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Review Article

Acute Effects of Exercise to Mitigate Cancer-Related Fatigue: A State-of-the-Art Review

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Cancer-related fatigue (CRF) is one of the most common and distressing symptoms experienced by cancer survivors. While exercise interventions have shown efficacy in reducing CRF, the acute effect of exercise on CRF is not well understood. In this state-of-the-art review, we first provided historical context for the potential for exercise to provide immediate relief of CRF by summarizing plausible physiological and psychological mechanisms, then reviewed studies that have been done to date examining the acute effects of exercise on CRF, and finally, suggested directions for future research.

Keywords: acute; cancer-related fatigue; cancer survivors; exercise

1. Introduction

1.1. Statement of the Problem. Recent advances in cancer screenings and treatment(s) have led to a growing number of individuals living with and beyond cancer (i.e., cancer survivors), with 32 million survivors worldwide [1]. This number is expected to grow due to improvements in cancer screening and treatment(s), with two-thirds of cancer survivors living for more than 5 years after diagnosis [2]. Despite the improving efficacy of various cancer treatment(s), the impact of negative treatment-related side effects is a persistent problem among cancer survivors [3]. Cancer-related fatigue (CRF) is one of the most prevalent and distressing cancer- and treatment-related side effects, reported by 49–62% of cancer survivors [4–6].

The National Comprehensive Cancer Network (NCCN) [7] describes CRF as “a distressing, persistent subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and that interferes with usual functioning.” [7] CRF tends to be most severe during adjuvant treatment; however, 37% of breast cancer survivors report fatigue 2–6 years postsurgery [8]. CRF is a significant burden on the everyday lives of cancer survivors, impairing patients’ physical, psychological, and/or occupational functions and limiting their ability to perform daily activities [9].

Thus, there has been a pressing need to determine effective therapeutic strategies to help manage CRF, and previous systematic reviews and meta-analyses have determined the most efficacious approaches include physical activity/exercise, cognitive behavioral therapy (CBT), and mindfulness-based activities [10–13]. The European Society for Medical Oncology (ESMO) guidelines for management of CRF suggest physical activity, cognitive-behavioral interventions, and yoga [2]. The NCCN recommends exercise, yoga, massage, and CBT to manage CRF [7], and the American Society of Clinical Oncology (ASCO) also endorses exercise, CBT, and movement therapies like yoga, tai chi, and qigong for reducing the severity of fatigue during treatment [14]. However, of these approaches, the efficacy of exercise (i.e., a subset of physical activity that is structured, planned, and intended to improve some aspect of health and/or fitness [15]) is most consistently supported by randomized controlled trials (RCTs) [16–18]. Exercise targets physiological and psychological mechanisms and offers a sustainable, evidence-based approach to alleviating CRF across all stages of survivorship [19]. Cross-sectional evidence has consistently demonstrated an inverse association between exercise and CRF [9], and a seminal review found that exercise interventions were more effective for reducing CRF compared to pharmacological treatments [11]. Most recently, an umbrella review synthesizing 44 systematic reviews and meta-analyses found consistent evidence to support the efficacy of exercise interventions for reducing CRF [20]. Taken together, this evidence suggests that "chronic exercise" or exercise training (i.e., multiple exercise sessions done over several weeks or months) reduces CRF [12, 16, 21]. Although the underlying physiological mechanisms have not fully been elucidated, current evidence suggests that the relationship between exercise training and CRF is complex and may be influenced by a variety of physiological and psychological mechanisms [22, 23].

Despite this robust evidence for the benefits of chronic exercise or exercise training on CRF, cancer survivors are less likely than those without a history of cancer to achieve exercise guidelines, with only 14% estimated to be regularly engaging in aerobic and resistance exercise [24]. Paradoxically, a common barrier to initiating exercise among cancer survivors is CRF [12, 25, 26], and many report a lack of knowledge about how exercise can be used to manage CRF [25]. Consequently, it can be daunting for cancer survivors who are experiencing moderate or high levels of CRF to begin or adhere to regular exercise when the benefit is somewhat distal (i.e., weeks or months before seeing reductions in CRF). Thus, as an underlying premise for this review, we suggest that a promising strategy to reduce the barrier of low engagement in exercise due to CRF may be to explore the immediate or "acute" effect of exercise on CRF. Acute exercise is defined as a single, short-duration bout of exercise [27] and is distinct from chronic exercise, which involves repeated bouts of exercise over a longer period [28–30]. Although clinical guidelines support chronic exercise as an effective intervention to reduce CRF [3], there is very little information about the "acute" effects of exercise on CRF. Thus, this state-of-the-art review will focus on the effects of exercise on CRF from immediately before to immediately and several hours following a single bout of exercise. Specifically, this review aims to

1. Provide a historical context for the premise that exercise may have the potential to acutely reduce CRF by summarizing (a) what is known about the acute effects of exercise on fatigue in other (noncancer) populations and (b) the plausible physiological and psychological mechanisms underlying the acute effects of exercise on CRF.
2. Review previous studies that have examined the acute effect of exercise on CRF and provide a narrative synthesis.
3. Provide suggestions for future studies.

2. Methodology

A state-of-the-art literature review intends to address current matters, offer new perspectives on issues or topics, and/or point out areas for further research [31]. A state-of-the-art literature review synthesizes how the main characteristics of a topic have changed over time to give rise to current understanding, and these reviews have been used in many fields, such as biomedical science, medicine, and engineering, to provide information on the current understanding of a topic, the historical roots that shaped the understanding, and potential next directions for future research [32]. Currently, there are no established guidelines for reporting standards for state-of-the-art reviews, but according to Barry et al. [32], "a state-of-the-art literature review can be deemed a success if it provides a coherent description regarding the current state of knowledge of a phenomenon (i.e., this is where we are now in our current understanding of this topic. This is how we got here. This is where we could go next)."

For Objective 1, we summarized existing reviews, and for Objective 2, we searched relevant literature within a state-of-the-art review, as outlined by Barry et al. [33]. For Objective 2, the process consisted of (1) determining an initial research question to define the scope of the review ("Is there an acute effect of exercise on CRF?"); (2) establishing the timeframe for the review, which was 2010–2024, reflecting the time frame since the release of the first American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors in 2010 [34]; (3) developing a search strategy (described below); and (4) conducting a narrative synthesis of the included studies. The search strategy for Objective 2 used four databases: PubMed, Web of Science, CINAHL, and SPORTdis, and included the following terms: [(acute OR immediate OR single bout OR individual) AND (neoplasm OR cancer OR malignancy) AND (exercise OR physical activity) AND cancer-related fatigue]. For a study to be included in the review, it had to meet two inclusion criteria: (i) CRF measured before and after (within the same day) one or more exercise sessions and (ii) participants had to have been diagnosed with cancer. The search yielded 93 titles and abstracts, of which 86 did not meet the inclusion criteria. Following the initial screening, the remaining seven articles were retrieved. Three of these articles were further excluded because CRF was not measured immediately before and after exercise, which left $N = 4$ studies to be included in this review. Information was synthesized narratively, and there were no quantitative analyses performed. Finally, for Objective 3, based on findings from Objectives 1 and 2, we postulate potential future research directions in this area.

3. Results

3.1. Historical Context

3.1.1. Acute Effects of Exercise on Fatigue in Noncancer Populations. Previous studies have examined the acute effect of exercise on fatigue and energy in noncancer populations (e.g., college students [35], individuals with major depressive disorder [36], and healthy adult men [37]). In a systematic review summarizing these studies, Loy et al. reviewed 16 studies involving a total of 678 participants aged 18–55 years [38]. Fatigue and energy were self-reported, but specific definitions were not included in search terms, and the measures varied. Four studies focused on resistance exercise, while the remaining studies exclusively examined aerobic exercise. Exercise intensity varied across all studies and was measured using percentages of one-repetition maximum (RM) (15%–80%), predicted heart rate max (40%–80%), heart rate reserve, and oxygen consumption (VO_2). Findings demonstrated that energy increased immediately following a single exercise session; however, the effects of fatigue were inconsistent [38]. Interestingly, a significant three-way interaction was detected for changes in fatigue immediately after exercise that depended upon increases in energy, the intensity, and the duration of exercise. When increases in energy were at least moderate, fatigue was reduced after light-to-moderate intensity exercise, but not after vigorous exercise lasting longer than 20 min. Although these studies in noncancer populations (primarily college-age students) provide some support for the premise that exercise can reduce fatigue immediately afterwards, these findings may not be directly transferable to CRF, given the differences in the etiology of general fatigue (i.e., usually temporary; resolving with rest, recovery, and other lifestyle factors) versus CRF (i.e., debilitating exhaustion that is not alleviated by rest and that can persist for months to several years) [39]. Thus, this highlights and supports the need to further explore whether these relationships are similar for CRF.

3.1.2. Plausible Physiological Mechanisms Underlying the Acute Effects of Exercise on CRF. The physiological mechanisms that can explain the positive effect of exercise training (i.e., chronic exercise) on CRF have been well described [22, 40, 41]. However, the underlying mechanisms for how exercise may reduce CRF immediately afterwards (i.e., acutely) have not yet been fully elucidated. Although it is outside the scope of this state-of-the-art review to provide a comprehensive review of all potential physiological mechanisms, we aim to summarize two plausible pathways by which a single bout of exercise could reduce CRF (Figure 1).

Cancer and its treatments (i.e., chemotherapy, radiation, immunotherapy, and/or hormonal therapy) are used to treat a variety of cancer types and can activate the proinflammatory cytokine network. For example, cytokines may be produced in response to tissue damage. This damage has been associated with chronically increased levels of proinflammatory cytokines (i.e., interleukin-6 [IL-6] and tumor necrosis factor alpha [TNF-α]), which have been linked to inflammation-induced conditions, including CRF [40, 41]. Chronic exercise training has been shown to have anti-inflammatory effects, including increased interleukin-10 (IL-10) and reduced TNF-α expression [22]. Thus, one plausible mechanism for the acute effect of exercise on reducing CRF may be via anti-inflammatory pathways, specifically, transient increases in IL-6. Previous studies have examined acute IL-6 changes following exercise, finding patterns such as increased IL-6 immediately postexercise, which is more pronounced with higher-intensity and longer-duration exercise, peaking within 1–2 h postexercise and declining towards baseline values within 24 h [42, 43].

This acute increase in IL-6 immediately following exercise could upregulate the production of anti-inflammatory cytokines, including IL-10, interleukin-1 receptor antagonist (IL-1Ra), and transforming growth factor beta (TGF-β), dampening the inflammatory response, potentially leading to acute reductions in CRF [44].

Another plausible mechanism that supports the potential for the acute effect of exercise on CRF is the endocannabinoid system (ECS). The ECS regulates many systemic physiological processes in the human body, including emotions, mood, and somatic perception (e.g., the subjective perception of pleasure and pain) [45]. Emerging evidence suggests the ECS may be altered in the presence of cancer. A recent review reported that dysregulation of the ECS via changes in receptor expression and signaling has been documented in many cancer types, suggesting that the ECS system might be a target for anticancer therapies, including exercise [45]. Exercise has been shown to elevate circulating levels of endocannabinoids (eCBs), particularly anandamide (AEA), with increases observed as soon as 15 min postexercise, and the highest levels (2–3x increase) observed 30–45 min following exercise [46, 47]. The release of eCBs following exercise has also been referred to as "runner's high," characterized by increased sensations of euphoria and decreased pain up to 30 min postexercise [48]. Therefore, given the positive emotional arousal that can result from the release of eCBs immediately following exercise, there may be potential for this response to contribute to a feeling of reduced CRF. However, to our knowledge, there are no studies that have examined ECS responses to exercise among individuals living with and beyond cancer.

3.2. Literature Review of Previous Studies That Have Examined the Acute Effect of Exercise on CRF. Only four previous studies have examined the acute effect of exercise on CRF. Two studies were pilot RCTs [49, 50], one was a secondary analysis [51], and one was a retrospective study [52]. The retrospective study by Matsugaki et al. examined CRF among cancer survivors before and after a single inpatient exercise session [52]. The secondary analysis by Gomes et al. examined changes in CRF from before to immediately after exercise sessions during a videoconference-delivered exercise program [51]. One RCT by Cohen et al. [49] examined the immediate effects of aerobic exercise

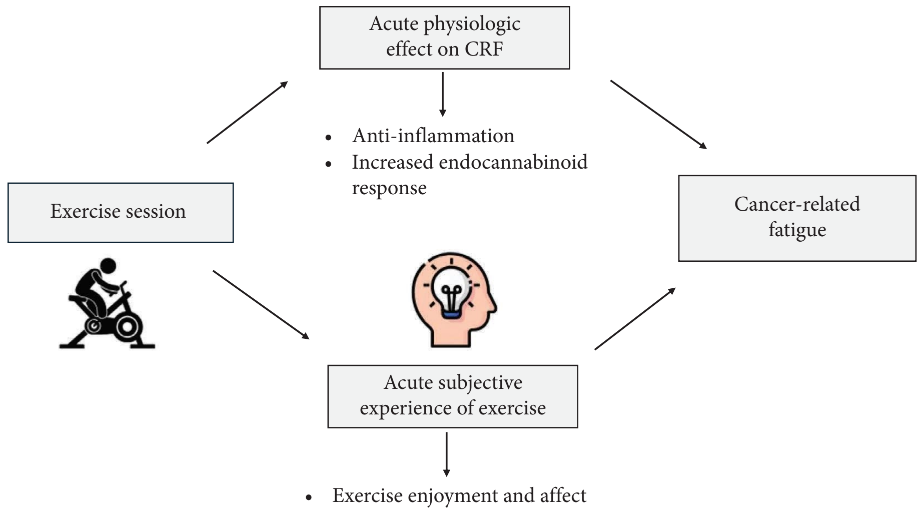

Figure 1: Conceptual model of the potential for the acute effects of exercise on cancer-related fatigue (CRF).

combined with relaxation training compared to aerobic exercise and relaxation alone on CRF, and the other RCT by Siebert et al. [50] evaluated the effects of four exercise interventions with varying intensity and type. Study details and results are described in Table 1.

Despite preliminary evidence suggesting that exercise may acutely reduce CRF, several limitations across the four existing studies limit the ability to draw definitive conclusions. Most notably, only one out of the four studies included a control condition. Sample sizes were small in two of these studies, with a limited number of CRF observations (i.e., only one exercise session per participant), and only one study reported the effects of an exercise session on CRF throughout the course of the day, but due to small sample size, only trends were reported. Additionally, studies were designed to determine feasibility [49, 50], or findings were derived from a secondary analysis [51], with no study designed a priori to examine the acute effects of exercise on CRF. These limitations underscore the need for additional studies as outlined in the section below to fully elucidate the acute effect of exercise on CRF.

3.3. Future Research Directions. A substantial literature base exists to support the benefits of exercise interventions (i.e., "chronic exercise") for reducing CRF [12, 16, 21]. However, whether exercise can provide immediate relief of CRF remains a pressing scientific question, with substantial practical and clinical implications. Currently, only four studies have examined the acute effect of exercise on CRF, but promising findings from these studies, and the presence of plausible underlying physiological mechanisms for this phenomenon, support the need for further investigation and a promising direction of research in the field of exercise oncology. Below, we outline three suggested future directions that will build upon the information provided in Objective 1 and the results of Objective 2.

3.3.1. Establishing the Efficacy of Exercise to Reduce CRF From Immediately Before to Immediately After Exercise. To more definitively determine the acute effect of exercise on CRF, additional studies with an RCT design are needed. RCTs will establish a causal relationship between exercise and immediate reductions in CRF. We suggest a within-person crossover RCT design in order to minimize between-person variability in CRF, with participants randomized to either an exercise session or an attention-matched control (e.g., seated rest or light stretching) with a washout period between.

To enhance internal validity, future RCTs should consider several key inclusion/exclusion criteria or stratify randomization based on treatment(s) received, demographics (e.g., age, sex, and socioeconomic status), and baseline level of CRF, as these factors may influence the magnitude of effect for exercise on CRF.

Additional considerations for future RCTs that aim to determine the acute effect of exercise on CRF include careful selection of CRF measures and the impact of exercise type, intensity, duration, and timing. First, in order to detect meaningful reductions in CRF immediately following exercise, the appropriate CRF measure is of vital importance. Many widely tested, valid, and reliable instruments exist [57]; however, these tools typically have six or more questions and have been used to assess fatigue either cross-sectionally or to capture changes over weeks to months. Thus, it is unclear whether these instruments would be too burdensome to assess CRF before and after exercise and whether they would be sensitive enough to capture acute or immediate changes in CRF. Due to their brevity, visual analog scales (VAS) may offer a feasible option for assessing CRF before and after exercise sessions and have also been tested for reliability and validity to measure CRF [56, 58]. However, additional testing of the psychometric properties for sensitivity to change and clinical meaningfulness of this change is needed. Second, given that exercise type, intensity, and duration have been shown to impact the acute effects of exercise on fatigue in general populations [38] and the acute

Table 1: Literature review study characteristics (Objective 2).

Study	Participant characteristics	Study design	Intervention exercise prescription	CRF timepoints	CRF measurement	Study findings
Matsugaki et al. (2018)	$N = 18$ Hematologic cancer Currently undergoing treatment	Retrospective study	F; single session I: RPE of 4/10 T: 20–40 min T: standing, sitting, and walking	"Immediately" before and after the session	Cancer fatigue scale (CFS) [53]	CRF was significantly reduced for physical ($p = 0.023$) and total ($p = 0.006$) domains
Cohen et al. (2019)	$N = 40$ Breast cancer Not currently undergoing treatment	RCT	Aerobic only: F: 3 sessions (≥ 24 h apart) I: 50%–70% age-predicted HRmax T: 20 min each (40 total) T: Stationary bike and quiet seated rest Relaxation only: F: 3 sessions (≥ 24 h apart) T: 20 min each (40 total) T: Technology-based MBSR and quiet seated rest Combined: F: 3 sessions (≥ 24 h apart) I: 50%–70% age-predicted HRmax T: 20 min each (40 total) T: Stationary bike and technology-based MBSR	Before and after session (exact timeframe not specified)	Piper fatigue scale (PFS) [54]	There was a large effect (Cohen's $d = 0.91$) in CRF reduction from pre- to postexercise in the combined group only

Table 1: Continued.

Study	Participant characteristics	Study design	Intervention exercise prescription	CRF timepoints	CRF measurement	Study findings
Siebert et al. (2022)	$N = 33$ Various cancer types Not currently undergoing treatment	RCT	Moderate endurance: F: 3x for 4 weeks I: 50%–60% of VO_2max T: 30 min T: cross-trainer or bicycle ergometer Vigorous endurance: F: 3x for 4 weeks I: 70%–80% of VO_2max T: 30 min T: cross-trainer or bicycle ergometer Moderate strength: F: 3x for 4 weeks I: 50%–60% of 1RM T: 30 min T: weight machines Vigorous strength: F: 3x for 4 weeks I: 70%–80% of 1RM T: 30 min T: weight machines	Before and after session + three additional times per day (unspecified)	Numerical rating scale (NRS) [55]	The change in CRF from before to immediately after each exercise session was not reported.
Gomes et al. (2025)	$N = 55$ Various cancer types and mixes of treatment status	Secondary analysis	F: 1x for 8 weeks I: RPE 3–6/10 T: 60 min T: Aerobic, resistance, and balance circuits	Before and after session (within 15 min)	Visual analog scale (VAS) [56]	CRF was significantly reduced pre- to postexercise session ($p < 0.01$)

Note: min = minute, VO_2max = maximal oxygen uptake.
Abbreviations: CRF = cancer-related fatigue, FITT = frequency, intensity, time, and type, HRmax = heart rate max, MBSR = mindfulness-based stress reduction, RCT = randomized controlled trial, RM = repetition max, RPE = rate of perceived exertion.

physiological response to exercise [59, 60], future RCTs should be attentive to exercise prescriptions and potentially consider comparisons across exercise type (e.g., aerobic vs. resistance), intensity (e.g., light vs. moderate-vigorous), or duration. Finally, the time of day when exercise is performed has been shown to have important implications for its effects on metabolic outcomes (e.g., obesity, Type 2 diabetes, dyslipidemia, and hypertension) [61], suggesting that this may also be a factor to consider when designing future RCTs that examine the acute effect of exercise on CRF (i.e., standardizing the timing of exercise sessions within and across participants).

3.3.2. The Effect of an Exercise Session on CRF Throughout the Day. In addition to determining the efficacy of exercise to immediately reduce CRF, exploring the impact of an exercise session on CRF throughout the remainder of the day may also have significant practical and clinical implications. Cancer survivors frequently report the negative impact of CRF on their ability to successfully perform activities of daily living (ADLs) [62]; thus, exploring the effect of an exercise session to reduce CRF for the rest of the day may have implications for reducing impairments in ADLs and improving functional independence. Siebert et al. [50] is currently the only study to assess CRF at three additional timepoints throughout the exercise day; however, results were not reported. When conceptualizing future studies to examine the time course of CRF throughout the day following an exercise session, we suggest beginning with a longitudinal, observational design with the following considerations. First, determining when and how frequently to measure CRF following an exercise session and appropriate methods for assessing CRF multiple times throughout the day. The timepoints at which to measure CRF (e.g., how many minutes or hours following the exercise sessions) are important considerations because it is currently unknown when reductions in CRF peak following exercise or when these levels return to baseline. Evidence from previous studies that have examined acute exercise effects on circulating inflammation markers [42, 43] suggests that measurement timepoints could begin as early as 15 min postexercise and extend up to 24 h following exercise. In terms of frequency of measurement, previous studies in cancer populations have found three to five measurements of CRF per day to be feasible and acceptable to participants [63, 64]. In terms of measurement methods, future studies may consider collecting these data in real time utilizing ecological momentary assessment (EMA). EMA is often used to examine within-person changes that occur over relatively short time periods (minutes, hours, and days) [65], may help overcome the limitation of recall bias [65, 66], and previous studies have established that EMA is feasible in cancer populations to measure CRF [67].

In addition, given that CRF can fluctuate throughout the day due to various individual and treatment-related factors [68], when measuring changes in CRF following an exercise session, future studies should also consider measuring CRF on nonexercise days. Assessing CRF at the same timepoints on a nonexercise day will help isolate the effects of the exercise session outside of "typical" daily variability. Finally, these studies should also consider additional factors that can impact CRF throughout the day, such as nonexercise physical activity, sedentary behavior, sleep, and treatment schedules [69, 70]. These activities can be monitored using a variety of devices that have been previously tested for feasibility, acceptability, reliability, and validity among cancer survivors [71].

3.3.3. Elucidating Underlying Mechanisms for the Acute Effect of Exercise on CRF. To better understand how exercise can immediately reduce CRF both immediately and over the course of a day, future studies are needed that examine the underlying physiological mechanisms, as no current studies have assessed the mechanisms of CRF acutely in the context of a single exercise bout and self-reported CRF. Although the mechanisms by which exercise can acutely reduce CRF are not well-established, an exciting and emerging area for future research may include the role of the ECS in how exercise may provide immediate relief of CRF [45]. Adaptations in the ECS system may induce positive emotional arousal following exercise [72], yet no studies have explored the ECS responses to exercise in a cancer population and the subsequent impact on CRF. Thus, future studies are needed to determine a direct link between ECS activation during exercise and the effect on CRF, which may include biomarker assays of circulating eCB levels. Based on previous studies that evaluated the relationship between a runner's high following endurance exercise and eCB levels [46], future studies seeking to examine this response among cancer survivors experiencing CRF may consider measuring circulating levels of eCBs (e.g., AEA) before and 15–60 min postexercise. We suggest that these measures could be added to a within-person crossover RCT, where participants are randomized to exercise or an attention-matched control condition, with blood draws immediately before and after (e.g., 15–60 min post) to assess changes in circulating eCBs.

3.3.4. Exploring the Impact of Acute Reductions in CRF on Long-Term Exercise Adherence. CRF is one of the most common barriers to exercise among cancer survivors [12, 25, 26], and a promising strategy to overcome this barrier may be to emphasize the potential for exercise to provide immediate relief of CRF. When exercise elicits a positive emotional response, it may increase the likelihood of the continuation of that behavior [62]. This phenomenon, consistent with the hedonistic principle linking positive emotional arousal or "affect" to subsequent exercise behavior (i.e., we sustain participation in activities that give us enjoyment or pleasure) [75, 76], suggests that it is reasonable to posit that if cancer survivors experience immediate relief of CRF following an exercise session, this could lead to continued engagement in this behavior even while experiencing CRF [77, 78]. To examine this relationship, future studies should examine associations between acute changes in CRF following exercise sessions and long-term adherence to exercise behavior. This could be accomplished using a longitudinal design with exercise behavior measured several weeks and/or months following an exercise intervention or program in which CRF is assessed immediately before and after exercise sessions.

4. Conclusion

The acute effect of exercise on CRF is an understudied area of research with potential for important practical and clinical implications. Only four studies have examined the acute effects of exercise on CRF, and despite promising results, limitations in sample size and variability of intervention type and CRF measure prevent drawing definitive conclusions. Directions for future research include RCTs to establish efficacy for the acute effect of exercise on CRF, assessing the time course of CRF throughout the day following an exercise session, exploring potential mechanisms (e.g., inflammation and/or the ECS), and how a focus on immediate relief of CRF following exercise could contribute to exercise adherence. Determining whether exercise has an acute effect for reducing CRF could have the potential to profoundly influence how oncology clinicians and exercise professionals discuss and prescribe exercise to their patients with the intent of alleviating CRF.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Conflicts of Interest

The authors declare no conflicts of interest.

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