



Exercise Across the Phases of Cancer Survivorship: A Narrative Review

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Exercise has long been recognized as an important component of treatment for various diseases. However, the benefits and risks of exercise interventions must be carefully evaluated to ensure the former outweighs the latter. As cancer patients undergo diverse treatment modalities with distinct objectives, a systematic approach partitioning the cancer journey into distinct phases is necessary to inform tailored exercise prescriptions. This narrative review summarizes exercise benefits and mechanisms for cancer patients and survivors across four distinct survivorship periods—before surgery, after surgery and before adjuvant treatment, during nonsurgical treatment (adjuvant and neoadjuvant), and during extended survival. In summary, exercise reduces the risks of complications and declines in physical functioning while improving fatigue, quality of life, and the ability to manage treatment effects. Although additional research is warranted, existing evidence is sufficient to integrate exercise into clinical oncology practice and cancer survivorship programs.

Key Words: Exercise, neoplasms, cancer survivors, adjuvant chemotherapy

INTRODUCTION

Is exercise a medicine? This inquiry, while contemporary in its phrasing, builds upon the longstanding recognition that exercise and physical activity have historically been vital components in the treatment paradigm for various diseases.¹ When evaluating novel therapeutic interventions, a comprehensive analysis of the associated benefits and risks is imperative, ensuring that the former significantly outweighs the latter. In this

context, the systematic implementation of exercise-based cardiac rehabilitation, structured according to the phases of cardiac rehabilitation, has a long and well-established history supported by robust evidence. This approach is delineated into four phases: Phase I: Inpatient rehabilitation; Phase II: Outpatient rehabilitation; Phase III: Maintenance and community-based programs; and Phase IV: Long-term exercise and lifestyle management.² Each phase is strategically designed to cater to the dynamic needs of cardiac patients throughout their recovery trajectory. This structured, phase-based methodology empowers clinicians to customize exercise-based cardiac rehabilitation protocols, aligning with the distinctive risk-benefit profile inherent to each stage of patient convalescence and recovery. Although the primary objectives of exercise regimens and the multifaceted treatment modalities for cancer patients diverge substantially from those for cardiac patients, the potential applicability of a systematic, phase-based approach in oncological care may find parallels in cardiac rehabilitation.

As exercise specialists, we routinely encounter inquiries con-

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cerning the safety and efficacy of exercise interventions for cancer patients. In response, we assess the patient's precise position within their cancer treatment continuum. This inquiry entails ascertaining whether the patient is in the preoperative or postoperative phase, undergoing neoadjuvant or adjuvant therapy, receiving maintenance therapy, or receiving palliative care. These questions are of paramount significance within the scope of our practice, as they underscore the critical point that the safety and potential benefits of exercise regimens are inherently dependent on the specific phase of a patient's oncological journey. Exercise prescription is intrinsically linked to the targeted objectives or anticipated outcomes of the exercise regimen. Within this framework, reference can be made to the organizational model devised by Courneya and Friedenreich³ entitled "Physical Exercise Across the Cancer Experience (PEACE)." This model segments the cancer journey into six distinct temporal points: two pre-diagnosis and four post-diagnosis stages. This structured approach offers a comprehensive perspective to discern the appropriate exercise interventions tailored to each specific phase of the patient's cancer trajectory,³ somewhat comparable to phases of cardiac rehabilitation. It has also laid a critical foundation for comprehending the potential benefits and underlying mechanisms of exercise interventions, guided by expected outcomes, within the realm of cancer care.

Another temporal framework, which holds significant relevance to cancer survivorship, is the "Seasons of Survival" framework. Propounded by Fitzhugh Mullan, drawing from his personal confrontation with a cancer diagnosis and treatment, this framework demarcates the cancer survivorship continuum into three distinct phases: acute survivorship, extended survivorship, and permanent survivorship. Such delineation offers profound insights into the evolving challenges and needs of patients as they navigate their unique cancer journeys, emphasizing the multifaceted nature of survivorship and the diverse interventions required at each juncture.⁴ While the "Seasons of Survival" framework does not explicitly address the domain of physical activity and exercise, it offers valuable insights into the evolving phases of survivorship.

In the acute survivorship phase, patients undergo a spectrum of therapeutic modalities, including surgery, as well as neoadjuvant and adjuvant treatments. Although supportive care measures can ameliorate some of the side effects arising from these therapies, the majority of cancer survivors continue to grapple with varying degrees of treatment-related adverse effects. Miller, et al.,⁵ in their work, extended the "Seasons of Survivorship" framework, introducing the concept of "transitional survivorship" and further refining the definitions of "extended survivorship" and "permanent survivorship". This expansion and diversification of the framework provided a more nuanced understanding of the survivorship experience. It caters to the multifaceted and evolving needs of cancer survivors as they progress through their unique journeys, thereby enriching the conceptual landscape of survivorship within the context of can-

cer care.⁵ "Transitional survivorship" encompasses a phase that includes periods of "watchful waiting" or the continuation of some form of maintenance therapy. During this phase, the level of involvement from the medical team tends to decrease, and it becomes increasingly important for patients to actively manage their health and well-being. Exercise and physical activity can play a crucial role during this time, offering not only physiological benefits but also significant psychological advantages. Engaging in regular physical activity can help cancer survivors regain a sense of control over their bodies, reduce anxiety, and improve their overall quality of life (QoL) during this transitional period.

In the context of cancer survivorship, the combination of the "Seasons of Survivorship" and PEACE framework allows for a more detailed categorization of the "acute survivorship" phase, encompassing not only the post-treatment aspect but also the pre-treatment phase, which can be referred to as "prehabilitation." The "Seasons of Survivorship" framework, specifically "acute survivorship", primarily focuses on the post-treatment phase. Meanwhile, the PEACE framework emphasizes the entire cancer journey, including the pre-treatment period. To provide a more comprehensive understanding of this combined approach, the current narrative review divides cancer survivorship into four distinct periods: 1) after cancer diagnosis and before surgery: prehabilitation; 2) after surgery and before adjuvant treatment; 3) during nonsurgical treatments (adjuvant and neoadjuvant); and 4) during extended survival including transitional survivorship, which may include transitional survivorship or resumption, emphasizing the evolving needs of survivors who are post-treatment (Fig. 1). This narrative review summarized the benefits of exercise that cancer survivors may experience along their treatment journey.

BENEFICIAL EFFECTS OF EXERCISE FOR CANCER SURVIVORS

After cancer diagnosis and before surgery:

Prehabilitation

After the diagnosis of cancer, patients usually have an average waiting period of more than 1 month before surgery^{6,7} and experience high anxiety, depression, and feelings of loss.⁸ In addition, lower physical and psychological conditions preceding surgery not only induce delayed postoperative recovery (i.e., extended hospital stay and increased likelihood of post-surgical complications) but also elevate the risk of overall mortality in cancer survivors.⁹⁻¹¹ Thus, the period between cancer diagnosis and the initiation of treatment has recently emerged as more than a mere waiting time; it is now recognized as a critical window of opportunity to prepare patients for challenging cancer treatments.

Cancer prehabilitation is defined as a targeted intervention between the time of cancer diagnosis and the initiation of acute

PEACE	Seasons of survival	Current review
Prescreening		
Screening		
Pretreatment	Acute survivorship	After cancer diagnosis and before initiating active treatment
Treatment		After surgery before initiating adjuvant treatment
		During nonsurgical treatment
Posttreatment	Extended survivorship	Extended survival including transitional survivorship
Resumption	Permanent survivorship	

Fig. 1. Comparison of the phases of cancer trajectory in the current review. PEACE, Physical Exercise Across the Cancer Experience.

treatment, and is implemented to alleviate physical and psychological vulnerabilities caused by cancer treatment.^{12,13} Exercise serves as a crucial interventional method in cancer prehabilitation, exerting a positive influence on the patient's treatment prognosis and subsequent post-surgical recovery. A review paper reported that cancer patients with higher levels of physical activity before surgery had shorter length of hospital stay [odds ratio (OR)=3.66; 95% confidence interval (CI)=1.38 to 9.6] and higher QoL after surgery (OR=1.29; 95%CI=1.11 to 1.49) compared to their counterparts.¹⁴ Moreover, preoperative exercise benefits weight and fat loss in obese cancer patients and lowers the risk of surgery-related adverse effects, including surgical complications, blood loss, and prolonged surgical durations.¹⁵⁻¹⁷ It also helps preserve muscle mass in individuals with esophageal cancer¹⁸ and enhances cardiopulmonary function and muscle strength in those with lung cancer.¹⁹

The phase after cancer diagnosis and before surgery provides a valuable opportunity for behavioral change.^{16,20} Preoperative exercise has been reported to be an important factor in completing the patient's planned treatment, promoting recovery after treatment, and having a positive effect on cancer prognosis. Therefore, increasing literacy among patients about the importance of exercise and intensively modifying their behavior to make it a habit might play a leading role in completing the cancer treatment journey during this period. The American Society for Clinical Oncology²¹ now recommends exercise for lung cancer patients prior to surgery. Additional research will likely expand this recommendation to other cancer patients prior to surgery and prior to other first-line treatments.

After surgery and before adjuvant treatment

Surgery is one of the primary therapeutic modalities for achieving cure or complete or partial tumor resection.²² Despite advancements in surgical techniques, approximately one-third of cancer patients undergoing surgery encounter various complications and postoperative issues, such as pain, decreased phys-

ical function, and reduced QoL.^{23,24} In particular, muscle mass loss after surgery in cancer patients has a significant impact on survival rates.^{25,26} In many clinical settings, cancer patients may have 4–6 weeks of recovery after surgery prior to initiating adjuvant therapy. Furthermore, delayed initiation of chemotherapy due to prolonged postoperative recovery has an adverse effect on survival.²⁷⁻²⁹

Postoperative exercise, or rehabilitation, is a major intervention that facilitates patient recovery and positively affects prognosis. Early mobilization, and a representative postoperative exercise intervention, effectively reduces postoperative cardiopulmonary complications, prevents thromboembolism, alleviates pain, mitigates bowel obstruction, and enhances gastrointestinal activity.^{30,31} Ahn, et al.³² suggested that preserving lower body strength is more critical for recovery of post-surgery colorectal cancer patients. A follow-up study that examined the efficacy of postoperative exercise in a clinical pathway setting also found that a resistance and balance exercise program for postoperative colorectal cancer patients shortened hospital stay, improved readiness for discharge, and enhanced body composition and fitness.³³ In particular, post-surgery exercise could contribute to alleviating surgery-related complications and side effects.³⁴ For example, postoperative exercise in breast cancer patients improved shoulder function, pain, and QoL, facilitating recovery after surgery.³⁵ A recent meta-analysis in colorectal and lung cancer patients found that post-surgery exercise improves physical health-related QoL and enhances physical function and fatigue management.³⁶

In summary, postoperative exercise contributes to alleviating surgery-related physical function decline and muscle loss, as well as providing relief from treatment-induced pain. Additionally, it has the potential to reduce psychological anxiety and depression, facilitating patient recovery and enhancing their physical and psychological readiness for subsequent adjuvant treatments. While postoperative exercise may impact cancer prognosis, the scientific foundation for timing and evidence-based exercise programs remains limited. Long-term benefits and implications for future treatment and prognosis require further large-scale studies across different cancer types and populations.

During nonsurgical treatments (adjuvant and neoadjuvant)

The positive effects of exercise during nonsurgical treatments (e.g., chemotherapy, radiation therapy, hormone therapy, targeted therapy, immunotherapy) have been reported in many systematic reviews and meta-analyses. Most of these studies have focused on breast and colorectal cancers, although there are several that have investigated mixed cancer patients. The main benefits of exercise during nonsurgical cancer treatment include reducing side effects and improving treatment-related outcomes based on incorporating evidence.

The most common side effect examined in previous studies

was fatigue. Several systematic reviews and meta-analyses³⁷⁻⁴⁰ consistently reported that exercise significantly reduced fatigue during adjuvant treatment (e.g., chemotherapy and/or radiation therapy) in breast cancer. Moreover, the positive effects were even larger when pooling the results of the supervised interventions only.^{38,40} In the case of colorectal cancer patients, there were not as many systematic reviews or meta-analyses available as there were for breast cancer studies. However, the findings showed results consistent with those of breast cancer studies.^{41,42} Physical fitness was the second most common outcome examined. The findings showed that exercise intervention during adjuvant therapy significantly improved cardiorespiratory fitness,³⁹ muscular strength,^{39,43} and lean mass⁴³ in breast cancer patients. One study³⁹ reported additional benefits on breast cancer-specific outcomes, such as shoulder mobility, upper body function, arm mobility, and lymphedema, during treatment, demonstrating the efficacy of exercise as a rehabilitation therapy after surgery. For colorectal cancer patients, one meta-analysis found no significant effects of exercise during chemotherapy on aerobic fitness, muscular strength, and body composition.⁴¹ Regarding psychological outcomes, the results were controversial, possibly due to differences in assessment instruments among studies. One meta-analysis³⁷ showed significant effects of exercise on depression and borderline significant effects on anxiety, while another meta-analysis³⁹ reported results from individual studies demonstrating non-significant effects on anxiety, distress, and self-esteem during breast cancer treatment. For colorectal cancer, one meta-analysis⁴¹ reported no significant difference in depression between the exercise and the control groups. The evidence on QoL was also controversial for both breast and colorectal cancer patients. Carayol's meta-analysis³⁷ reported significant beneficial effects, while Lipsett's meta-analysis⁴⁰ reported non-significant effect in breast cancer patients. For colorectal cancer, Lund's meta-analysis⁴¹ found that exercise significantly improved QoL; however, Dun's meta-analysis⁴² reported inconsistent results depending on the subscale of QoL, with significant beneficial effects on the QoL-social factor but non-significant effects on the QoL-cognitive and physiological factors. Furmaniak, et al.³⁹ reported additional beneficial effects of exercise on physical activity behavior in breast cancer patients from a meta-analysis of seven studies.

Another crucial aspect of exercise during nonsurgical cancer treatments involves improving treatment-related outcomes, such as treatment tolerance, cancer-related biomarkers, and potential cancer recurrence. This aspect is significantly important to demonstrate the potential of exercise as a cancer treatment, as noted by Courneya and Booth⁴⁴ in the Exercise as Cancer Treatment (EXACT) Framework. However, as there is still insufficient evidence from systematic reviews and meta-analyses on these outcomes, we will introduce several individual studies. Bland, et al.'s⁴⁵ systematic review examined the impact of exercise on chemotherapy completion rate based on

eight randomized controlled trials. Out of the eight trials included, only two trials^{46,47} that were conducted in breast cancer patients reported significant beneficial effects of exercise on chemotherapy completion. Specifically, the START trial by Courneya, et al.⁴⁶ compared three arms (aerobic exercise, resistance exercise, and usual care group) and showed that resistance exercise significantly improved chemotherapy completion compared to the usual care groups. Additionally, both the aerobic and resistance exercise groups exhibited trends toward improving disease-free and overall survival, although these results did not reach statistical significance. Another randomized controlled trial, PACES by van Waart, et al.,⁴⁷ compared a home-based low-intensity exercise, a supervised moderate- to high-intensity combined aerobic and resistance program, and a usual care group. The results demonstrated that the supervised moderate to high-intensity exercise group required approximately four times fewer dose adjustments in the prescribed chemotherapy regimen compared to the usual care and low-intensity exercise group ($p=0.002$). Additionally, the average dose reduction in the two exercise groups was significantly lower (10%) than the usual care group (25%) ($p=0.014$). More recently, Courneya and his team pooled data from the START and another RCT, the CARE trial, to explore the predictors of chemotherapy completion in 543 breast cancer patients.⁴⁸ The findings showed that cardiovascular fitness and muscular strength before chemotherapy were the strongest predictors of chemotherapy completion, which underscored that exercise to improve physical fitness before treatment may improve treatment tolerance.

For colorectal cancer patients, Van Vulpen's study⁴⁹ reported that the relative dose intensity was higher (82%) in the exercise intervention group compared to the usual care group (76%), although the result was not statistically significant ($p=0.8$). A Phase II RCT, EXERT,⁵⁰ found that the number of participants who achieved a pathologic complete response/near pathologic complete response was significantly higher in the exercise group (56%) compared to the usual care group (18%) ($p=0.020$) in rectal cancer patients undergoing neoadjuvant chemoradiation therapy. As additional benefits, one systematic review⁵¹ reported that exercise improved biomarkers, such as insulin-like growth factor (IGF)-1, IGF-II, CD-4 cells, immune function, and decreased inflammatory markers in mixed cancer patients during and after treatment. Based on existing evidence, the American Society of Clinical Oncology²¹ now recommends exercise during treatment with curative intent to improve fitness, symptom management, and QoL for all cancer patients. Evidence for exercise as a cancer treatment was deemed insufficient.

During extended survival (including transitional survivorship)

Exercise is gaining growing recognition as a crucial approach for aiding the recovery and rehabilitation of individuals who have survived cancer. Numerous studies have shown that en-

gaging in exercise helps alleviate various physical and psychological issues after cancer treatment. Cancer survivorship after cancer treatment can be separated into an acute rehabilitation period and a longer-term disease prevention/health promotion period (long-term survivorship).⁵²

During the rehabilitation period, the objective is to manage the immediate treatment-related side effects and support a return to the level of health experienced prior to treatment. When examined in clinical trials, the impact of exercise on cancer patients who completed their treatment approximately within 1–2 years revealed compelling evidence.⁵³ These trials, including mixed but primarily breast cancer, revealed that exercise interventions comprising aerobic and/or resistance training programs led to notable enhancements in various aspects of health, including physical functioning, strength, levels of physical activity, QoL, fatigue, immune function, hemoglobin concentrations, potential markers of recurrence, as well as body composition.

Exercise was shown to be beneficial for cancer patients not only in the immediate rehabilitation periods but also after several years of cancer treatment (long-term survivorship). For post-treatment breast cancer patients, there is strong evidence that exercise interventions, such as aerobic, resistance and stretching exercises, can significantly improve pain, fatigue, upper limb dysfunction, lymphoedema, and QoL.^{54,55} Moreover, exercise appears safe and feasible overall, particularly for alleviating shoulder pain and improving mobility. Similarly, for post-treatment colorectal cancer patients, exercise was feasible and effective for improving physical function (e.g., cardiopulmonary fitness), metabolic growth factors (e.g., insulin and insulin resistance), and tumor related biomarkers, while less consistent results were shown for body composition and psychological outcomes.⁵⁶ Insufficient intervention studies have been conducted to provide concrete evidence of positive effects of exercise after cancer treatment for other types of cancer patients. It is worth noting that the majority of previous studies focused on breast cancer patients and had relatively small numbers of participants, ranging from 10 to 100. Some of the trials also used non-randomized group allocation. Despite some methodological limitations, available evidence suggests that incorporating exercise is both viable and potentially advantageous for the physical and psychological well-being of cancer survivors throughout the rehabilitation phase.

Although randomized controlled trials have rigorous study design for causal inference, it is less feasible to conduct clinical trials to investigate the effects of exercise on long-term survival. For this reason, a number of observational prospective cohort studies have been conducted to examine the long-term prognosis of cancer patients, and they showed that higher levels of physical activity after diagnosis (usually well after treatments) was associated with decreased risk of all-cause, breast cancer-specific, and colon cancer-specific mortality.⁵⁷ In 2018, the American College of Sports Medicine convened an Interna-

tional Multidisciplinary Roundtable to evaluate the epidemiological evidence on physical activity and cancer survival. They reported consistent and compelling conclusion that post-diagnosis physical activity is associated with improved long-term prognosis.⁵⁸ Compared to those in the lowest postdiagnosis physical activity group, cancer patients in the highest post-diagnosis physical activity group had approximately 26%–69% lower cancer-specific mortality and 21%–45% lower all-cause mortality. These findings were predominantly from breast, colorectal, and prostate cancer patients with limited evidence for other cancer sites.^{59,60} Based on this evidence, the American Cancer Society⁶¹ recommends exercise for long-term cancer survivors to reduce their risk of recurrence and improve survival.

PROPOSED MECHANISMS FOR BENEFICIAL EFFECTS OF EXERCISE FOR CANCER SURVIVORS

The roles of exercise as an effective therapeutic strategy for cancer have been widely studied through preclinical and clinical investigations. Beyond its roles in enhancing physical fitness/function and psychological health, exercise exerts intricate bio- and physiological effects that can modulate various cancer-related outcomes. Here, we will elucidate the biological and treatment-related mechanisms of exercise before and after surgery and during survivorship.

Before surgery

Exercise can be offered during the prehabilitation period (i.e., after diagnosis and before surgery), in which exercise may reduce or inhibit tumor suppression through various mechanisms. One mechanism is that exercise-induced stress responses modulate the production of inflammatory cytokines, increasing or reducing the chronic and systemic biomarkers of inflammation associated with cancer progression,⁶² such as lowering levels of C-reactive protein,⁶³ where anti-inflammatory effect may indirectly inhibit tumor growth and micro-metastasis. Moreover, exercise can increase the circulation of immune cells, such as natural killer (NK) cells and cytotoxic T cells, which are essential for recognizing and eliminating cancer cells.⁶⁴ For example, one study that investigated the effects of a short-term exercise (approximately 30 days) before surgery in breast cancer patients demonstrated upregulation of genes associated with anti-tumor inflammatory and immune response in tumor tissues (e.g., elevated NK cell-mediated cell cytotoxicity and T-cell signaling pathway).⁶⁵

Another mechanism is through blood vessels and perfusion around tumor cells. One of the hallmarks of cancer is the hypoxic status and thereby uncontrolled growth of abnormal cells, where exercise can increase the blood flow and deliver oxygen to induce apoptosis.⁶⁶ Additionally, exercise can enhance insulin sensitivity, potentially reducing the risk of insulin-driven

tumor growth.^{67,68} When it comes to neoadjuvant treatment settings to reduce the tumor size prior to surgery, exercise has been shown to have further benefits by facilitating the delivery of cancer treatments, such as chemotherapy and even radiation, and improving the efficacy of the treatments.⁶⁹ In this regard, significantly better pathological complete response (53% vs. 28%) among breast cancer patients who were randomly assigned to exercise and nutritional intervention during neoadjuvant chemotherapy is worth noting.⁷⁰ Lastly, exercise can alter tumor metabolism by increasing glucose uptake and oxidative stress in cancer cells, which can make cancer cells more vulnerable to the cytotoxic effects of neo-adjuvant chemotherapy and radiation therapy.⁷¹

After surgery

Surgery induces a potent inflammatory response that can impair wound healing and increase the risk of complications. Regular exercise after surgery can attenuate this post-surgical inflammatory response, leading to improved wound healing and reduced risk of postoperative complications.^{72,73} Furthermore, postoperative pain and fatigue are common concerns for cancer surgery patients. Exercise has analgesic effects through the release of endorphins and anti-inflammatory biomarkers, which in turn could reduce not only the pain and fatigue itself but also the need for pharmacological intervention to manage pain or fatigue, minimizing the risk of their side effects.^{74,75} In addition, physical conditioning and movement immediately after surgery in colorectal cancer patients can potentially help early hospital discharge by recovering physical functioning and facilitating gut movements.³²

During nonsurgical treatments

Another emerging yet plausible mechanism is that exercise may improve treatment outcomes through various biological mechanisms. Exercise has been shown to improve the function of blood vessels not only at systemic levels but also at peripheral and tumoral levels, which can enhance the delivery and perfusion of chemotherapy to the target tumor cells.⁶⁹ This can also be applied to radiation treatment, where exercise could reduce radiation-induced damages through enhancing antioxidant activity and DNA repair,⁷⁶ and may act as a “radiosensitizer” to increase the efficacy of radiation therapy through inhibiting tumor hypoxia, which is a key limiting factor of radiation therapy.⁵⁰ Moreover, it has been reported that exercise can improve cancer treatment tolerance and completion rate, which is directly associated with disease-free survival. The mechanism through which this occurs is by improving physical fitness, lean muscle mass, and managing side effects, such as fatigue and pain.⁴⁵

Survivorship

Cancer survivors often face elevated risks of comorbidities, such as cardiovascular and metabolic diseases, as certain cancer treatments induce long-term cardiotoxicity (e.g., anthracycline-

based chemotherapy)⁷⁷ or metabolic dysregulation (e.g., sex hormone suppressing treatment for breast and prostate cancers).^{78,79} It is well-established that regular exercise helps reduce cardiometabolic risk factors, including hypertension, dyslipidemia, and insulin resistance, thereby reducing the risks of developing comorbidities and improving long-term health.⁸⁰ Additionally, many cancer survivors report cognitive impairments commonly referred to as “chemo brain.” Exercise interventions have demonstrated potential in improving cognitive function through mechanisms that enhance neuroplasticity, neurogenesis, and cerebral blood flow.⁸¹ Moreover, cancer survivors frequently experience psychological distress, including anxiety and depression. Regular exercise has well-documented mood-regulating effects, attributed to the release of endorphins and neurotransmitter modulation, which reduce symptoms of anxiety and depression, improving the overall psychological well-being.⁸² It is important to note that such comorbidities and treatment symptoms can be present in the survivorship period but can start to develop during cancer treatment or even before treatment (e.g., psychological distress after diagnosis), which warrants to consider that exercise can be incorporated as early as possible to manage comorbidities and side effects.

Another potential role of exercise during survivorship could be its role in reducing the risks of cancer recurrence, metastasis, and eventually improving disease-free survival.⁶⁶ Although evidence exists from epidemiological and preclinical research with a lack of clinical research, the suggested mechanisms include the following: 1) Increased immuno-surveillance: Exercise can stimulate the infiltration and activation of immune cells (e.g., NK cells), which can recognize and kill tumor cells; 2) Decreased vascular permeability and metastasis: Exercise can reduce the leakiness of tumor blood vessels, which may prevent cancer cells from escaping into the circulation and forming metastatic sites. Exercise may also maintain the integrity of the blood-brain barrier, thus protecting the brain from metastatic invasion; and 3) Increased tumor perfusion and oxygenation: Exercise can enhance blood flow and oxygen delivery to the tumor tissue, thus reducing hypoxia and inducing apoptosis. Exercise may also induce vascular remodeling and maturation in the tumor microenvironment, resulting in more uniform and stable perfusion.⁶⁶

Exercise has emerged as a valuable adjunctive tool in cancer care, with its mechanisms surrounding the phases of cancer treatment. A comprehensive understanding of the biological and treatment-related mechanisms of exercise is critical for the development of personalized exercise interventions that can improve cancer outcomes, minimize treatment-related complications, and enhance the overall well-being and QoL for cancer patients and survivors. However, further research, especially translational and clinical research, is warranted to further explore such mechanisms in clinical settings in order to refine exercise prescriptions, optimize timing, and establish guidelines for integrating exercise into routine cancer care protocols.⁸³

SUMMARY AND IMPLICATIONS

Exercise plays an important role across the entire cancer continuum. Exercise prescriptions must be tailored to the phase of the cancer trajectory. From a supportive care perspective, exercise helps cancer patients prepare for treatments, cope with treatments, and recover after treatments. From a cancer treatment perspective, exercise may help cancer patients complete treatments, respond to treatments, and lower their risk of recurrence and death from cancer. Although additional research is warranted, existing evidence is sufficient to implement exercise interventions in clinical oncology practice and cancer survivorship programs.

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AUTHOR CONTRIBUTIONS

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