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REVIEW ARTICLES

Can physical exercise help people with irritable bowel syndrome? How substantial is the evidence?

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Abstract

Purpose: Irritable bowel syndrome is one of the most common gastrointestinal disorders worldwide that negatively affect health and quality of life and imposes high costs. Increasing attention is being paid to non-pharmacological therapies, like physical exercise, to manage and alleviate irritable bowel syndrome symptoms, but the underlying mechanism is unclear, and the evidence is inconclusive. This article aims to provide an overview analysis of the recent evidence that links physical exercise with irritable bowel symptoms.

Material and methods. For the last five years of research (2018-2023), we searched several international scientific databases, including Web of Science, Scopus, Science Direct, ADI, the Cochrane Central Register of Controlled Trials, PubMed, Medline, Clinical trials.gov, Google Scholar, and the WHO database.

Results. Generally, exercise exerts variable effects on gut physiology, integrity, and health. Much research recommended adopting regular light-to-moderate aerobic exercise and relaxation anaerobic exercise to enhance the patient's psychological well-being and alleviate global irritable bowel syndrome symptoms. These types of exercise are purported to improve bowel function, motility, tone, habits, immunity, microbial diversity, and quality of life due to a decrease in psychological stress, depression, anxiety index, irritable bowel syndrome symptom severity score, intestinal hypersensitivity, and gut permeability. In contrast, more studies reported several disruptive effects of vigorous aerobic exercise on gut integrity and physiology that can compromise irritable bowel syndrome symptoms by inducing splanchnic hypoperfusion, gastrointestinal epithelial wall damage, malabsorption, dysbiosis, and bacterial translocation, thus calling into question the positive outcomes of the exercise.

Conclusions. There is overwhelming evidence recommending regular light-to-moderate aerobic exercise and anaerobic relaxation exercises for patients with IBS. However, this evidence seems low-quality, making it challenging to confirm the actual impacts of exercise. Ethnicity, study design, type and intensity of exercise, and methodological issues are among the reasons that are put forward to account for this low-quality evidence. Thus, well-designed plausible studies, particularly randomized controlled trials and research on individualized exercise intervention settings that consider exercise frequency, intensity, time, type, volume, and progression, are highly demanded to enable drawing specific exercise recommendations for irritable bowel syndrome patients without adverse effects.

Key words: irritable bowel syndrome symptoms, exercise, physical activity, life quality, anxiety, depression

Анотація

Муса Нуман Ахмад, Обада Мансур Тнайба. Чи можуть фізичні вправи допомогти людям із синдромом подразненого кишечника? Наскільки вагомі є докази?

Мета: Синдром подразненого кишечника є одним із найпоширеніших розладів шлунково-кишкового тракту в усьому світі, що негативно впливає на здоров'я та якість життя та вимагає великих витрат. Все більше уваги приділяється немедикаментозним методам лікування, таким як фізичні вправи, для лікування та полегшення симптомів синдрому подразненого кишечника, але основний механізм неясний, а докази непереконливі. Ця стаття має на меті надати оглядовий аналіз нещодавніх доказів, які пов'язують фізичні вправи з симптомами синдрому подразненого кишечника.

Матеріал і методи. За останні п'ять років дослідження (2018-2023) ми здійснили пошук у кількох міжнародних наукових базах даних, зокрема Web of Science, Scopus, Science Direct, ADI, Кокранівський центральний реєстр контрольованих досліджень, PubMed, Medline, Clinical trials.gov, Google Scholar, і база даних ВООЗ.

Результати. Загалом фізичні вправи по-різному впливають на фізіологію кишечника, цілісність і здоров'я. Багато досліджень рекомендували регулярні легкі та помірні аеробні вправи та релаксаційні анаеробні вправи для покращення психологічного благополуччя пацієнта та полегшення глобальних симптомів синдрому подразненого кишечника. Ці види вправ мають на меті покращити функцію кишечника, моторику, тонус, звички, імунітет, мікробне різноманіття та якість життя завдяки зниженню психологічного стресу, депресії, індексу тривоги, оцінки тяжкості симптомів синдрому подразненого кишечника, гіперчутливості кишечника та проникності кишечника . Навпаки, інші дослідження повідомляли про кілька руйнівних впливів інтенсивних аеробних вправ на цілісність кишечника та фізіологію, які можуть скомпрометувати симптоми синдрому подразненого кишечника шляхом індукції внутрішньої гіпоперфузії, пошкодження епітеліальних стінок шлунково-кишкового тракту, мальабсорбції, дисбактеріозу та бактеріальної транслокації, що ставить під сумнів позитивні результати вправ при синдромі подразненого кишечника.

Висновки. Існують переконливі докази, що рекомендують регулярні аеробні вправи легкої та помірної інтенсивності та вправи на анаеробну релаксацію для пацієнтів із синдромом подразненого кишечника. Однак ці докази здаються низькоякісними, тому підтвердити фактичний вплив фізичних вправ складно. Етнічна приналежність, дизайн дослідження, тип та інтенсивність фізичних вправ, а також методологічні проблеми є одними з причин, які висуваються для пояснення цих низькоякісних доказів. Таким чином, добре сплановані правдоподібні дослідження, зокрема рандомізовані контрольовані дослідження та дослідження індивідуальних налаштувань втручання, які враховують частоту, інтенсивність, час, тип, об'єм і прогресування вправ, дуже потрібні для того, щоб скласти конкретні рекомендації щодо вправ для пацієнтів із синдромом подразненого кишечника без побічних ефектів.

Ключові слова: симптоми синдрому подразненого кишечника, вправи, фізична активність, якість життя, тривога, депресія

Аннотация

Муса Нуман Ахмад, Обада Мансур Тнаибат. Могут ли физические упражнения помочь людям с синдромом раздраженного кишечника? Насколько существенны доказательства?

Цель: Синдром раздраженного кишечника является одним из наиболее распространенных во всем мире желудочно-кишечных заболеваний, негативно влияющих на здоровье и качество жизни и требующих больших затрат. Все больше внимания уделяется нефармакологическим методам лечения, таким как физические упражнения, для лечения и облегчения симптомов синдрома раздраженного кишечника, но основной механизм неясен, а доказательства неубедительны. Эта статья призвана предоставить обзорный анализ последних данных, которые связывают физические упражнения с симптомами синдрома раздраженного кишечника.

Материал и методы. За последние пять лет исследований (2018-2023 гг.) мы провели поиск в нескольких международных научных базах данных, включая Web of Science, Scopus, Science Direct, ADI, Кокрановский центральный регистр контролируемых исследований, PubMed, Medline, Clinical Trials.gov, Google. Ученый и база данных ВОЗ.

Результаты. Как правило, физические упражнения оказывают различное влияние на физиологию, целостность и здоровье кишечника. Многие исследования рекомендовали регулярные легкие и умеренные аэробные упражнения и расслабляющие анаэробные упражнения для улучшения психологического благополучия пациента и облегчения общих симптомов синдрома раздраженного кишечника. Предполагается, что эти виды упражнений улучшают функцию кишечника, моторику, тонус, привычки, иммунитет, микробное разнообразие и качество жизни за счет снижения психологического стресса, депрессии, индекса тревоги, оценки тяжести симптомов синдрома раздраженного кишечника, гиперчувствительности кишечника и проницаемости кишечника.

Выводы. Имеются убедительные данные, рекомендующие регулярные легкие и умеренные аэробные упражнения и анаэробные релаксационные упражнения для пациентов с синдромом раздраженного кишечника. Однако эти доказательства кажутся некачественными, что затрудняет подтверждение фактического воздействия упражнений. Этническая принадлежность, дизайн исследования, тип и интенсивность упражнений, а также методологические проблемы являются одними из причин, которые выдвигаются для объяснения этих доказательств низкого качества. Таким образом, хорошо спланированные правдоподобные исследования, особенно рандомизированные контролируемые испытания и исследования индивидуальных параметров вмешательства с упражнениями, которые учитывают частоту, интенсивность, время, тип, объем и прогрессирование упражнений, крайне необходимы для разработки конкретных рекомендаций по упражнениям для пациентов с синдром раздраженного кишечника без побочных эффектов.

Ключевые слова: симптомы синдрома раздраженного кишечника, физические нагрузки, физическая активность, качество жизни, тревожность, депрессия

Abbreviations

BAQ: Body awareness questionnaire responsiveness	GI: Gastrointestinal
BDNF: Brain-derived neurotrophic factor	GSRS: Gastrointestinal symptom rating scale
BGA: Brain–gut axis	IL: Interleukins
BRS: Baroreceptor sensitivity	IL-1β: Interleukin-1β
BRS2: Perceived mind-body connection	LPS: Lipopolysaccharides
CLDN: Claudin	LFMD: Low-Fodmap diet
CV: Cardiovascular	METs: Metabolic equivalent units
FITT-VP: Frequency, intensity, time, type, volume, & progression	NK: Natural killer
HADS: Hospital anxiety and depression scale	NPY: Neuropeptide Y
5-HT: 5-hydroxytryptamine	RCT: Randomized controlled trial
HPA: Hypothalamic–pituitary–adrenal axis	ROS: Reactive oxygen species
IBS: Irritable bowel syndrome	SCFA: Short chain fatty acids
IBS-C: IBS with constipation	SIgA: Secretary immunoglobulin A
IBS-D: IBS with diarrhoea	TLR: Toll-like receptors
IBS-SSS: Irritable bowel syndrome- symptom severity score	TNF-α: Tumor necrosis factor-α
IBS-QoL: Irritable bowel syndrome- quality of life	ZO-1: Zonula occludens-1

Introduction

Irritable bowel syndrome (IBS) is one of the most common disorders of gut-brain interactions [1, 2]. It is heterogeneous, with poorly understood pathophysiology and no specific laboratory examinations [1, 3]. It is well-acknowledged that genetics and lifestyle factors, such as nutrition, physical activity, psychological comorbidity, sleeping hours, gut dysfunction, the gut-brain axis, microbiome, and visceral hypersensitivity, are associated with IBS etiology [3, 4]. The IBS is a serious health problem widespread among various groups of the global communities [5], with diverse ranges [5-7] and being more common in females than in males [3, 7]. The underlying mechanism for this gender difference is largely unknown. The IBS prevalence varies between nations because of ethnicity or heterogenicity in diagnostic methods [5, 7]. Worldwide, the estimated prevalence of IBS is 21% [8], and its pooled value is 9.2% according to Rome III and 3.8% according to the Rome IV criteria [7].

Although IBS is not a life-threatening syndrome, people with IBS have a reduced quality of life (QoL) [9, 10]. The IBS is also closely linked to several psychological comorbidities, such as anxiety and depression, which are the most prominent causes of global disability [11]. In essence, the disorder presents a variety of irritating symptoms, particularly abdominal pain, bloating, constipation, or diarrhea which interfere with patients' lifestyles and result in higher absenteeism and costs, poor productivity, and reduced educational, social, and occupational achievements [5-12]. Patients with IBS utilize more healthcare resources and services than healthy people [11]. About 11% of American adults have IBS [13, 14], and its direct and indirect annual cost exceeds US$21 billion [15].

The management of IBS in modern conventional medicine is based on medical and pharmacological interventions and lifestyle modifications, particularly physical exercise and dietary measures [7, 8]. Unfortunately, the IBS treatment shows a limited effect as the cause of the syndrome is not fully known [3-5]. To date, IBS remains a clinical challenge, with an increase in many patients [3]. Current IBS therapies result in several side effects, such as gastrointestinal (GI) problems, and produce serious complications related to poor health and QoL [7]. Thus, due to their low cost, minimal side effects, and therapeutic value, physical exercise has currently gained much interest and popularity [16-18].

There is plenty of evidence to suggest that physical exercise plays a vital role in reducing many types of stress and maintaining good physical and mental health [19-21]. Physical exercise has also been associated with a marked reduction in the risk for many chronic diseases and related mortality

and morbidity [22, 23].This benefit can be obtained from even a slight increase in physical activity [22]. Although the notion that physical exercise provides many benefits for people with IBS has been proposed, the evidence is not yet consistent. Physical activity can alleviate several symptoms by decreasing GI transit time and bloating and flourishing gut microbiota that may be positively mediated via the brain-gut axis (BGA) [1, 3, 4, 6]. However, several studies, with considerable controversy are available. Physical exercise improved some IBS symptoms in some people and did not influence other symptoms or individuals [1, 3, 8, 17, 18, 24-29]. The evidence that links the physical exercise type, intensity, pattern, and dose to IBS symptoms is relatively limited and inconsistent [1, 3].

Purpose: to provide an overview analysis of the recent evidence for the link between physical exercise and Rome IV IBS symptom-based criteria, highlighting the substantiality of this evidence.

Material and methods

An up-to-date literature search was conducted to review the evidence that links physical exercise and IBS symptom-based Rome criteria. The search process was limited to the most recent English publications, focusing on those covering the last five years (2018-2023). Relevant articles were principally identified through an online search of the Web of Science, Scopus, Science Direct, ADI, the Cochrane Central Register of Controlled Trials, PubMed, Medline, Clinical trials.gov, Google Scholar, and the WHO database. The search was performed using the following keywords or combinations: Physical exercise or activity or sport, IBS symptom-based criteria, and IBS. Included articles were mainly original experimental, clinical, intervention, randomized controlled trials (RCT), and cross-sectional research. Lead review articles were also used. For search accuracy, reference lists of works were checked for additional publications from the major databases.

Results

Symptoms of irritable bowel syndrome

The IBS diagnosis is challenging, and its symptoms change over time and overlap with other disorders [2, 30]. No specific laboratory or imaging tests for IBS diagnosis are known, rather diagnosis is based on symptoms, along with certain worrisome features exclusion [30, 31]. Nevertheless, the current IBS diagnosis is based on the well-defined version of Rome IV criteria that is timely updated with a better understanding of the condition to be a multicultural-oriented clinical application (3-6, 30-32). These evidence-based criteria have gained worldwide acceptance as a reference for IBS symptom-based diagnosis for clinical and research purposes [33].

The IBS symptoms can be relatively mild or severe and can influence all quality aspects of the patient's life [4, 34]. The syndrome is often characterized by recurrent abdominal pain or discomfort with changes in bowel habits without noticeable organic pathology or biomarkers [1-6]. It is categorized into four specific subtypes based on prevailing bowel habits: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), IBS with mixed bowel habits (IBS-M), or IBS-unsub typed (IBS-U) [33, 35]. Table 1 presents a summary of the IBS symptoms and subtypes according to Rome IV criteria.

Table 1

Irritable bowel syndrome diagnosis and subtypes in Rome IV diagnostic criteria.

IBS-subtypes in Rome IV criteria*	
IBS-subtype	Description
IBS-C (IBS with predominant constipation)	>25% of bowel movements with Bristol stool form types 1–2 and <25% of bowel movements with Bristol stool form types 6–7
IBS-D (IBS with predominant diarrhoea)	>25% of bowel movements with Bristol stool form types 6–7 and <25% of bowel movements with Bristol stool form types 1–2
IBS-M (IBS with mixed bowel habits)	>25% of bowel movements with Bristol stool form types 1–2 and >25% of bowel movements with Bristol stool form types 6–7

IBS-U (IBS-unclassified)	Patients who meet criteria for IBS, but do not fall into one of the other three subgroups according to Bristol stool form type
IBS Symptoms as diagnosed by Rome IV criteria	
Recurrent abdominal pain, on average, at least one day/week in the last three months, associated with two or more of the following criteria: • Related to defecation. • Associated with a change in frequency of stool. • Associated with a change in the appearance of stool. Criteria fulfilled for the last three months with symptom onset at least six months before diagnosis.	

*Classification based on only days with symptomatic bowel movement [32, 34]. IBS: Irritable bowel syndrome.

General classes of physical exercise

Physical exercise is classified according to the type and intensity into dynamic and static, and based on muscle metabolism, into aerobic and anaerobic [36, 37]. Most static exercises, such as muscle building, weightlifting, Tai Chi, and Yoga and Benson relaxation, are performed anaerobically, while dynamic exercises lasting for more than several minutes require increased heart and breathing rates to maintain exercise sessions, and could be low-to-moderate, such as walking, jogging, and cycling, and vigorous exercise, like football, treadmill running and swimming [37-39].

Furthermore, metabolic equivalent units (METs) are often used to classify aerobic physical exercise as light-to-mild, moderate, or vigorous, where METs refer to the amount of oxygen consumed during exercise compared to the rest status, and 1 MET typically equals 3.5 ml O_2/kg body weight/minute [36]. Accordingly, the low-to-mild, moderate, and vigorous exercises equal (1.6-2.9 METs), (3-6 METs), and (> 6 METs), respectively [38].

Psychological interactions between exercise and irritable bowel syndrome

Anxiety and depression are among the most prevalent psychological disorders, and they are also one of the leading causes of disability worldwide [11]. Much research has investigated the relationship between IBS, anxiety, and depression. Patients with IBS are three times more likely to experience anxiety or depression than normal individuals [40], with a higher prevalence of these conditions in patients with IBS- constipation than the other IBS subtypes [17, 18]. Besides, anxiety or depression can aggravate IBS GI and extra-GI symptoms by modulating visceral sensation and gut microenvironment and impacting the microbiome-gut-brain axis, ultimately reducing the QoL [40-42]. These findings posit the prime role of IBS psychological therapies, such as mindfulness behavioral therapy, hypnotherapy, multicomponent psychotherapy, relaxation therapy, and psychodynamic therapy [43-45].

Recently dysregulation of the BGA was suggested as a cause for IBS symptoms and visceral hypersensitivity and may associate with psychiatric comorbidities such as anxiety and depression. The BGA represents the bidirectional interaction of physical, psychological, and hormonal signaling between the central nervous system and the peripheral functions of the GI tract [44, 45]. Patients with IBS often exhibit high rates of psychiatric comorbidities, such as anxiety and depression, that can be effectively treated by exercise [43-45]. Aerobic and mind-body physical activities such as Yoga and Tai chi can regulate physical, physiological, and psychological states and improve emotional and GI symptoms, especially in IBS patients [16, 46, 47].

Do physical exercises impact irritable bowel syndrome, and how?

Generally, regular aerobic exercise with moderate intensity and an appropriate duration is considered beneficial for the body, mind regulation, and health, which can lessen many somatic symptoms and alleviate the stress and pain associated with various diseases, such as IBS [48]. However, the mechanism of the effect of exercise on IBS symptoms is not fully understood [8, 24]. Lacking exercise could compromise symptoms and reduce the QoL in IBS patients [12]. Physically inactive persons are 3.5 times more likely to suffer from IBS symptoms compared to physically active persons [49]. Increasing physical activity is viewed as one of the initial management strategies for preventing chronic morbidities, enhancing GI and psychological health, and improving overall IBS symptoms, including GI and extra-GI symptoms, such as fatigue, depression, anxiety, and stress [16-18,25,47], especially in IBS-C patients [17, 18, 42, 50]. Even though physical activity positively affects physiological, physical, and psychological factors in IBS patients, the exact mechanisms until now are not well understood, and the evidence is still insufficient and inconclusive [12-

20, 26, 42]. Figure 1 shows the proposed impacts of low-to-moderate versus vigorous physical activity on the IBS, with their possible mechanisms.

The effect of physical activity on IBS might be due to modulating the BGA, and hepatobiliary-gut axis, increasing abdominal gas clearance, bowel transit [26-28], and increased gut microbial diversity [3]. For instance, Yoga relaxation is reported to improve headaches, anxiety, depression, and chronic fatigue and relieve many symptoms of IBS by enhancing bowel energy circulation [51, 52] and correcting stress-induced underactive parasympathetic nervous system [53]. In several studies, unfortunately, many IBS patients are considered less motivated to increase their physical activity, and thus changing their attitude to adopt long-term physical activity is crucially recommended [3, 28].

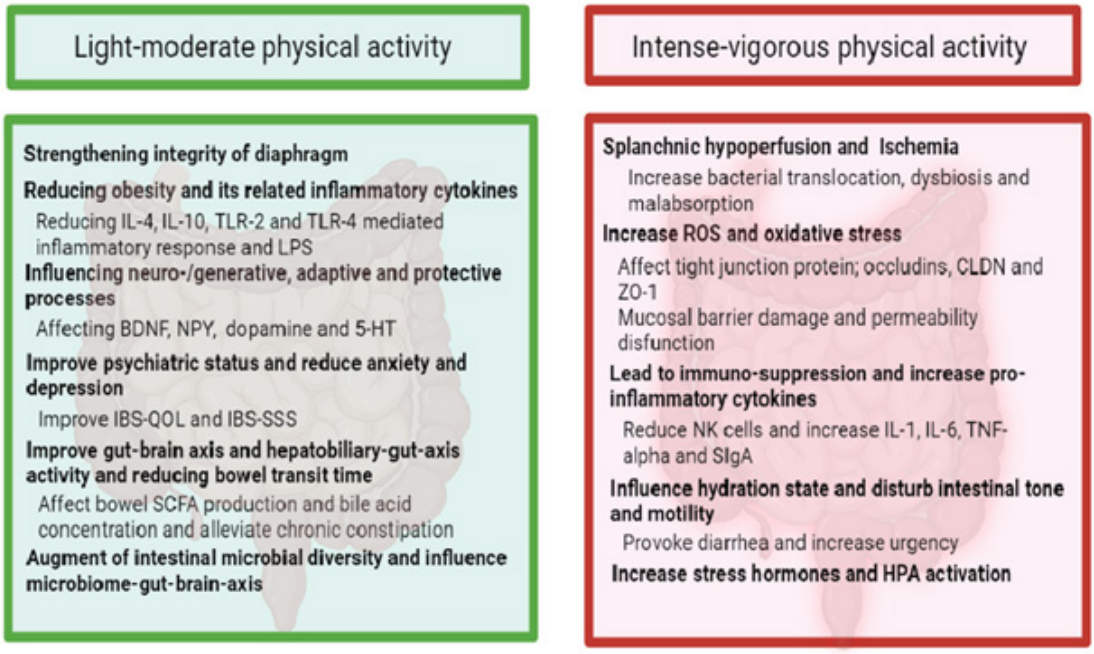

Fig. 1. Proposed impacts and mechanisms of low-to-moderate versus vigorous exercise in irritable bowel syndrome:

Abbreviations. BDNF: Brain-derived neurotrophic factor; CLDN: Claudin; HPA: Hypothalamic-pituitary-adrenal; 5-HT; 5-hydroxy-tryptamine (Serotonin); IL: Interleukins; IBS: Irritable bowel syndrome; LPS: Lipopolysaccharides; NK: Natural killer; NPY: Neuropeptide Y; QoL: Quality of life; ROS: Reactive oxygen species; SIgA: Secretary immunoglobulin; SCFA: Short chain fatty acids; SSS: Symptom severity score; TLR: Toll-like receptors; TNF: Tumor necrosis factor; ZO-1: Zonula occludens-1

Light-moderate exercise can improve IBS QoL, immune function, and GI symptoms by affecting hypothalamic–pituitary–adrenal axis response, modulating gut motility, and microbiota, and reducing systematic inflammation [3, 54]. Physical exercise can enhance the function of the serotonergic system by increasing serotonin synthesis and activity of the central nervous system, which may reduce anxiety and depression and improve IBS QoL [29, 52]. Physical exercise can also protect gut integrity by increasing mucus secretion and preventing pathogens' adhesion to the intestinal epithelium [54-56]. In contrast to vigorous exercise, light-moderate exercise can increase the secretion of secretory immune globulin A, which plays a significant role in boosting the immune system and providing protection against different pathogens [57, 58]. Increasing physical activity is also associated with enhanced intestinal immune function due to increased microbial diversity resulting in increased short chain fatty acids (SCFA), which can modulate energy balance, increase nutrient availability, and promote intestinal barrier maintenance and homeostasis [12, 38, 59, 60].

On the other hand, vigorous exercise can induce oxidative stress and increase reactive oxygen species (ROS) production, which results in dysbiosis, pro-inflammatory response, intestinal mucosal barrier damage, and permeability dysfunction [61]. Unfortunately, dysbiosis negatively affects mucin

production and intestinal peristalsis and influences depression by affecting hypothalamic–pituitary–adrenal axis and modulating neurotransmitters synthesis such as brain-derived neurotrophic factor (BDNF) and serotonin [62, 63]. The BDNF can play a role in neuroprotection, neuroplasticity, and neuronal activity [64]. Additionally, oxidative stress is associated with decreasing intestinal tight junction proteins such as Claudin (CLDN) and Zonula occludens (ZO-1), inducing lipopolysaccharides (LPS) translocation and increasing cytokines production, mainly tumor necrosis factors-α (TNF-α), TNF-β, and interleukin-6 (IL-6) in IBS patients [65]. Moreover, increasing stress hormones such as corticosteroids and catecholamines induced by exercise can negatively affect gut motility, microbiota, and SCF production and reduce GI transport activity [66]. Thus, decreasing SCF can result in dysregulation of visceral sensation and associate with constipation and IBS symptoms [67].

Although physical activity can exhibit an advantageous effect on various GI symptoms, such influence depends mainly upon the exercise mode, duration, and intensity [68]. For example, prolonged repetitive physical activity such as running can impair BGA signaling and sensitization, intestinal barrier integrity, GI motility, esophageal sphincter tone and ultimately induce GI dysfunction and severe symptoms [69, 70] such as nausea, diarrhea, and GI bleeding [68]. Nevertheless, this evidence seems low-quality to make specific recommendations to use physical activity as therapy for patients with IBS as it is based on the heterogeneity of study designs, interventions, and outcome measures [56].

The associations between physical exercises and IBS symptoms with their proposed mechanisms are presented in table 2. Several studies evaluated the effect of Yoga, Tai chi, and the Benson relaxation technique on IBS-related variables [53, 71, 72]. In the study by Schumann *et al.*, 2018 [53], Yoga and low-Fodmap diet (LFMD) interventions that lasted for 12-24 weeks resulted in significant improvement in the IBS- severity symptoms scores (IBS-SSS), while only Yoga induced marked clinical progress in the body awareness questionnaire (BAQ) responsiveness, perceived mind-body connection, psychological levels of anxiety in hospital anxiety and depression scale (HADS), psycho-neuro-immune axis markers, and psycho-social relationship domains compared to baseline results. However, three depressive incidences in the LFMD group were noticed [53]. Staller *et al*., 2022 [71] showed that Tai Chi relaxation for seven weeks had a notable improvement in the IBS-SSS and IBS-QoL scores compared to values before the treatment in IBS-constipation (IBS-C) patients. The same technique reduced the abdominal discomfort measured by the visual analog scale, improved satiety, constipation, and bloating measured by the GI symptom rating scale (GSRS), and diminished GI fears, food fears, and social impairment in IBS patients [53]. Ebrahimloee *et al.*, 2022 [72] found that the IBS-SSS and IBS-QoL scores were improved after three weeks of the Benson relaxation technique for 20min/twice/day compared to the control group, who only received the typical medical therapy without adverse effects.

Many studies also demonstrated the effects of several types of physical activities like walking, running, jogging, and Yoga on outcomes such as SRS, IBS-SSS, IBS-QoL, and vital markers including cardiovascular (CV) activity, baroreceptor sensitivity (BRS), antioxidants status, and pro-inflammatory cytokines [73-77]. Eid *et al*., 2020 [73] and Fani *et al*., 2019 [74] in RCT, found that the IBS-SSS and IBS-QoL were significantly lower in the physical activity groups than in the control groups (either with routine medical care or usual day activity) without any adverse effects. Davydov *et al*., 2019 [75] studied the impacts of 16 sessions of walking (60 min/twice /week) as a moderate non-aerobic exercise versus Yoga (60 min/ twice/week). They found that the IBS patient's pretreatment BRS and CV activity markers were differentially related to clinical outcomes for the treatment groups [75].

In contrast to walking, Yoga diminished parasympathetic tone by decreasing BRS linked with increased heart rate [75]. The Yoga group with a low BRS had a marked reduction in pain severity, but in the walking group, this reduction was seen in individuals with a higher resting BRS [75]. Davydov *et al*., 2019 [75] recommended individualized exercise intervention programs for patients with IBS based on a personal pre-treatment assessment. In a one-week cohort study, Hamaguchi *et al*., 2020 [76] reported significant improvements in GSRS in IBS patients with increasing locomotor activity measured by pedometer counts without adverse effects. They also noted that a 50% reduction in the IBS-SSS was observed with increasing the daily step count from 9500-to-4000 steps [72]. Maleki *et al*. 2018 [77] investigated the effect of 24 weeks of low-moderate intensity exercise on sedentary IBS patients. This exercise included walking or jogging (25-30 minutes/day, 3–4 days/week) for 12 weeks, followed by a treadmill (40–45 minutes/day, 4–6 days/week) for

12 weeks [77]. Results were significant improvement in IBS symptoms, reduction in pro-inflammatory cytokines such as interleukins (IL-1β, IL-6, IL-8, IL-10), and TNF-α and enhancement of indicators of antioxidant status, including superoxide dismutase, catalase, and glutathione peroxidase compared to the non-exercise group [77].

Furthermore, Sadeghian *et al.,* 2018 [78] noted a significant positive association between the sedentary physical activity of participants measured by using the general practice physical activity questionnaire and the prevalence of IBS among normal-weight individuals (Table 2). Another cross-sectional study by Sajitha and Kumari, 2021 [79] found that an increase in physical activity based on the international physical activity questionnaire significantly regularizes bowel habits and reduces constipation compared to a sedentary lifestyle. In retrospective qualitative studies by Groenendijk *et al*., 2022 [42] and Johannensson *et al*., 2018 and 2019 [80, 81], IBS female patients reported varied symptoms with physical activities where some patients noted both negative and positive attitudes to the IBS-QoL, GI, extra-GI and psychological symptoms. Moreover, Gaskell *et al*., 2023 [82] examined the impact of exercise duration (for 1, 2, and 3 hours) in endurance runners on IBS symptoms; and found that the incidence of GI symptoms and discomfort was significantly higher in the 2-hour and 3-hour duration groups compared to 1-hour groups. IBS athletes experienced more frequent symptoms during exercise and at rest; about 60% of endurance athletes experienced at least one of the GI symptoms, such as abdominal cramps, pain, bloating, the urge to defecate, and diarrhea during or after the training and competition [83].

Table 2

The association between physical exercise and irritable bowel syndrome symptoms.

Reference (Country)	Study design	Sample size	Exercise type	Main findings (Side effects)
{82} Gaskell et al., 2023 (Australia)	Prospective cohort study	16 endurance runners	Endurance running * 1, 2, and 3 hours	The incidence of bowel discomfort and GIS was lower after 1 hour of the exercise. (Severity of bowel discomfort and total GIS increased during all trials)
[42] Groenendijk et al., 2022 (Netherlands)	Retrospective qualitative study	11 IBS women, 20-54 years	Sedentary-to-elite athlete physical activity	Experiences of negative and positive symptoms were reported. (Some patients reported GIS, especially with intense exercise)
[72] Ebrahimloee et al., 2022 (Iran)	Randomized control trial	60 IBS children, 10-15 years	20 minutes*3/ day * 3 weeks- Benson relaxation	Significant improvements in IBS-SSS and IBS-QoL were reported. (Not reported)
[71] Staller et al., 2022 (USA)	Prospective cohort study	27 patients with IBS-C, constipation	8 sessions of Tai Chi weekly * 7 weeks	Significant improvements in IBS-SSS and IBS-QoL with notable improvements in IBS symptom scoring measures were reported. (1 participant had mild exacerbation of sciatica)
[79] Sajitha and Kumari, 2021 (India)	Cross sectional study	591 medical students, 17-25 years	Sedentary-to-moderate lifestyle	Moderate physical activity did regularize bowel habits and reduce constipation. (Not reported)
[73] Eid et al., 2020 (Egypt)	Randomized control trial	30 postchole-cystectomy patients, 25-40 years	Treadmill 3 times/ week * 4 weeks	Significant difference in IBS-SSS and IBS-QoL (Not reported)
[76] Hamaguchi et al., 2020 (Japan)	Cohort study	101 (78 female students), >20 years	Daily physical activity * 1 week (pedometer)	Significantly correlated with improving severity of gastrointestinal symptoms rating scale. (Not reported)

[75] Davydov et al., 2019 (USA)	Randomized pilot study	27 IBS patients, 18-65 years	16 sessions: 2*60 minute/week-walking vs. Yoga	Significant decrease in pain severity, somatic symptoms and cardiovascular activity markers. (IBS symptoms were reported according to patients with baroreceptor-sensitivity)
[74] Fani et al., 2019 (Iran)	Randomized control trial	20 IBS female patients, 29-33 years	30 minutes*2/ week*6 weeks-treadmill vs. control	Significant improvements in IBS-SSS and IBS-QoL (Not reported)
[80,81] Johannensson et al., 2018 & 2019 (Sweden)	Retrospective qualitative study	15 (10 female) IBS patients), 30-48 years	Patients self-reported daily physical activity	Physical activity had positive and negative effects on QoL, gut, extra-gut, and psychological symptoms. (Some patients reported bowel symptoms)
[77] Maleki et al. 2018 (Iran)	Randomized control trial	60 IBS participants, 34 years mean age	Waking/jogging + treadmill * 12 weeks each vs. control	Significantly enhanced antioxidants status and decreased pro-inflammatory cytokines and improved IBS-SSS. (Not reported)
[78] Sadeghian *et al.,* 2018 (Iran)	Cross-sectional	4763 participants (21.5% IBS), 36.5 years mean age	Physically active vs. inactive	Significant correlations between physical inactivity and IBS. (Not reported)
[53] Schumann et al., 2018 (Germany)	Randomized control trial	59 IBS patients, 18-75 years	Yoga (2 times/ week) vs. LFMD *12 weeks	Significantly improved IBS-SSS, BAQ, BRS2 and psychological levels of anxiety in HADS. (3 depressive episodes in the LFMD group)

Abbreviations. IBS: Irritable bowel syndrome; BAQ: Body awareness questionnaire responsiveness; BRS2: Perceived mind-body connection; BRS: Baroreceptor-sensitivity; GIS: Gastrointestinal symptoms; HADS: Hospital anxiety and depression scale; IBS-SSS: Irritable bowel syndrome severity scoring system; QoL: Quality of life; LFMD: Low-Fodmap diet.

Discussion

In contrast to walking, Yoga diminished parasympathetic tone by decreasing BRS linked with increased heart rate [75]. The Yoga group with a low BRS had a marked reduction in pain severity, but in the walking group, this reduction was seen in individuals with a higher resting BRS [75]. Davydov *et al*., 2019 [75] recommended individualized exercise intervention programs for patients with IBS based on a personal pre-treatment assessment. In a one-week cohort study, Hamaguchi *et al*., 2020 [76] reported significant improvements in GSRS in IBS patients with increasing locomotor activity measured by pedometer counts without adverse effects. They also noted that a 50% reduction in the IBS-SSS was observed with increasing the daily step count from 9500-to-4000 steps [72]. Maleki *et al*. 2018 [77] investigated the effect of 24 weeks of low-moderate intensity exercise on sedentary IBS patients. This exercise included walking or jogging (25-30 minutes/ day, 3–4 days/week) for 12 weeks, followed by a treadmill (40–45 minutes/day, 4–6 days/week) for 12 weeks [77]. Results were significant improvement in IBS symptoms, reduction in pro-inflammatory cytokines such as interleukins (IL-1β, IL-6, IL-8, IL-10), and TNF-α and enhancement of indicators of antioxidant status, including superoxide dismutase, catalase, and glutathione peroxidase compared to the non-exercise group [77].

Furthermore, Sadeghian *et al.,* 2018 [78] noted a significant positive association between the sedentary physical activity of participants measured by using the general practice physical activity questionnaire and the prevalence of IBS among normal-weight individuals (Table 2). Another cross-sectional study by Sajitha and Kumari, 2021 [79] found that an increase in physical activity based on the international physical activity questionnaire significantly regularizes bowel habits and reduces constipation compared to a sedentary lifestyle. In retrospective qualitative studies by Groenendijk *et al*., 2022 [42] and Johannensson *et al*., 2018 and 2019 [80, 81], IBS female patients reported varied symptoms with physical activities where some patients noted both negative and positive attitudes to the IBS-QoL, GI, extra-GI and psychological symptoms. Moreover, Gaskell *et al*., 2023 [82] examined the impact of exercise duration (for 1, 2, and 3 hours) in endurance runners on IBS symptoms;

and found that the incidence of GI symptoms and discomfort was significantly higher in the 2-hour and 3-hour duration groups compared to 1-hour groups. IBS athletes experienced more frequent symptoms during exercise and at rest; about 60% of endurance athletes experienced at least one of the GI symptoms, such as abdominal cramps, pain, bloating, the urge to defecate, and diarrhea during or after the training and competition [83].

How substantial is the evidence linking exercise and irritable bowel syndrome?

Individuals with IBS have different characteristics regarding IBS subtype, symptom severity, physical fitness, psychological status, and preferences for the physical exercise type [70-80]. The effect of physical activity on GI symptoms varies and depends mainly on the exercise attributes, namely frequency, intensity, type, duration, volume, and progression [68]. Despite the controversy mentioned earlier and the low-quality evidence that relates exercise to IBS, there are overwhelming recommendations for regular light-to-moderate aerobic exercise and anaerobic relaxation exercises for patients with IBS. Table 3 summarizes the evidence linking irritable bowel syndrome symptoms and related conditions with the type of physical exercise. Generally, anaerobic strength exercise has higher adverse effects than aerobic endurance exercise [37, 39]. Vigorous exercise, such as competitive running, can impair brain-gut axis signaling, trigger splanchnic ischemia and blood hypoperfusion where blood is moved forward the working muscles, exacerbating nutrient absorption, increasing intestinal permeability and motility dysfunction, and aggravating the severity of IBS GI and extra-GI symptoms [68-70, 82-86].

Table 3

Summary of the evidence linking irritable bowel syndrome symptoms and related conditions with the type of physical exercise.

IBS symptoms and related conditions	Aerobic exercise		Anaerobic exercise
	Light-to-moderate	Vigorous	
Abdominal pain	***+ve [8,50,74,79] *-ve [78,81]	*-ve-to-***-ve [49, 55, 82, 84]	***+ve [16]
Bloating	***+ve [3]	*-ve-to-***-ve [49, 84]	***+ve [16]
Constipation	***+ve [8,50,74,79]	*-ve [49, 84]	***+ve [8, 50]
Fatigue	***+ve [42,74]	*-ve [87, 88]	***+ve [51, 52]
Anxiety	***+ve [8,74] *-ve [81]	*-ve [87, 88]	***+ve [2, 31, 33]
Depression	***+ve [8, 74, 78]	Not reported	*+ve-to-***+ve [8, 52, 87]
IBS-symptom severity score	***+ve [3, 8, 42, 73-77]	*-ve-to-***-ve [49, 84]	***+ve [8, 28, 42, 51-53, 72]
IBS-quality of life	*+ve-to-***+ve [8, 73, 74, 78]	Not reported	***+ve [8, 51, 52, 72]

Denotations: *+ve-to-***+ve: Mild-to-strong positive or favorable effects; *-ve-to-***-ve: Mild-to-strong negative or adverse effects; IBS: Irritable bowel syndrome.

Running works against the organized structure of the intestinal tract inside the abdominal cavity by gravity force which may lead to diaphragm spasm, dysbiosis, an increase of serotonin production, affects pain sensitization of afferent nerves, and induce IBS symptoms [85, 89]. Many IBS patients avoid running due to the belief that the abdominal bouncing up and down during running may be responsible for inducing abdominal complaints and delaying defecation onset. Abdominal mechanical bouncing can increase intra-abdominal pressure and organ movement and interfere with prostaglandin release, which affects intestinal motility and causes exercise-induced abdominal complaints such as runner's diarrhea [42].

Increasing intensity and exercise duration associated with lowering gastric emptying and increasing levels of plasma intestinal-fatty acid binding protein and luminal tight junction proteins such as ZO-1 and eventually results in structural epithelial damage, tight-junction disruption, and disturbance production of secretory immunoglobulin A (SIgA), mucins and antimicrobial molecules [90-94]. In a study by Ruiz-Iglesias *et al*., 2022 [92] intensive training program in Wistar rats decreased the salivary IgA concentration, impaired the CLDN and ZO-1 gene expression, and altered the mesenteric lymphocyte composition. Increasing exercise intensity is associated with the activation of the sympathetic nervous system, releasing of stress hormones, decreasing of natural killer (NK) cells, and stimulation of pro-inflammatory modulators such as TNF-α, IL-1, IL-6, Interleukin-1 receptor antagonist, LPS translocation, and Toll-like receptors (TLR)-mediated recognition of gut commensal bacteria, which alters gut motility and leads to immunosuppression, localized and systemic inflammation [84, 89, 94]. Furthermore, vigorous repetitive exercise causes cellular damage, may compromise the mesenteric redox environment by weakening the activity of antioxidant enzymes and produces oxidation markers ROS, and leads to unfavorable intracellular biochemical changes [90, 95], such as macromolecules peroxidation and ZO-1 phosphorylation [90].

The FITT-VP principle and irritable bowel syndrome

Exercise can improve brain health by regulating neurogenesis and neuroplasticity by affecting BDNF and serotonin production, reducing inflammatory markers, and improving BGA signaling [28, 38, 96]. During moderate aerobic exercise, brain functions are modulated, and areas such as the frontal lobe and the parietal cortex are activated, which, in turn, results in escaping excessive nervous activity, regulating brain balance, and thus effectively relieving the pain [16, 47, 51-53]. On the other hand, vigorous-to-strenuous exercise in athletes, especially those who go into competitive sports, might be associated with increasing neurophysiological stress and different risks [97, 98]. Thus, the FITT-VP principle is recommended for prescribing exercise to attain maximum health benefits and physical fitness [97, 98]. This principle (FITT-VP) denotes the exercise frequency (how often is an exercise done each week), intensity (how hard is the exercise), time (how long is the exercise duration), type (what is a mode of exercise), volume (what is the total amount of exercise), and progression (how is the program advanced) [97, 98].

The proposed association between physical activity and GI and extra-GI symptoms in IBS individuals is shown in Figure 2. Any IBS patient has a definite ability to exercise depending on health status and physical fitness. The IBS subtype and the ability to perform the selected exercise in line with the FITT-VP principle should be initially determined. Typically, it is difficult to predict and generalize the effect of physical activity on GI symptoms in IBS patients [75] due to the vast diversity of different exercises regarding frequency, intensity, duration, and mode. For example, relatively light-moderate physical activity is associated with a beneficial effect on GI symptoms, while physical inactivity and vigorous physical activity can compromise GI symptoms. Intense physical activities that exceed 80% $\dot{V}O_2$ max can negatively delay GI function and gastric emptying [Chen et al., 2020]. Focusing on the optimum physical activity to the intensity, frequency, and mode of exercise is considered a critical, beneficial, and promising strategy for improving health [57].

The volume of any physical activity, estimated as the intensity and duration, is considered an essential factor for appearing neurological, physiological, and psychological symptoms in response to exercise [55-57]. Additionally, an individual's pretreatment measurements, such as rated perceived exertion, baroreceptor-sensitivity, CV activity markers, and accelerometry measures, can play a role in differentiating a person's response to physical activity [75]. The American College of Sports Medicine established and recommended using the FITT-VP principle in the prescription of physical

activity as a means to individualize physical activity intervention to maintain health and improve physical fitness [99].

Scientists may still hesitate to prescribe specific exercises for IBS management due to the lack of accurate indicators of the most appropriate suggestions to give patients [86]. Proper and correct exercise intervention based on the sympathetic and parasympathetic reactivity and tone phenotypes is crucially recommended to obtain the beneficial effect of exercise on IBS symptoms and psychic status, like mood [78,76,81]. Thus, for suitable exercise prescription, exercise attributes typified in the FITT-VP-principle should be considered, to attain maximum health benefits and physical fitness [97-99].

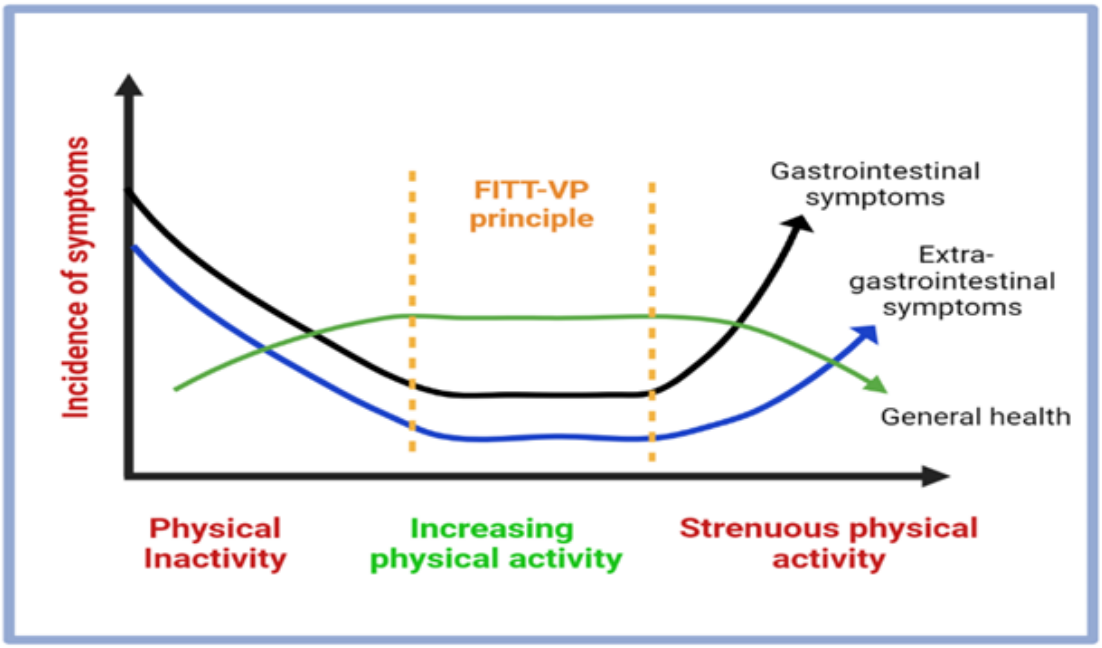

Fig. 2. The proposed association between physical activity and gastrointestinal and extra-gastrointestinal symptoms in IBS individuals.

Abbreviations. FITT-VP: Frequency (number of exercise occurrence), intensity (difficulty of the exercise bout), time (length of intervention), type (mode of the exercise bout), volume (total amount of exercise), and progression (change in difficulty in the exercise program over time)

Conclusions

IBS is a functional GI disorder characterized by recurrent abdominal pain and changes in bowel habits. It depicts a crucial health problem worldwide, reduces the QoL, and imposes a substantial economic burden. A physical exercise is a reasonable option for managing IBS symptoms, but this depends on exercise attributes, including type, frequency, intensity, duration, volume, and progression. There is great evidence recommending regular light-to-moderate aerobic exercise and anaerobic relaxation exercises for patients with IBS. In contrast to vigorous exercise, individualized light-moderate aerobic physical activity or the relaxation anaerobic exercise techniques enhance GI and psychological well-being by reducing anxiety, stress, and depression and relieving main IBS symptoms and improving the QoL. However, the evidence seems low-quality to make specific recommendations to use physical activity as therapy for patients with IBS as it is based on the heterogeneity of study designs, samples, interventions, and outcome measures. Thus, well-designed plausible studies, particularly RCT and research on individualized exercise intervention settings that consider all exercise attributes, are warranted.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

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