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The Impact of Physical Activity and Exercise on Endometriosis Related Symptoms with Particular Emphasis on Pain – Systematic Review

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Abstract:
Endometriosis is common chronic condition that can cause acute and chronic pain. It affects 5 - 10 % of women in their reproductive years. It is characterized by the presence of endometrial - like tissue outside the uterus and it is associated with pelvic pain and infertility. Diagnosis of endometriosis requires laparotomy or laparoscopy. Therefore, there is often a delay from initial symptoms to diagnosis and treatment. There is no effective treatment. Current therapeutic methods aim to reduce pain and treat infertility. It include surgery, hormonal treatments and analgesics in case of a pain. Additionally, this methods have their limitations in form of side effects and unsatisfactory therapeutic effect. [1,2] Wherefore physical activity (PA) and exercise have been suggested as alternative treatments.[3] In this study authors perform a systematic review to evaluate the effect of PA and exercise on endometriosis-related symptoms.

Keywords:
endometriosis, pelvic pain, endometriosis and physical activity, endometriosis and lifestyle

Methods:
Pubmed electronic database was searched using keywords such as: endometriosis, pelvic pain, endometriosis and physical activity, endometriosis and physical exercises, endometriosis and lifestyle. The authors performed study selection, quality assessment and data extraction. The primary product was pain intensity but other benefits were taken into final account. Four studies were selected for detailed analysis.[6,7,8,9]

Introduction:
Endometriosis is a chronic estrogen-dependent disorder characterized by the presence of ectopic endometrial implants situated outside the uterine cavity, primarily within the pelvic cavity, including the ovaries, uterosacral ligaments, peritoneum, as well as in the gastrointestinal tract and urinary bladder. These ectopic lesions trigger a chronic inflammatory cascade, often leading to fibrosis and adhesion formation. It affects approximately 5-10% of women in their reproductive years.[1] The clinical spectrum of endometriosis is highly variable, often manifesting as chronic pelvic pain syndrome. Depending on the anatomical distribution of endometriotic foci, patients may experience deep dyspareunia, dysuria, and gastrointestinal disturbances such as bloating, nausea, and dyschezia. Infertility is a frequent complication, further complicating the clinical picture. The cumulative burden of these symptoms significantly diminishes the quality of life of affected individuals. Endometriosis predominantly occurs in women of reproductive age; however, it has been documented in premenarcheal females and as recurrent disease in postmenopausal women. [1-2] Recent research indicates that physical activity and specific exercise regimens may attenuate pain and improve quality of life in individuals diagnosed with endometriosis.[10]

Pathogenesis:
The pathophysiology of endometriosis is complex and multifactorial, involving genetic predisposition, environmental influences, immune dysregulation, and aberrant hormonal signaling. Despite extensive research, the precise mechanisms underpinning the ectopic implantation and survival of endometrial tissue remain incompletely understood.[11]

Treatment:
In the absence of a definitive curative approach, the therapeutic management of endometriosis primarily aims at alleviating pain and facilitating fertility. Current treatment strategies encompass pharmacotherapy, including hormonal suppression, and surgical intervention for the excision of endometriotic lesions. [1,2] However, the efficacy of these approaches is often suboptimal and associated with significant adverse outcomes, prompting ongoing exploration of alternative therapeutic avenues. Physical activity is increasingly recognized as a beneficial adjunct in the management of chronic pain syndromes, with emerging evidence supporting its anti-inflammatory properties and potential to improve outcomes in patients with endometriosis.

Review question:
The main goal was to establish the impact of PA and exercise on endometriosis associated symptoms with particular emphasis on pain.

Quality Assessment:
Three of the four studies [6,8,9] were rated as being of poor quality. The RCT by Gonçalves et al.[7] was rated as being of moderate quality. The primary limitation of the conducted studies was the small sample sizes, and in the studies by K.F.S. Petrelluzzi et al.[9] and Eman Awad et al.[8], an additional drawback was the absence of a control group. Another significant limitation was the lack of objective pain assessment in the studies. The RCT by Gonçalves et al.[7] had significant differences between the intervention and control groups - the intervention group had significantly more years of education than the non-yoga practicing group. Furthermore, none of the studies assessed the long-term outcomes of the interventions.

Physical Activity and Exercise Programs:
In the study by Gonçalves et al.,[7] patients participated in yoga sessions for 8 weeks. In other studies, physical activity included corrective exercises, breathing exercises, proprioception and muscle relaxation training, stretching exercises, and aerobic activities such as walking. The exercise programs lasted between 8 and 12 weeks. All activities were supervised by experienced physiotherapists, and efforts were made to keep the exercise groups small to avoid poor adherence.

Pain:
In the study by Petrelluzzi et al.[9], pain intensity was quantified using a Visual Analogue Scale (VAS) before and after treatment, with each patient recording their pain intensity on a scale from 0 (no pain) to 10 (the most intense pain). No significant improvement in pain relief was found. Gonçalves et al.[7], registered a significant reduction in daily pain intensity on the VAS among women practicing yoga, while in the non-yoga group, pain levels tended to increase. Similarly, in the study by Awad E, et al.[8] , there was a statistically significant reduction in pain levels after 12 and 24 weeks of exercise compared to baseline values.

Study	Pain assessment methods
Petrelluzzi et al. [9]	Visual Analogue Scale (VAS) (0-10)
Zhao et al. [6]	Indirect assessment (via HRQoL)
Goncalves et al.[7]	Visual Analogue Scale (VAS) (0-10)
Awad et al.[8]	Present Pain Intensity Scale (0-4)
Pain Assessment Tool	

Quality of Life, Well-being, and Mental State:

In the study by Petrelluzzi et al.[9] researchers did not observe significant differences in domains such as physical role, general health, social functioning, emotional role, and mental health. However, there were significant improvements in vitality and physical functioning domains. The program effectively reduced perceived stress, as measured by the Perceived Stress Questionnaire, increased vitality, and improved physical functioning. In contrast, in Gonçalves et al. [7] study, women practicing yoga showed improved quality of life, measured by EHP-30, in the following domains: pain, control and powerlessness, emotional well-being, self-image, and social support. Zhao et al.[6] reported significant improvements in overall quality of life at the end of the study in both the intervention and control groups. The intervention group also demonstrated significant improvement in psychological symptoms, while the control group showed no statistically significant effects in reducing depression and anxiety. Additionally, the PMR (Progressive Muscle Relaxation) group showed significant improvement in all QoL (Quality of Life) domains, while the control group showed improvements in physical health areas such as general health and pain relief, as well as in two mental health domains (vitality and social functioning). This study suggests that PMR effectively alleviates anxiety, depression, and improves the quality of life in patients with endometriosis treated with GnRH agonists. The researchers specifically selected GnRH agonists due to reports that they induce anxiety and depression in patients with endometriosis. GnRH agonists can both lower mood and improve it by alleviating endometriosis symptoms. This concept is supported by the fact that the control group did not show significant improvement in anxiety and depression after GnRH agonist treatment, while there was a significant improvement in the reduction of endometriosis symptoms across all physical health domains of QoL.

Additional Outcomes:

Petrelluzzi et al.[9] found that physical therapy and psychological intervention normalize cortisol levels. In Gonçalves et al. [7], no significant changes were observed in the menstrual patterns of either the intervention or control groups.

However, in the group of women practicing yoga, there was a reduction in quality of life values in the following domains: work, relationships with their children, treatment, and sexual intercourse. In In the study of Awad et al. [8] demonstrated a significant reduction in the degree of kyphosis before the study, after 12 weeks, and after 24 weeks.

	F. S. Petrelluzzi et al. [9]	Zhao et al.[6]	Goncalves et al.[7]	Awad et al.[8]
Study Objective	The impact of physical activity on stress levels, health-related quality of life, and salivary cortisol levels.	Effects of PMR training on anxiety, depression and quality of life of endometriosis patients under gonadotrophin-releasing hormone agonist therapy	The Impact of Practicing Yoga on Quality of Life (QoL) and Pain Symptoms	The impact of exercise on pelvic pain and posture associated with endometriosis
Study Duration	10 weeks	12 weeks	8 weeks	8 weeks
Sample Size	30	100 (50 intervention vs 50 controls)	40 (28 intervention vs 12 controls)	20
Study Program	2.5-hour sessions, once a week; physical therapy, body awareness training, breathing exercises, stretching exercises	GnRH agonist therapy + PMR training based on a classic muscle relaxation program by Jacobson twice a week	Yoga program twice a week	Posture correction breathing exercises, diversion drill training, positional education stretching; exercises for lower back muscles, walking on treadmill, three times a week

Population Criteria	Women diagnosed with laparoscopy or laparotomy plus biopsy; and having chronic pelvic pain (CPP) ≥ 7 years	Women diagnosed with laparoscopy or laparotomy plus biopsy; CCP; an above-elementary school education; no surgical treatment; no GnRH treatment	Women with endometriosis and CPP, in past treated with hormonal therapy, laparoscopy, etc.; no regular exercise (> 3 times a week)	Inclusion cr: unspecified Exclusion cr: diabetes mellitus presence, gynecological hemorrhage, impaired sensation, tubo-ovarian abscess, chest diseases, scoliosis or previous trauma or fractures in the spine, pelvis, and lower limbs
Age	Average 32 ± 1.30 years	18–48 years	18–50 years	26–32 years
Control Group Treatment	No control group	One dose of depot leuprolide, 11.25 mg IM	Medical or physiotherapy session a week	No control group
Main Purpose	Pain (VAS; 0-10); Stress level (PSQ)	Anxiety, depression	Quality of Life (QoL; EHP 30)	Pain (PPIS, 0-4); posture (raster stereography system)
Side Purpose	Health-Related Quality of Life (HRQoL; SF-36); Salivary cortisol levels	Health-Related Quality of Life (HRQoL; SF-36)	Pain (VAS; 0-10), menstrual pattern	None
Data Parallel of included studies				

Discussion:

In numerous previous studies, the positive impact of physical activity on chronic conditions associated with inflammatory responses [15, 16], as well as the alleviation of pain related to such diseases [17], has been widely described. Additionally, chronic diseases, including endometriosis, are often associated with chronic mood disorders, depression, anxiety, and chronic stress, which contribute to a decline in overall quality of life. Stress has been linked to the exacerbation of autoimmune diseases and other conditions where excessive inflammation plays a significant role [18].

Studies suggest that moderate-intensity exercise may be an optimal intensity of exercise for promoting mental health by decreasing pro-inflammatory cytokines (e.g., TNF-α, IL-6, IL-1β) [19, 20]. According to numerous studies on clinical populations with chronic inflammatory diseases, regular aerobic exercise can reduce depression. [19]

In this review, the authors meticulously analyzed four studies regarding the impact of physical activity (PA) on symptoms related to endometriosis. The review included 186 women suffering from the condition. Despite the careful selection of studies, numerous confounding factors arose during the trials, making it impossible to treat PA and exercise as the sole factors influencing the symptoms of the women studied. Due to the numerous limitations of the conducted studies (which are listed in this paper), the conclusions are divergent, and it is not possible to provide a definitive answer to the posed question based on them. However, certain trends can be observed- in three out of the four analyzed studies, researchers recorded a positive impact of physical activity on pain symptoms.

On this basis, it can be inferred that physical exercise has a positive effect on the symptoms of women with endometriosis. Additionally, in three studies (references), where the impact of PA on quality of life was examined, a positive effect was observed on most of the evaluated domains. Another benefit, investigated by F.S. Petrelluzzi et al.[9] and Zhao et al. [6], is the undeniable impact on improving mental health, reducing stress levels, depression, and anxiety in patients engaging in PA.

None of the studies reported any adverse effects associated with exercise.[6,7,8,9] Additionally, it is possible that physical activity may reduce the risk of developing endometriosis. A crucial aspect to consider is the selection of physical activities that are feasible for women who often balance full-time work and childcare responsibilities. In the study by Gonçalves et al. [7], although 28 women initially enrolled in the program, only 16 completed the full 2 months of practice. Twelve women dropped out after a few sessions, citing a lack of available childcare during the sessions and the commencement of full-time employment, while one participant withdrew due to health reasons. This example highlights the importance of tailoring exercise programs to fit into participants' lifestyles.

Unfortunately, based on the presented data, it is not possible to definitively determine the actual impact of physical activity on endometriosis. The authors agree that further research is necessary, with well-designed clinical trials and stringent criteria to minimize the risk of bias.

During the preparation of this review, the authors also analyzed two highly promising ongoing studies on this topic.[5, 12] These studies are being conducted with large clinical cohorts, and we have high hopes that their outcomes will provide reliable information. An additional advantage of MDM Salinas-Asensio et al. [5] study is the evaluation of patients one year after the conclusion of the intervention, a follow-up period that, according to the researchers, has not been included in any previously published studies.

Additionally, in three of four studies (references provided) that investigated the impact of physical activity on quality of life, a positive effect was observed across most of the evaluated domains. Another benefit, examined by F.S. Petrelluzzi et al.[9] and Zhao et al.[6] was the clear improvement in mental health, stress levels, depression, and anxiety among patients engaging in physical activity. None of the studies reported any adverse effects associated with exercise. Moreover according to few other studies, it is possible that physical activity may reduce the risk of developing endometriosis.[13,14]

A crucial aspect to consider is the selection of physical activities that are feasible for women who often balance full-time work and childcare responsibilities. In the study by Gonçalves et al.[7] although 28 women initially enrolled in the program, only 16 completed the full 2 months of practice. Twelve women dropped out after a few sessions, citing a lack of available childcare during the sessions and the commencement of full-time employment, while one participant withdrew due to health reasons. This example underscores the importance of tailoring exercise programs to fit into participants' lifestyles.

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Conclusion:

Further research is needed to confirm and refine the findings. The authors of this review have high expectations for the ongoing studies mentioned[5,12]. Physicians and physiotherapists should inform women with endometriosis about the potential positive effects of physical activity on symptoms, especially since no adverse effects were found in the studies reviewed, , as well as the exact cause of this disease is still not fully understood [21], and medical treatment focuses on managing symptoms rather than reducing the number of abnormal cells. Additionally, surgery often leads to a high likelihood of the disease returning. [22]

Abbreviations:

CPP: Chronic pelvic pain

EHP-30: Endometriosis Health Profile-30 (five domains: pain, control and powerlessness, emotional well-being, social support and self-image), Scoring ranges from 0 to 100, with higher scoring representing a worse health status.

PA: Physical activity

PPSI: Present Pain Intensity Scale (0-4)

PRM: Progressive Muscle Relaxation

PSQ: Perceived Stress Questionnaire

SF-36: 36-Item Short-Form Health Survey,(following domains: physical function, role limitation caused by physical problems, body pain, general health perception, vitality-energy, social function, role limitations caused by emotional problems, and mental health

VAS: Visual analogue scale (0-10)

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