone in older exercised animal if compared with the sedentary ones. Moreover, they benefited from augmented mitochondrial antioxidant capacity and increased levels of antioxidant enzymes (super oxide dismutase [SOD] 1 and SOD 2) that lead to an improved capacity to recover from cellular stress.

Before concluding we would like to underline some limitation. Included studies were not homogeneous and performed physical activity was different among groups analyzed. Moreover, we did not account on other putative risk factors related to health (*i.e.* diabetes, smoking, etc.) or also genetic characters (*i.e.* related genes). Moreover, studies weight is sometimes very different in plot and these could influence final results, included studies numbers were small and had high heterogeneity in forest plot, however a leave one out meta-analysis or an individuation of potential outliers can't be performed due to the small number of studies included and for these reasons other clinical studies are necessary to confirm the findings of this meta-analysis; next step could be the investigation of the effect of physical activities on genomic in male infertility. Finally, studies did not report data on markers of oxidative stress that may justify these findings.

On the other hand, strengths of the present meta-analysis are the inclusion of randomized controlled trials and full assessment of male infertility.

CONCLUSIONS

We demonstrated that physical activity is significantly associated with amelioration of semen parameters and may be crucial in improving or even reverting male infertility. Further studies may be warranted to confirm and strengthen our findings.

Conflict of Interest

The authors have nothing to disclose.

Funding

None.

Acknowledgements

None.

Author Contribution

Conceptualization: ALG, GIR. Methodology: GIR. Validation: SC, GM, AC. Formal analysis: MF, IS, PC, AM. Investigation: ALG. Data curation: ALG. Writing - original draft preparation: ALG. Writing - review and editing: MGA. Visualization: SC. Supervision: GIR. Project administration: GIR. All authors have read and agreed to the published version of the manuscript.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.5534/wjmh.230106.

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