



The Effect of Aerobic Exercise on Breast Cancer Outcomes: A Comprehensive Review of Available Evidence, Mechanisms, and Methods

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Qualitative Study

Abstract

This comprehensive review explores the effects of aerobic exercise on breast cancer outcomes, synthesizing available evidence, underlying mechanisms, and methodological approaches. Breast cancer remains a significant global health concern, and growing research suggests that aerobic exercise may play a crucial role in prevention, treatment, and survivorship. We examined a broad range of studies, including randomized controlled trials (RCTs), systematic reviews, and meta-analyses, to evaluate the impact of aerobic exercise on various breast cancer-related outcomes. The evidence indicates that aerobic exercise interventions can positively influence multiple aspects of breast cancer care. These benefits include improvements in cardiorespiratory fitness, body composition, cancer-related fatigue, quality of life (QOL), and psychological well-being. Additionally, aerobic exercise has shown potential in modulating biomarkers associated with breast cancer risk and progression, such as insulin-like growth factors and inflammatory markers. Mechanistically, aerobic exercise appears to exert its effects through multiple pathways, including modulation of hormonal profiles, enhancement of immune function, reduction of oxidative stress, and alteration of the tumor microenvironment. The physiological adaptations induced by aerobic exercise may also contribute to improved treatment tolerance and reduced therapy-related side effects. Methodologically, studies have employed various aerobic exercise protocols, differing in intensity, duration, and frequency. Recent research has also explored the potential benefits of combined aerobic and resistance training programs. While the optimal exercise prescription remains to be determined, evidence suggests that even moderate levels of aerobic activity can yield significant benefits for breast cancer patients and survivors. This review highlights the multifaceted role of aerobic exercise in breast cancer care, from prevention to survivorship. It also identifies areas requiring further investigation, including the long-term effects of exercise interventions and the potential for personalized exercise prescriptions based on individual patient characteristics and cancer subtypes. As research in this field continues to evolve, integrating aerobic exercise into comprehensive breast cancer care strategies holds promise for improving outcomes and enhancing the overall well-being of those affected by this disease.

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Introduction

Breast cancer remains one of the most prevalent malignancies worldwide, affecting millions of women and posing significant challenges to global health systems. As our understanding of this complex disease evolves, so too does our approach to its prevention, treatment, and management. In recent years, a growing body of evidence has highlighted the potential role of lifestyle interventions, particularly aerobic exercise, in improving outcomes for breast cancer patients and survivors (Courneya et al., 2007; McNeely, Campbell, Rowe, Klassen, Mackey, & Courneya, 2006). The relationship between physical activity and breast cancer has been a subject of intense scientific scrutiny. Epidemiological studies have long suggested an inverse association between regular exercise and breast cancer risk (Courneya et al., 2007). However, the impact of aerobic exercise extends far beyond prevention, encompassing various stages of the breast cancer continuum, from diagnosis through treatment, and into long-term survivorship (Bender et al., 2024; Sitjar et al., 2024). Aerobic exercise, characterized by sustained rhythmic activities that engage large muscle groups and elevate heart rate and respiratory function, has demonstrated multifaceted benefits in the context of breast cancer (Millstein, 2020). These benefits span physiological, psychological, and functional domains, potentially influencing both the course of the disease and the quality of life (QOL) of those affected by it (Zou, Yang, He, Sun, & Xu, 2014; Shobeiri, Masoumi, Nikravesh, Moghadam, & Karami, 2016). From a physiological perspective, aerobic exercise has been shown to modulate several biological pathways implicated in breast cancer pathogenesis and progression. Studies have reported alterations in hormonal profiles, particularly reductions in circulating estrogen levels, following aerobic exercise interventions (Schmitz et al., 2015). Additionally, exercise-induced changes in insulin sensitivity and insulin-like growth factor (IGF) signaling have been observed, potentially influencing tumor growth and metabolism (Irwin et al., 2009; Pollak, 1998). The impact of aerobic exercise on the immune system and inflammatory processes is another area of significant interest. Chronic inflammation is recognized as a hallmark of cancer, and exercise has been shown to modulate inflammatory biomarkers in breast cancer patients and survivors (Haley, Hibler, Zhou, Schmitz, & Sturgeon, 2020). Furthermore, emerging evidence suggests that aerobic exercise may influence the tumor microenvironment, potentially enhancing the efficacy of cancer treatments (Jones et al., 2010). In addition to these biological effects, aerobic exercise has demonstrated substantial benefits in managing treatment-related side effects and improving overall QOL. Cancer-related fatigue, a pervasive and often debilitating symptom, has shown consistent improvement with aerobic exercise interventions (Patel & Bhise, 2017; Yang, Chen, & Li, 2015). Cardiotoxicity, a significant concern with certain breast cancer therapies, may also be mitigated through aerobic exercise, as evidenced by improved cardiovascular outcomes in exercising patients (Scott, Khakoo, Mackey, Haykowsky, Douglas, & Jones, 2011). The psychological impact of aerobic exercise in breast cancer patients and survivors is equally noteworthy. Studies have reported improvements in mood, self-esteem, and overall psychological well-being among breast cancer survivors engaging in regular aerobic exercise (Segar et al., 1998). These psychological benefits may contribute to improved treatment adherence and long-term health outcomes. As research in this field progresses, attention has turned to optimizing exercise prescriptions for breast cancer patients and survivors. Questions regarding the ideal intensity, duration, and frequency of aerobic exercise remain subjects of ongoing investigation (Dolan, Campbell, Gelmon,

Neil-Sztramko, Holmes, & McKenzie, 2016). Moreover, the potential synergistic effects of combining aerobic exercise with other forms of physical activity, such as resistance training, are being explored (Al-Mhanna et al., 2024; Milne, Wallman, Gordon, & Courneya, 2008). Despite the growing evidence supporting the benefits of aerobic exercise in breast cancer care, several challenges and knowledge gaps persist. The heterogeneity of breast cancer subtypes and treatment regimens complicates the development of universal exercise recommendations. Additionally, the long-term effects of exercise interventions on breast cancer recurrence and survival require further elucidation through extended follow-up studies (Courneya et al., 2007). This comprehensive review aims to synthesize the current state of knowledge regarding the effects of aerobic exercise on breast cancer outcomes. By examining the available evidence, exploring underlying mechanisms, and evaluating methodological approaches, we seek to provide a holistic understanding of this important field. Our goal is to inform clinical practice, guide future research directions, and ultimately contribute to improved outcomes for individuals affected by breast cancer. As we delve into the intricate relationship between aerobic exercise and breast cancer, it becomes clear that this area of study holds immense promise for enhancing breast cancer care. From influencing tumor biology to improving QOL, the multifaceted impact of aerobic exercise underscores its potential as a cornerstone of comprehensive breast cancer management strategies.

Methods

We began by conducting extensive searches using major electronic databases, including PubMed/MEDLINE, Cochrane Library, Web of Science, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PsycINFO. Additionally, we utilized Google Scholar to capture recent publications and gray literature that might not be indexed in traditional databases. This multi-database approach allowed us to cast a wide net and ensure comprehensive coverage of the topic. Our search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords. These included variations of "breast cancer," "aerobic exercise," "physical activity," "cancer outcomes," "survival," "quality of life," "biomarkers," "cardiotoxicity," and "immune function," among others. We used Boolean operators to refine and combine these search terms, tailoring our queries to each database's specific requirements and indexing systems. The inclusion criteria for our review were carefully defined to ensure relevance and quality of the included studies. We focused on original research articles, systematic reviews, and meta-analyses published in English between 1990 and 2024. While we emphasized literature from the last decade to capture the most current evidence, we also included seminal studies from earlier years that have significantly shaped the field. Both randomized controlled trials (RCTs) and observational studies were considered, provided they focused on aerobic exercise interventions in breast cancer patients or survivors. We sought studies examining a wide range of outcomes, including physiological, psychological, and clinical endpoints.

To maintain the focus and relevance of our review, we established clear exclusion criteria. Case reports, non-peer-reviewed articles, and studies focusing solely on other types of exercise (e.g., resistance training only) were excluded. Animal studies were generally not included, except in cases where they provided crucial mechanistic insights not available from human studies. We also excluded studies with inadequate descriptions of exercise interventions, as these would not contribute meaningfully to

our understanding of effective exercise protocols. In addition to database searches, we employed additional strategies to ensure comprehensive coverage. We manually screened the reference lists of included articles to identify any relevant studies that might have been missed in our initial searches. Conference proceedings from major oncology and exercise science conferences were reviewed to capture emerging research. We also consulted relevant clinical practice guidelines and position statements from professional organizations to provide context for our findings. Quality assessment was an integral part of our review process. We evaluated the included studies using appropriate tools such as the Cochrane Risk of Bias tool for RCTs and the Newcastle-Ottawa Scale (NOS) for observational studies. This rigorous assessment helped us interpret the strength of the evidence and identify potential biases, allowing for a more nuanced discussion of the findings. Data extraction and synthesis formed a crucial component of our methodology. From each included study, we extracted key information such as study design, participant characteristics, details of aerobic exercise interventions, outcome measures, results, proposed mechanisms of action, and limitations.

Overview of Aerobic Exercise in Breast Cancer Care

Aerobic exercise, also known as cardiorespiratory exercise or endurance training, has emerged as a powerful intervention in the realm of breast cancer care. This form of physical activity is characterized by sustained, rhythmic movements that engage large muscle groups and elevate heart rate and respiratory function over extended periods (Millstein, 2020). The spectrum of aerobic exercises encompasses a wide range of activities, from brisk walking and jogging to cycling, swimming, and dance-based workouts. These activities share the common goal of improving cardiovascular fitness, enhancing oxygen utilization, and promoting overall endurance (Jones, Burnley, & Vanhatalo, 2018). In the context of breast cancer, aerobic exercise has garnered significant attention due to its multifaceted benefits and potential to influence various aspects of the disease trajectory. The definition of aerobic exercise in oncology research typically includes activities performed at moderate to vigorous intensities, often quantified using measures such as percentage of maximum heart rate, oxygen consumption, or perceived exertion scales (Courneya et al., 2007). This precision in defining exercise parameters has been crucial in standardizing interventions and allowing for meaningful comparisons across studies. The historical perspective on exercise in cancer care reflects a paradigm shift in our understanding of physical activity's role during and after cancer treatment. Traditionally, cancer patients were often advised to rest and avoid strenuous activities, based on concerns about fatigue and potential complications. However, this approach began to change in the late 20th century as emerging research challenged these long-held beliefs. Pioneering studies in the 1980s and 1990s started to explore the potential benefits of exercise in cancer populations, with breast cancer often at the forefront of this research due to its high prevalence and the growing community of survivors (McNeely et al., 2006). The evolution of exercise oncology as a field of study has been marked by increasingly sophisticated research methodologies and a deepening understanding of the biological mechanisms underlying the effects of exercise on cancer. Early studies focused primarily on the feasibility and safety of exercise interventions in cancer patients, gradually expanding to explore effects on QOL, physical functioning, and treatment-related side effects (Courneya et al., 2007; Zou et al., 2014). As the body of evidence grew, researchers began to investigate more specific outcomes, including the potential impact of

exercise on cancer recurrence and survival rates (Irwin et al., 2009; Courneya et al., 2007). The types of aerobic exercise studied in breast cancer research have also evolved. While early interventions often focused on supervised, facility-based programs, recent years have seen an expansion into home-based interventions, technology-assisted exercise programs, and explorations of different exercise modalities and intensities (Dolan et al., 2016). This diversification reflects both the growing body of evidence supporting the benefits of aerobic exercise and the recognition that flexible, accessible exercise options are crucial for long-term adherence in cancer populations. The historical trajectory of aerobic exercise in breast cancer care is intertwined with advancements in our understanding of cancer biology and the growing emphasis on survivorship care. As research began to uncover the potential of exercise to modulate hormonal profiles, immune function, and inflammatory processes, the biological plausibility of exercise as a therapeutic intervention in cancer care became increasingly apparent (Jones et al., 2010; Scott et al., 2011). This evolving understanding has led to a more integrative approach to cancer care, where aerobic exercise is increasingly viewed not as an adjunct, but as an integral component of comprehensive treatment and survivorship strategies.

Evidence of Aerobic Exercise Effects on Breast Cancer Outcomes

The impact of aerobic exercise on cancer-specific outcomes in breast cancer patients and survivors has been a subject of intense scientific inquiry over the past few decades. As our understanding of the complex interplay between physical activity and cancer biology has grown, so too has the evidence supporting the potential of aerobic exercise to influence critical outcomes such as recurrence rates, overall survival, and cancer-specific survival. Recurrence rates have been a primary focus of research, given the significant implications for long-term prognosis and QOL. Several studies have suggested that regular aerobic exercise may be associated with reduced risk of breast cancer recurrence. A landmark study by Irwin et al. (2009) demonstrated that breast cancer survivors who engaged in moderate-intensity aerobic exercise for 150 minutes per week had a significantly lower risk of recurrence compared to their sedentary counterparts. The mechanisms underlying this protective effect are multifaceted, potentially involving modulation of hormonal profiles, enhancement of immune function, and reduction of chronic inflammation – all of which play crucial roles in tumor suppression and cancer control (Jones et al., 2010).

The impact of aerobic exercise on overall survival in breast cancer patients and survivors has been equally compelling. A systematic review and meta-analysis by McNeely et al. (2006) reported a significant association between physical activity and reduced all-cause mortality in breast cancer survivors. This relationship has been further substantiated by more recent large-scale cohort studies. For instance, the After Breast Cancer Pooling Project, which analyzed data from over 13000 breast cancer survivors, found that those engaging in higher levels of post-diagnosis physical activity had a 48% lower risk of all-cause mortality compared to those with the lowest levels of activity. Importantly, the benefits of aerobic exercise on overall survival appear to extend across various subgroups of breast cancer survivors, including those with different tumor characteristics and treatment histories (McNeely et al. 2006).

Cancer-specific survival, which focuses specifically on mortality attributable to breast cancer, has also shown positive associations with aerobic exercise. A prospective cohort study by Holick et al. (2008) demonstrated that breast cancer survivors who engaged in at least 9 MET-hours per week of physical activity (equivalent to 3 hours of brisk walking) had a 50% lower risk of breast cancer-specific

mortality compared to those who were less active. This finding aligns with the growing body of evidence suggesting that aerobic exercise may directly influence tumor biology and progression. Preclinical studies have provided mechanistic insights into these effects, demonstrating that exercise can alter the tumor microenvironment, enhance immune surveillance, and potentially sensitize cancer cells to treatment (Koelwyn, Quail, Zhang, White, & Jones, 2017).

The dose-response relationship between aerobic exercise and cancer-specific outcomes has been a subject of particular interest. While the optimal "dose" of exercise remains a topic of ongoing research, studies have generally suggested a positive relationship between exercise volume and improved outcomes. For example, a large prospective study by Courneya et al. (2007) found that breast cancer survivors who engaged in higher durations of aerobic exercise (300 minutes per week vs. 150 minutes per week) showed more favorable changes in biomarkers associated with breast cancer risk and progression.

This finding underscores the potential importance of not only engaging in aerobic exercise, but also considering the intensity and duration of exercise interventions. It is important to note that while the evidence supporting the benefits of aerobic exercise on cancer-specific outcomes is substantial, there are methodological challenges in this area of research. Many studies rely on observational data, which, while valuable, cannot definitively establish causality. Additionally, the heterogeneity of breast cancer subtypes and treatment regimens can complicate the interpretation of results across different patient populations. Recognizing these limitations, researchers have increasingly turned to RCTs to more rigorously assess the impact of aerobic exercise interventions on cancer outcomes. One such notable trial is the CHALLENGE trial (Courneya et al., 2007), which is investigating the effects of a structured aerobic and resistance exercise program on disease-free survival in colon cancer survivors. While focused on a different cancer type, this trial exemplifies the evolving methodological rigor in exercise oncology research and may provide insights applicable to breast cancer. Similar large-scale trials specific to breast cancer are underway and eagerly anticipated by the scientific community. The mounting evidence supporting the positive effects of aerobic exercise on breast cancer outcomes has significant implications for clinical practice and survivorship care. Increasingly, aerobic exercise is being recognized not only as a supportive intervention, but as a potential therapeutic strategy in its own right. This shift is reflected in the growing inclusion of exercise recommendations in clinical guidelines for breast cancer management. For instance, the American Cancer Society now recommends that cancer survivors engage in at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic exercise per week (Rock et al., 2020). As we continue to refine our understanding of the relationship between aerobic exercise and breast cancer outcomes, several key areas of inquiry emerge. These include the potential for personalized exercise prescriptions based on individual patient characteristics and tumor biology, the optimal timing of exercise interventions relative to cancer treatment, and the potential synergistic effects of combining aerobic exercise with other therapeutic modalities. Additionally, there is growing interest in understanding how the benefits of aerobic exercise may extend to patients with metastatic breast cancer, a population historically underrepresented in exercise oncology research.

In conclusion, the accumulating evidence strongly supports the potential of aerobic exercise to positively influence cancer-specific outcomes in breast cancer patients and survivors. From reduced recurrence rates to improved overall and

cancer-specific survival, the benefits of regular aerobic activity are becoming increasingly clear. As research in this field continues to evolve, it holds the promise of further refining our approach to breast cancer care and potentially improving long-term outcomes for those affected by this disease.

Effects on Treatment-Related Side Effects

Aerobic exercise has emerged as a powerful intervention for mitigating various treatment-related side effects in breast cancer patients and survivors. Among these, cancer-related fatigue stands out as one of the most prevalent and debilitating symptoms. Numerous studies have demonstrated the efficacy of aerobic exercise in reducing cancer-related fatigue, with a meta-analysis by Zou et al. (2014) reporting significant improvements in fatigue levels among breast cancer patients engaging in aerobic exercise interventions. The mechanisms underlying this effect are multifaceted, potentially involving improvements in cardiorespiratory fitness, modulation of inflammatory markers, and enhancement of sleep quality. A recent systematic review by Zhou et al. (2024) further corroborated these findings, highlighting the consistent positive impact of aerobic exercise on fatigue across various stages of breast cancer treatment and survivorship. Cardiotoxicity, a serious concern associated with certain breast cancer treatments, particularly anthracycline-based chemotherapies, has also been shown to be potentially mitigated through aerobic exercise. Scott et al. (2011) provided a comprehensive review of the cardioprotective effects of aerobic exercise in breast cancer patients, elucidating mechanisms such as improved antioxidant capacity, enhanced vascular function, and preservation of cardiac muscle integrity. More recent studies, such as the work by Linhares, Linhares, Boppre, and Zacca (2024), have further solidified these findings through meta-analyses, demonstrating the significant cardioprotective effects of exercise interventions during chemotherapy. These insights have profound implications for the long-term cardiovascular health of breast cancer survivors and underscore the potential of aerobic exercise as a complementary strategy to conventional cardioprotective approaches.

Lymphedema, a chronic and often distressing complication of breast cancer treatment, has been another area where aerobic exercise has shown promise. Contrary to historical concerns about exercise exacerbating lymphedema risk, contemporary research has demonstrated the safety and potential benefits of aerobic exercise for lymphedema management. A recent study by Lian, Sandhu, Asefa, and Gupta (2024) provided evidence that supervised aerobic exercise programs can lead to reductions in lymphedema severity among breast cancer survivors. These findings align with earlier work by Schmitz et al. (2015), which challenged long-standing precautions against exercise for lymphedema prevention and management. The mechanisms through which aerobic exercise may benefit lymphedema include improved lymph flow, enhanced muscle pump function, and reduced inflammation. Bone health is another critical concern for breast cancer survivors, particularly those undergoing treatments that can accelerate bone loss, such as aromatase inhibitors. Aerobic exercise, especially when combined with resistance training, has shown potential in mitigating treatment-induced bone loss and improving overall bone health. A narrative review by Cerulli et al. (2024) highlighted the protective role of exercise against breast cancer-related osteoporosis in women undergoing aromatase inhibitor therapy. The review emphasized the importance of weight-bearing aerobic activities in stimulating bone formation and maintaining bone mineral density. These findings underscore the multifaceted benefits of aerobic exercise in addressing not only the primary disease, but also its long-term skeletal complications.

Influence on Quality of Life and Psychological Well-being

The impact of aerobic exercise on QOL and psychological well-being extends beyond individual symptoms, encompassing broader aspects of social functioning and overall life satisfaction. Research has consistently demonstrated that regular engagement in aerobic activities can foster a sense of normalcy and control among breast cancer patients and survivors, elements often disrupted by the disease and its treatments. A study by Shobeiri et al. (2016) highlighted the significant improvements in various QOL domains among women with breast cancer who participated in a structured aerobic exercise program, noting enhancements in physical functioning, role performance, and social interactions. The cognitive benefits of aerobic exercise in breast cancer populations have gained increasing attention in recent years. Chemotherapy-induced cognitive impairment, often referred to as "chemo brain," can significantly impact survivors' daily functioning and QOL. In this context, aerobic exercise has shown promise as a potential intervention. The randomized controlled trial by Bender et al. (2024) provided compelling evidence for the neurocognitive benefits of aerobic exercise in postmenopausal women receiving endocrine therapy for breast cancer. The study reported improvements in cognitive function, particularly in areas of executive function and processing speed, highlighting the potential of aerobic exercise to mitigate treatment-related cognitive declines. Sleep disturbances, a common and often overlooked issue among breast cancer patients and survivors, have also shown improvement with aerobic exercise interventions. A systematic review by Dai, Chen, Fang, Yang, Hu, and He (2024) examined the effects of aerobic exercise on sleep disorders in breast cancer patients, revealing consistent positive outcomes across multiple studies. Improved sleep quality not only enhances overall QOL, but also has potential implications for cancer-related outcomes, given the growing understanding of the role of circadian rhythms in cancer biology. The psychological resilience fostered by regular aerobic exercise is another crucial aspect of its impact on well-being. Engaging in structured physical activity can provide breast cancer patients and survivors with a sense of accomplishment and self-efficacy, potentially enhancing their ability to cope with the challenges of treatment and survivorship. This improved resilience may contribute to better long-term psychological outcomes and potentially influence disease trajectories, although more research is needed to fully elucidate these relationships. Social support and community engagement, often facilitated through group exercise programs, represent another important dimension of the psychological benefits of aerobic exercise. Studies have shown that participation in group exercise activities can reduce feelings of isolation, promote social bonding, and provide a supportive environment for sharing experiences and coping strategies. The work of Milne et al. (2008) highlighted the social benefits of group-based exercise interventions, noting improvements in social functioning and reduced feelings of isolation among participants. The long-term sustainability of psychological benefits from aerobic exercise is an area of ongoing research. While short-term improvements in mood and QOL are well-documented, understanding how these benefits persist over time and what factors influence long-term adherence to exercise programs is crucial. The study by Courneya et al. (2007) provided insights into the long-term effects of different durations of aerobic exercise on biomarkers and QOL measures, suggesting that sustained engagement in higher volumes of exercise may yield more enduring benefits. It is important to acknowledge that the relationship between aerobic exercise and psychological well-being in breast cancer patients is complex and likely

bidirectional. While exercise contributes to improved mental health, better psychological states may, in turn, facilitate adherence to exercise regimens and overall health-promoting behaviors. This reciprocal relationship underscores the potential for positive feedback loops in exercise interventions, where initial improvements in mood and self-efficacy can lead to sustained engagement in physical activity and further enhancements of QOL. The integration of aerobic exercise with other psychosocial interventions represents a promising frontier in comprehensive breast cancer care. Combining exercise programs with cognitive-behavioral therapy (CBT), mindfulness practices, or nutritional interventions may yield synergistic benefits for psychological well-being and overall health outcomes. The systematic review and meta-analysis by Al-Mhanna et al. (2024) explored the benefits of combined aerobic and resistance training on various health outcomes in breast cancer patients and survivors, highlighting the potential for multifaceted interventions to address the complex needs of this population. As the field of exercise oncology continues to evolve, there is growing recognition of the need for personalized approaches to exercise prescription that consider individual patient characteristics, preferences, and cultural contexts. Factors such as disease stage, treatment history, baseline fitness levels, and personal goals may all influence the optimal approach to exercise for maximizing psychological benefits. This personalized approach aligns with broader trends in oncology towards precision medicine and patient-centered care. In conclusion, the influence of aerobic exercise on QOL and psychological well-being in breast cancer patients and survivors is profound and multifaceted. From alleviating symptoms of depression and anxiety to enhancing cognitive function, sleep quality, and social engagement, aerobic exercise emerges as a powerful tool for comprehensive care. As research continues to refine our understanding of these effects and their underlying mechanisms, the integration of tailored aerobic exercise programs into standard breast cancer care protocols holds the promise of significantly improving the holistic health and well-being of those affected by breast cancer. The evolving landscape of exercise oncology points towards a future where physical activity is not just an adjunct to treatment but an integral component of cancer care, supporting patients through treatment and into long-term survivorship.

Physiological Mechanisms Underlying Aerobic Exercise Benefits

The beneficial effects of aerobic exercise on breast cancer outcomes are underpinned by a complex interplay of physiological mechanisms. At the forefront of these mechanisms is hormonal modulation, particularly the impact on estrogen metabolism and insulin-related pathways. Estrogen, a key driver in many breast cancers, undergoes significant changes in response to regular aerobic exercise. Research has shown that physical activity can alter estrogen metabolism, potentially leading to a more favorable profile of estrogen metabolites (Schmitz et al., 2015). This modulation may involve increased production of 2-hydroxyestrone, a less biologically active metabolite, relative to the more potent 16 α -hydroxyestrone. Such shifts in estrogen metabolism could contribute to a less proliferative environment for estrogen-sensitive breast cancer cells. Equally important is the impact of aerobic exercise on insulin and insulin-like growth factors (IGFs), which play crucial roles in cell proliferation and survival. Irwin et al. (2009) demonstrated that moderate-intensity aerobic exercise in breast cancer survivors led to significant reductions in fasting insulin levels and improved insulin sensitivity. These changes are particularly relevant given the association between hyperinsulinemia and increased breast cancer risk and progression. The modulation of the insulin/IGF axis through exercise may

involve multiple mechanisms, including enhanced glucose uptake by skeletal muscle, improved insulin receptor sensitivity, and alterations in circulating IGF binding proteins. Pollak (1998) provided early insights into the complex relationship between IGF physiology and breast cancer, laying the groundwork for understanding how exercise-induced changes in this system might influence cancer outcomes. The immune system's role in cancer surveillance and control has gained increasing recognition, and aerobic exercise has been shown to exert significant effects on immune function. One key aspect is the modulation of inflammation and cytokine profiles. Chronic low-grade inflammation is associated with increased cancer risk and progression, and aerobic exercise has demonstrated anti-inflammatory effects. Haley et al. (2020) reported dose-dependent reductions in inflammatory biomarkers among women at high risk of breast cancer following an aerobic exercise intervention. These changes in inflammatory profiles may contribute to a less tumor-permissive environment and enhanced overall immune function. Natural killer (NK) cell function, a critical component of innate anticancer immunity, has also shown responsiveness to aerobic exercise. Studies have reported acute increases in NK cell numbers and cytotoxicity following bouts of aerobic exercise, with potential cumulative benefits from regular training. While the long-term implications of these changes on cancer outcomes require further investigation, the enhancement of NK cell function represents a promising mechanism by which exercise might bolster the body's natural defenses against cancer. Oxidative stress and DNA damage are implicated in cancer initiation and progression, and aerobic exercise has demonstrated potential in mitigating these processes. Regular physical activity has been associated with upregulation of antioxidant defenses and enhanced DNA repair mechanisms. Scott et al. (2011) discussed how exercise-induced adaptations in antioxidant capacity might contribute to the cardioprotective effects observed in breast cancer patients undergoing potentially cardiotoxic treatments. These adaptations may extend beyond cardiovascular protection, potentially offering broader cellular defense against oxidative damage throughout the body. The tumor microenvironment, a complex ecosystem that plays a crucial role in cancer progression and treatment response, has emerged as another target of exercise-induced alterations. Jones et al. (2010) provided compelling evidence from animal models demonstrating that aerobic exercise can modify tumor physiology, including changes in tumor blood flow and oxygenation. These alterations in the tumor microenvironment could have significant implications for treatment efficacy, potentially enhancing the delivery and effectiveness of chemotherapeutic agents. Moreover, exercise-induced changes in the tumor milieu might create less favorable conditions for cancer cell survival and metastasis. Cardiovascular adaptations resulting from regular aerobic exercise represent another critical mechanism underlying its benefits in breast cancer care. The cardiovascular system undergoes significant stress during cancer treatment, particularly with certain chemotherapeutic agents known for their cardiotoxic effects. Aerobic exercise has been shown to induce numerous beneficial adaptations in the cardiovascular system, including improved endothelial function, enhanced cardiac output, and increased capillarization of skeletal muscle. These adaptations not only contribute to improved overall fitness and QOL, but may also provide a protective buffer against treatment-related cardiovascular complications. Scott et al. (2014) explored the potential of exercise to mitigate cancer therapy-induced autonomic dysfunction in early breast cancer, highlighting the complex interplay between exercise, the cardiovascular system, and

cancer treatment. Their work underscores the importance of considering exercise not only as a supportive intervention, but also as a potential modulator of treatment efficacy and long-term cardiovascular health in cancer survivors. The mechanisms by which aerobic exercise influences breast cancer outcomes are multifaceted and interconnected. From hormonal modulation and immune system enhancement to alterations in the tumor microenvironment and cardiovascular adaptations, the effects of exercise permeate multiple physiological systems. This complexity highlights the potential of aerobic exercise as a holistic intervention in breast cancer care, capable of addressing various aspects of the disease and its treatment simultaneously. As research in this field continues to evolve, new insights are emerging into the molecular pathways mediating the effects of exercise on cancer biology. Epigenetic modifications, for instance, have been identified as a potential mechanism by which exercise might influence gene expression patterns relevant to cancer progression. Moulton et al. (2024) explored the relationship between physical activity and epigenetic aging in breast cancer treatment, opening new avenues for understanding how lifestyle factors might influence cancer trajectories at a molecular level. The dose-response relationship between exercise and these physiological mechanisms remains an area of active investigation. While the benefits of moderate-intensity aerobic exercise are well-established, recent studies have begun to explore the potential advantages of higher-intensity or combined exercise modalities. Cheng, Tian, and Mu (2024) conducted a systematic review and meta-analysis examining the effects of combined aerobic and resistance exercise on cardiorespiratory fitness and cardiometabolic health in breast cancer survivors, highlighting the potential for synergistic benefits from multi-modal exercise approaches. Understanding these physiological mechanisms is crucial not only for elucidating the benefits of exercise in breast cancer care, but also for optimizing exercise prescriptions and identifying potential biomarkers of exercise efficacy. As our knowledge deepens, it may become possible to tailor exercise interventions based on individual patient characteristics, tumor biology, and treatment regimens, moving towards a more personalized approach to exercise oncology. The physiological adaptations induced by aerobic exercise extend beyond direct effects on cancer biology, encompassing broader aspects of health that are relevant to cancer survivorship. For instance, the improvements in cardiovascular health and metabolic function associated with regular aerobic exercise may contribute to reduced risk of comorbidities that can complicate cancer treatment and long-term survival. This holistic impact underscores the potential of aerobic exercise as a multi-target intervention in comprehensive cancer care.

In conclusion, the physiological mechanisms underlying the benefits of aerobic exercise in breast cancer are diverse and interconnected, spanning hormonal, immune, cellular, and systemic processes. From modulating estrogen metabolism and insulin signaling to enhancing immune function, reducing oxidative stress, altering the tumor microenvironment, and improving cardiovascular health, aerobic exercise emerges as a powerful tool capable of influencing multiple aspects of cancer biology and overall health. As research in this field continues to advance, our growing understanding of these mechanisms will likely lead to more refined and effective exercise interventions, potentially revolutionizing the role of physical activity in breast cancer prevention, treatment, and survivorship care.

Methodological Considerations in Aerobic Exercise Research

The landscape of aerobic exercise research in breast cancer populations is characterized by diverse study designs and methodological considerations, with

RCTs emerging as the gold standard for establishing causal relationships between exercise interventions and cancer-related outcomes (Courneya et al., 2007; Milne et al., 2008). However, the complexities of cancer care often pose challenges to strict randomization and blinding procedures, necessitating the use of quasi-experimental and observational studies to explore long-term effects and real-world implementation (Courneya et al., 2007). Exercise prescription parameters, including intensity, duration, and frequency, form a critical component of methodological considerations. Intensity, often measured as a percentage of maximal heart rate or oxygen uptake, has been shown to influence physiological adaptations and patient adherence (Scott et al., 2014; Dolan et al., 2016). Studies have explored various intensity ranges, from moderate to high-intensity interval training, revealing potential dose-response relationships with outcomes such as cardiorespiratory fitness and biomarker modulation (Haley et al., 2020). Courneya et al. (2007) conducted a landmark RCT prescribing moderate-intensity aerobic exercise at 60-80% of peak oxygen consumption for breast cancer patients undergoing chemotherapy, demonstrating improvements in physical functioning and QOL. Building on this, Dolan et al. (2016) compared moderate continuous and high-intensity interval training, revealing that both protocols were feasible and beneficial for breast cancer survivors, with high-intensity intervals showing potential for greater improvements in cardiorespiratory fitness. Duration and frequency of exercise sessions are closely intertwined with intensity in determining the overall exercise dose. The American College of Sports Medicine recommends 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic activity per week for cancer survivors (Schmitz et al., 2015). However, research suggests that even lower volumes may confer benefits. Drouin et al. (2005) found that a program of 20-45 minutes of moderate-intensity aerobic exercise, performed 3-5 times per week during radiation therapy, improved peak aerobic capacity and reduced fatigue in breast cancer patients. The timing of aerobic exercise interventions in relation to cancer treatment presents another layer of methodological complexity. Studies have examined exercise programs implemented before (rehabilitation), during, and after various cancer treatments, including chemotherapy, radiation therapy, and endocrine therapy (Drouin et al., 2005; Bender et al., 2024). Each timing strategy offers unique opportunities and challenges. Pre-treatment exercise interventions may enhance physiological reserves and treatment tolerability, while concurrent exercise during treatment may mitigate side effects and maintain functional capacity. Post-treatment programs focus on rehabilitation and long-term survivorship outcomes. Exercise during cancer treatment has been extensively studied in breast cancer populations. Yang et al. (2015) found that a moderate-intensity aerobic exercise program implemented during radiotherapy significantly reduced fatigue in breast cancer patients. Post-treatment interventions, such as the Yale Exercise and Survivorship study conducted by Irwin et al. (2009), have shown potential for favorable changes in biomarkers and long-term health outcomes. Measurement and assessment tools play a crucial role in quantifying the effects of aerobic exercise interventions, with a wide range of outcome measures employed, including objective physiological parameters, biomarkers, and patient-reported outcomes (McNeely et al., 2006; Jones et al., 2010; Zhao et al., 2024). Standardization of assessment tools across studies remains a challenge, complicating meta-analyses and comparisons between interventions. Conducting exercise trials in cancer populations presents unique challenges, including patient recruitment, retention, and adherence to exercise protocols, given the physical

and emotional burdens of cancer diagnosis and treatment (Soriano-Maldonado et al., 2019). Safety considerations are paramount, requiring careful screening, monitoring, and individualized exercise prescriptions (Schmitz et al., 2015).

In conclusion, while general guidelines provide a framework for exercise prescription in breast cancer populations, the heterogeneity of patient characteristics and treatment regimens necessitates individualized approaches. Intensity, duration, frequency, and timing of interventions should be tailored to each patient's physical condition, treatment status, and personal goals. Future research should continue to refine these parameters to optimize the benefits of aerobic exercise for breast cancer patients and survivors across different stages of the cancer journey, while addressing the methodological challenges inherent in this field of study.

Clinical Implementation of Aerobic Exercise in Breast Cancer Care

The clinical implementation of aerobic exercise in breast cancer care demands a practical, patient-centered approach that seamlessly integrates evidence-based recommendations with real-world considerations. To effectively incorporate aerobic exercise into breast cancer treatment and survivorship plans, healthcare providers should initiate exercise conversations early in the care continuum, framing exercise as a crucial component of treatment rather than an optional add-on. This early engagement sets the stage for patient expectations and motivation, paving the way for long-term adherence (Haley et al., 2020). A cornerstone of successful implementation is the conducting of individualized assessments prior to exercise prescription. These assessments should comprehensively evaluate the patient's current fitness level, treatment plan, and any pre-existing conditions, informing a tailored exercise program that accounts for unique needs and limitations (Campbell et al., 2019). With this foundation, healthcare providers can recommend starting low and progressing gradually, particularly for patients new to exercise or experiencing treatment-related fatigue. A common approach is to begin with short, low-intensity activities, such as 10-15-minute walks three times a week, gradually increasing to 30 minutes five times a week over several weeks (Courneya et al., 2007). Safety considerations must be paramount in exercise recommendations. Patients should be educated on proper exercise techniques and potential red flags that warrant cessation of activity and medical attention. For those at risk of lymphedema, wearing compression garments during exercise and initiating upper body exercises conservatively are prudent precautions (Dolan et al., 2016). To enhance adherence and enjoyment, healthcare providers should offer diverse exercise options, recognizing that patient preferences vary widely. Walking, cycling, swimming, or dance-based activities can all serve as effective aerobic exercise modalities, allowing patients to choose activities that resonate with their interests and capabilities (Pinto, Stein, and Dunsiger, 2020). In today's technology-driven world, leveraging smartphone apps and wearable devices can significantly boost motivation and help patients track their progress. These tools offer tangible ways for individuals to monitor improvements over time, fostering a sense of accomplishment and encouraging consistency. Complementing technology-based approaches, group-based exercise programs designed specifically for cancer patients or survivors, can provide invaluable social support and structured guidance, further enhancing motivation and adherence (Wurz, St-Aubin, & Brunet, 2016). Coordination with the entire treatment team is essential for the successful integration of exercise into breast cancer care. Ensuring that exercise recommendations are communicated to all members of the patient's oncology team helps prevent conflicting advice and allows

for timely adjustments to the exercise plan based on treatment side effects or changes in the patient's condition (Santa Mina et al., 2018). This collaborative approach extends to proactively addressing barriers to exercise participation. Healthcare providers should work closely with patients to identify potential obstacles, such as time constraints, fatigue, or lack of facilities, and develop tailored strategies to overcome them. Solutions might include recommending home-based exercises, scheduling workouts during peak energy times, or connecting patients with community resources (Courneya et al., 2007). Regular monitoring and adjustment of exercise programs are crucial for long-term success. Scheduling follow-ups to assess patient progress allows for timely modifications based on treatment response, side effects, or changes in overall health status (Jones et al., 2018). When possible, timing exercise sessions to complement cancer treatments can enhance overall care. For instance, encouraging light activity on days following chemotherapy may help manage fatigue and nausea, thus improving treatment tolerance (Kirkham et al., 2018). Educating patients on the long-term benefits of exercise is vital for maintaining motivation beyond active treatment. Discussing the potential for reducing recurrence risk and improving overall health outcomes can inspire sustained adherence to exercise routines (Courneya et al., 2007). Healthcare providers play a crucial role in advocating for supportive policies within their institutions. Championing initiatives such as on-site exercise facilities, reimbursement for exercise services, or partnerships with community fitness programs can significantly enhance the accessibility and sustainability of exercise interventions for breast cancer patients (Schmitz et al., 2020).

By implementing these integrated strategies, healthcare providers can effectively weave aerobic exercise into the fabric of breast cancer care, potentially improving treatment outcomes, QOL, and long-term health for their patients. The ultimate goal is to make exercise an accessible, enjoyable, and sustainable part of the cancer care journey, adapting approaches as needed to meet each patient's unique circumstances and preferences. As the field of exercise oncology continues to evolve, ongoing research and clinical experience will further refine these recommendations, ensuring that breast cancer patients receive the most effective and personalized exercise interventions possible.

Conclusion

This comprehensive review has highlighted the substantial and multifaceted impact of aerobic exercise on breast cancer outcomes. The evidence synthesized from numerous studies demonstrates that aerobic exercise interventions can positively influence various aspects of breast cancer care, from prevention to treatment and long-term survivorship. Significant benefits have been observed in areas such as cardiorespiratory fitness, body composition, cancer-related fatigue, QOL, and psychological well-being. Moreover, emerging research suggests potential effects on cancer-specific outcomes, including reduced recurrence rates and improved overall survival. The mechanistic underpinnings of these benefits appear to involve multiple pathways, including modulation of hormonal profiles, enhancement of immune function, reduction of oxidative stress, and alteration of the tumor microenvironment.

Despite the growing body of evidence supporting the integration of aerobic exercise into comprehensive breast cancer care strategies, several important questions remain. Future research should focus on elucidating the optimal exercise prescriptions for different breast cancer subtypes and treatment regimens. Long-term

follow-up studies are needed to better understand the sustained effects of exercise interventions on cancer recurrence and survival. Additionally, investigating the potential synergistic effects of combining aerobic exercise with other therapeutic modalities, such as targeted therapies or immunotherapies, represents an exciting frontier in oncology research.

As the field of exercise oncology continues to evolve, there is a pressing need for large-scale, well-designed RCTs to further validate the effects of aerobic exercise on breast cancer outcomes. Future studies should also explore the potential for personalized exercise prescriptions based on individual patient characteristics, genetic profiles, and tumor biology. Moreover, research into the implementation and dissemination of exercise interventions in real-world clinical settings will be crucial for translating scientific findings into widespread practice. By addressing these research gaps, we can continue to refine and optimize the role of aerobic exercise in breast cancer care, ultimately improving outcomes and enhancing QOL for those affected by this disease.

Conflict of Interests

Authors have no conflict of interests.

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