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REVIEW

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Exercise medicine for advanced prostate cancer

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Purpose of review
Exercise is a provocative medicine, known for its preventive, complimentary and rehabilitative role in the management of cancer. Impressively, exercise is also emerging as a synergistic and targeted medicine to enhance symptom control, modulate tumour biology and delay disease progression, with the potential to increase overall survival. Given the complex clinical presentation of advanced prostate cancer patients and their omnipresent comorbidities, this review describes the current and potential role of exercise medicine in advanced prostate cancer.

Recent findings
Exercise has been shown to be safe, feasible and effective for advanced prostate cancer patients, inclusive of patients with bone metastases; a previously excluded population due to patient and clinician fear of adverse events. Preclinical data provide insight into the ability of exercise to modulate cancer-specific outcomes, may synergistically increase the potency of chemotherapy and radiotherapy and may endogenously and/or mechanically suppress tumour formation, growth and invasion in visceral and skeletal tissue. Epidemiological studies have also shown an association between physical activity and increased survival.

Summary
Exercise oncology is rapidly evolving, with impressive possibilities that may directly improve patient outcomes in advanced prostate cancer. Research must focus on translating preclinical trials into human clinical trials and investigate the direct effect of exercise on overall survival.

Keywords
adjuvant, autoregulation, synergistic, targeted, tumour biology

INTRODUCTION

Prostate cancer represents the second most common cancer in men worldwide, and is predicted to substantially rise in developed nations owing to sustained population growth, increased life expectancies and an ageing population [1,2]. Fortunately, the advent and widespread adoption of serological prostate-specific antigen (PSA) screening programmes has notably improved the early detection, diagnosis, treatment and management of prostate cancer, demonstrably improving survival outcomes. Impressively, this has led to an increase in 5-year survival rates from ~68 to ~99.7% in recent decades, with a 10 and 15-year survival rate of ~99 and ~94%, respectively, when detected early [3,4]. As such, prostate cancer survivorship is an emerging and critically important field of study, focused on the effective management of new, recurrent and persistent symptoms across the disease spectrum to explicitly enhance patient health, wellbeing and quality of life [5,6]. Unfortunately, most studies exploring survivorship focus their attention on the initial years of posttreatment survival, with limited attention given to patient needs later in the disease trajectory [6,7▪] when recurrence, castrate resistance and/or metastatic proliferation inevitably result in progression to advanced prostate cancer, whereby patient needs magnify [7▪].

Advanced prostate cancer is characterized by the recurrence and/or invasion of the primary carcinoma to secondary sites (i.e. nodal, visceral or skeletal metastases) and/or the development of resistance to first-line hormone therapy (androgen deprivation therapy; ADT) whereby androgen independent progression occurs (castrate-resistant prostate cancer; CRPC) [8]. Men with advanced prostate cancer present a significant challenge to clinicians,

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KEY POINTS

- Exercise is a safe and effective medicine for advanced prostate cancer, including for patients with bone metastases; a historically excluded patient population with a high disease burden and magnified clinical needs. Advanced prostate cancer patients should therefore participate in exercise programmes, under clinical supervision.
- Exercise may act synergistically to improve the potency, delivery, effectiveness and tolerance of chemotherapy and radiotherapy in advanced prostate cancer patients. This has been presented in preclinical orthotopic models to date. Future studies should aim to translate findings to patient-focused human clinical trials.
- Exercise may endogenously and mechanically suppress tumour formation, growth and invasion in visceral and skeletal tissue by modulating cancer-specific outcomes. This has been demonstrated in preclinical orthotopic models to date. Future studies should aim to translate findings to patient-focused human clinical trials.
- Physical activity has been associated with lower risk of cancer-specific and all-cause mortality. However, exercise will likely yield even greater survival benefits, and this is being investigated by the INTERVAL-MCRPC clinical trial, using metastatic castrate-resistant prostate cancer patients, launched in 2016.
- Exercise programmes designed for advanced prostate cancer patients should always be supervised, individualized, periodized, progressive and autoregulated. Autoregulation is a particularly important for this patient population, given their disease profile, age, omnipresent comorbidities and associated treatment toxicities over time.

because of their high disease burden and omnipresent comorbidities, in addition to common treatment-related side-effects stemming from second-line hormone therapies (abiraterone and enzalutamide) [9], first-line and second-line chemotherapies (docetaxel and cabazitaxel) [10], radionuclear therapies (strontium-89, samarium-153 and radium-223) [11] and emergent immunotherapies [12], the optimal sequencing of which has yet to be determined. Indeed, the vast majority of advanced prostate cancer patients (>80%) will develop bone metastases, which is a currently incurable stage of disease leading to palliation, poor prognoses and numerous clinical complications [13,14▪]. It is therefore a high priority and of significant clinical interest to devise and implement strategies to safely and effectively reduce the disease burden and treatment toxicity profile of advanced prostate cancer patients; particularly, strategies which are inexpensive, non-invasive and able to be widely implemented. Exercise is an emerging and provocative therapy in oncology, inherently aligned with the 'exercise medicine' movement [15–17], which shows excellent promise to meet this patient need.

EXERCISE MEDICINE

Exercise was first considered a potential therapy for cancer patients and survivors in the mid-1980s [18–20], with only a further ~25 exercise oncology studies reported in the subsequent two decades [21]. Increasingly, over the last decade, exercise medicine has rapidly ascended as a key field of interest in the prevention [22] and management [23] of cancer, while emerging as a potential therapeutic agent to delay disease progression [24▪▪–26▪▪,27,28▪,29] and increase overall survival [29,30,31▪▪,32▪▪,33,34]. Primarily, researchers have focused their attention on the use of exercise in the neoadjuvant and adjuvant settings as a preventive, preparatory and rehabilitative tool for surgery (presurgical and postsurgical programmes) [35,36], and for symptom control during and/or following primary treatments, including radiotherapy, chemotherapy and hormone therapy (particularly ADT) postdiagnosis [37–40]. Collectively, this body of research has produced level 1 evidence [23], asserting the role of exercise for cancer patients to improve quality of life across several key metrics, including the mitigation of cancer-related fatigue [41▪] and restoration of physical function and exercise capacity [22,42], notably in response to treatment driven changes in body composition [23]. The effectiveness of exercise as a neoadjuvant and adjuvant therapy to minimize, manage and, in some cases, reverse the side-effects of primary therapies has been promising to date [42–46].

Exercise oncology (i.e. the application of exercise medicine in cancer) has also continued to broaden, with several novel avenues being explored through preclinical orthotopic models that have the potential to significantly improve outcomes in advanced prostate cancer patients once translated to human clinical trials [47,48,49▪▪,50▪▪,51–54]. Indeed, the impressive ability of exercise to potentially modulate cancer-specific outcomes is of direct clinical interest and warrants rigorous scientific inquiry. Beyond neoadjuvant and adjuvant applications, exercise is emerging as a synergistic medicine (i.e. increasing the potency or effectiveness of concomitantly applied therapies) and targeted medicine (i.e. exerting its own systemic and localized anticancer effects, independent of other therapies) to underpin delays in disease progression and improvements in survival for advanced cancer patients. For example, synergies between exercise

and chemotherapy have been identified [49▪▪,50▪▪,51], with aerobic exercise demonstrating an ability to interfere with tumour-driven dysregulation of angiogenesis; acting to restore and normalize tumour vasculature, thus improving blood supply and tumoral perfusion as mechanisms to enhance chemotherapeutic efficacy [49▪▪,50▪▪, 51–55]. This same angiogenic response may also synergistically improve the effectiveness of radiotherapy [51–55], as reversible DNA damage can be stabilized if sufficient oxygen is present (i.e. oxygen enhancing effect of radiotherapy) [55], which could be optimized through exercise driven provasculature changes, resulting in increased tumour cell death. This is yet another avenue of exploration for future research. When extrapolated, this may also lead to synergistic improvements in the potency of other systemically delivered therapies inclusive of emerging immunotherapies in the prostate cancer treatment mix, or endogenous immune agents produced by various organs in the body that are driven by exercise [15].

Provocative evidence also exists to promote the potential independent role of exercise medicine for advanced prostate cancer patients. Putatively, exercise is thought to alter tumour biology by numerous mechanisms in response to a variety of modes and dosages (Fig. 1) [24▪▪]; however, the direct influence of exercise on tumour biology remains largely unknown, despite many hypothesized mechanical and nonmechanical mechanisms of action [47,48,49▪▪,50▪▪,51–59,60▪]. Specifically, exercise regulates endocrine–paracrine activity, immune system function, blood glucose and cholesterol levels, insulin responses and body composition and may epigenetically modulate tumour cell

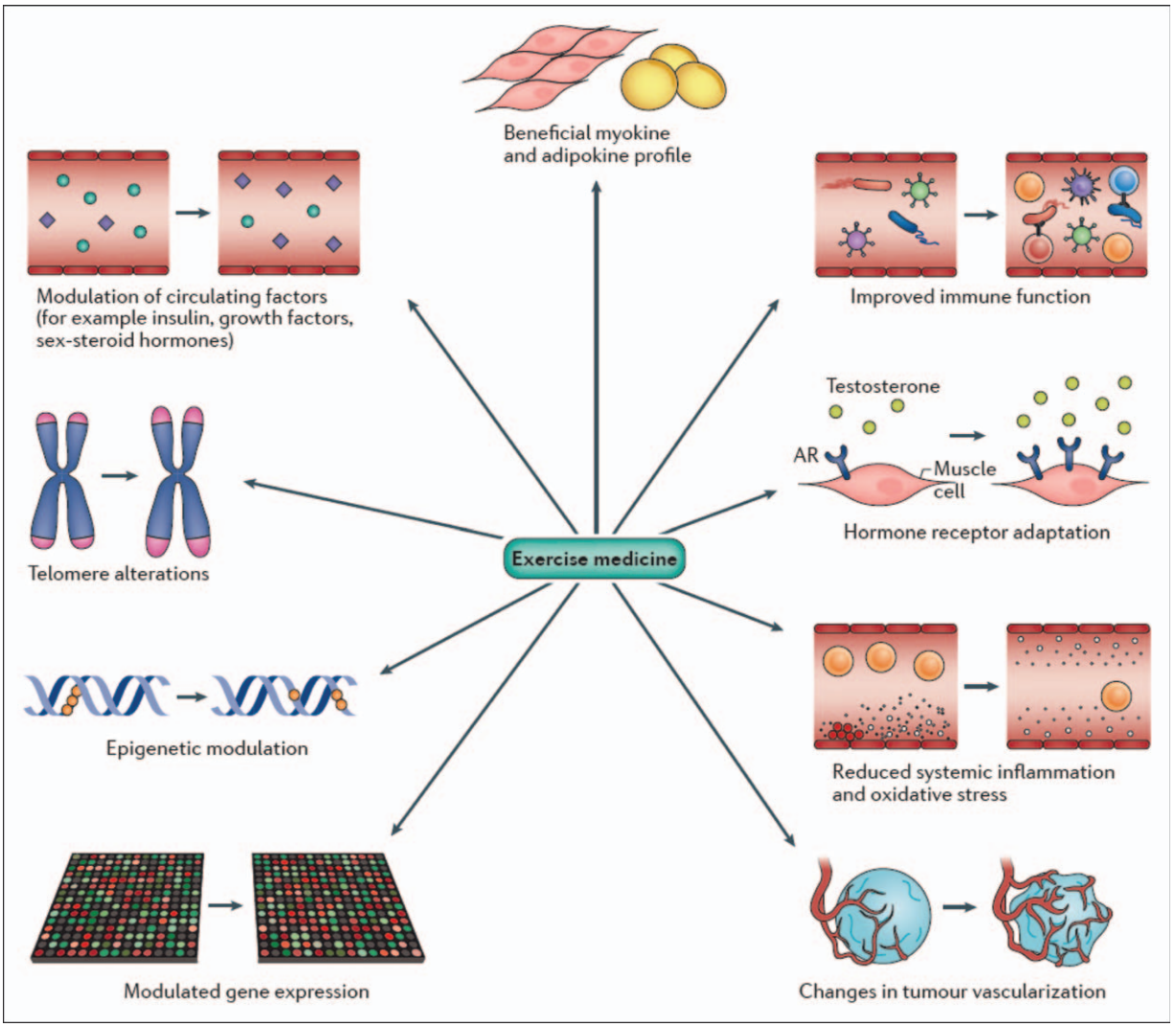

FIGURE 1. Potential mechanisms by which exercise might modulate tumour biology and delay disease progression. Thus far, the exact mechanisms of this effect have yet to be established; although, some evidence exists for a contribution from a variety of diverse mechanisms. Reprinted with permission [24▪▪].

proliferation, telomere length, telomere enzyme activity, tumour vascularity, oxidative stress capacity, platelet cloaking and platelet adhesion [61–66]. This emerging field of exercise medicine (i.e. biological alterations driven from biomechanical stimuli) [67] in exercise oncology presents practitioners with unique opportunities to target tumour formation, growth and invasion of primary or secondary prostate carcinomas through exercise interventions. For example, aerobic exercise has been shown to stimulate natural killer cell production, mobilization and infiltration in to tumours, producing an approximate 60% reduction in tumour incidence and growth across several different preclinical tumour models [68▪▪]. Similarly, controlled mechanical compressions of skeletal sites with known bone metastases have been shown to interfere with tumour-driven dysregulation of osteogenesis, producing an approximate 80% reduction in tumour growth rate in osteolytic models, while preserving skeletal integrity by approximately 70% in loaded versus unloaded conditions [47]. Cautiously, these preclinical findings use animal models over disparate time-periods, and require confirmatory human trials, some of which are currently in progress [69▪], though provide promising insights into exercise medicine independent of other therapies.

Epidemiological studies support the role of physical activity (i.e. incidental and/or nonspecific activities requiring bodily movement) and its association with delayed disease progression and increased overall survival [27,28▪,29,30,31▪▪,32▪▪,33,34]. Specifically, prediagnosis physical activity has been linked to tumour vessel normalization, which reduces the propensity of tumours to metastasize (i.e. delay disease progression) and has the potential to produce a 6.6–17.1-fold risk reduction in prostate cancer mortality [70▪▪,71]; whereby postdiagnosis moderate-to-vigorous physical activity has been linked to reductions in all-cause and prostate cancer-specific mortality of between 30 and 60% (pooled risk reduction = 0.62, 95% confidence interval: 0.47–0.82) [31▪▪,32▪▪,33,34,72▪], depending on the type, duration and frequency of physical activity reported. However, these studies provide associations using patient self-reported measures only and do not demonstrate a dose–response or load–adaptation insight into cause and effect between physical activity, disease progression or overall survival. Consequently, studies are yet to explore the role of exercise (i.e. purposeful, prescriptive, programmed and progressive activities of a specific nature; the nomenclature of which is often incorrectly used synonymously with physical activity) on disease-specific endpoints and such interventions would most certainly produce even greater benefits than those analysing self-reported physical activity. To address this need, a Global Action Plan (GAP4) has been funded by the Movember Foundation, with a multinational Phase III exercise trial (INTERVAL-MCRPC: https://clinicaltrials.gov/ct2/show/NCT02730338) launched, and currently underway to directly examine the effects of exercise medicine on disease progression and overall survival in metastatic castrate-resistant prostate cancer patients [73▪].

TREATMENTS, TOXICITIES AND EXERCISE

Exercise and antiandrogen therapies

Endocrine modification therapies are common first-line treatments for prostate cancer (beyond radical prostatectomy and radiation therapy), aiming to suppress testosterone released from the testes and/or to block androgen receptor uptake of testosterone by cancer cells, producing an environment commensurate with castration [74,75]. ADT remains the primary hormonal therapy for local and metastatic prostate cancer patients, proving an extremely successful pharmacological avenue to slow the progression of certain prostate cancers. On the contrary, long-term exposure to ADT inevitably leads to resistance, thus becoming ineffective due to tumour adaptability, desensitization to drug action and systemic acclimatization to the castrate environment [74–77]. This generates a rapid rise in PSA levels and velocity, indicating an advancement of the disease to CRPC. Consequently, extragonadal androgen sources start to sustain tumour growth despite castrate levels of testosterone, requiring second-line therapies to be introduced into the treatment mix [76,77].

Novel pharmacological agents which inhibit androgen receptors have recently been developed as second-line hormonal therapies to countenance extragonadal sources of androgen, including derivations from blood and bone marrow, successfully extending overall survival by ~4–5 months [78,79] in castrate-resistant patients. Specifically, Abiraterone Acetate (Zytiga; Janssen, Beerse, Belgium) and Enzalutamide (Xandti; Astellas, Illinois, USA) are prominent antiandrogen drugs in the standard of care landscape when treating CRPC patients, which act as selective inhibitors to obstruct androgen uptake and utilization by prostate carcinomas regardless of production site (gonadal or extragonadal), thus considered to be very effective at suppressing testosterone in the testes, adrenal glands and the tumour itself, reducing testosterone levels by a further 90% beyond castrate levels [74–80]. Although androgen-deprivation therapies are proving effective in slowing prostate cancer progression, with

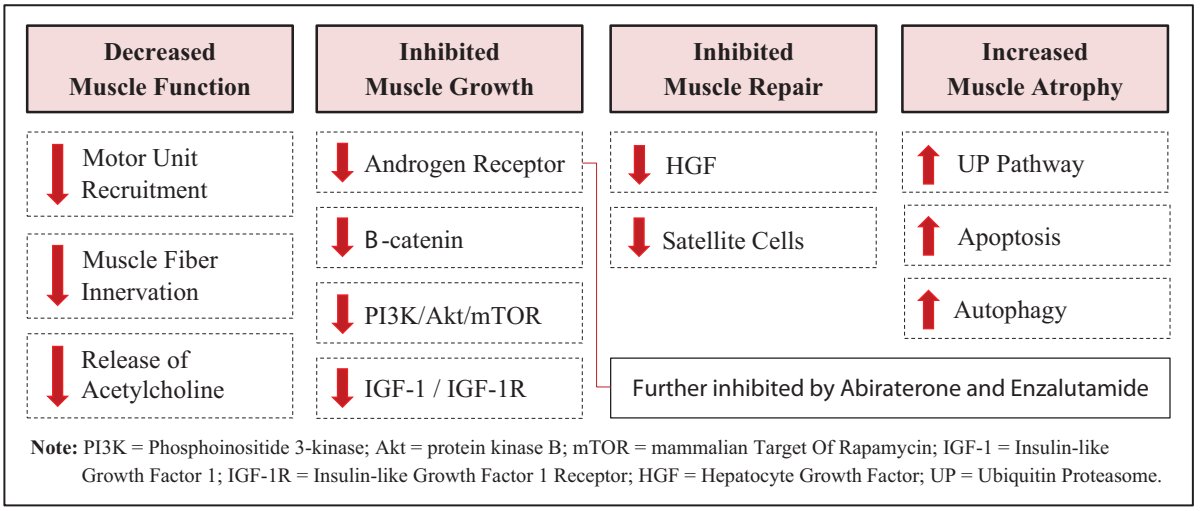

FIGURE 2. Skeletal muscle depletion (sarcopenia-related disorders) induced by androgen deprivation therapy, expected to be greater in severity for castrate-resistant prostate cancer patients treated with antiandrogen therapies generating maximal androgen suppression. Adapted with permission [82▪].

improvements to survival; observational and longitudinal evidence highlight the burden of treatment to patients, which may be exacerbated by novel antiandrogen therapies [81,82▪] (Fig. 2), yet could potentially be managed through exercise.

ADT induces rapid loss of muscle and bone mass, increased central adiposity and body fat, and is therefore a precursor for the onset of metabolic diseases and other comorbidities such as type II diabetes and/or cardiovascular disease; culminating in physical and functional decline, increased fatigue, heightened fragility, decreased psychosocial health and a reduced quality of life [37–40,41▪, 42–46,82▪,83–86]. Given that novel antiandrogen therapies induce an even greater blockade of androgen beyond castration levels (i.e. maximal androgen suppression), these reported side-effects are likely to be more pronounced (Fig. 3), presenting even greater clinical concerns for advanced prostate cancer patients. Although exercise is demonstrably

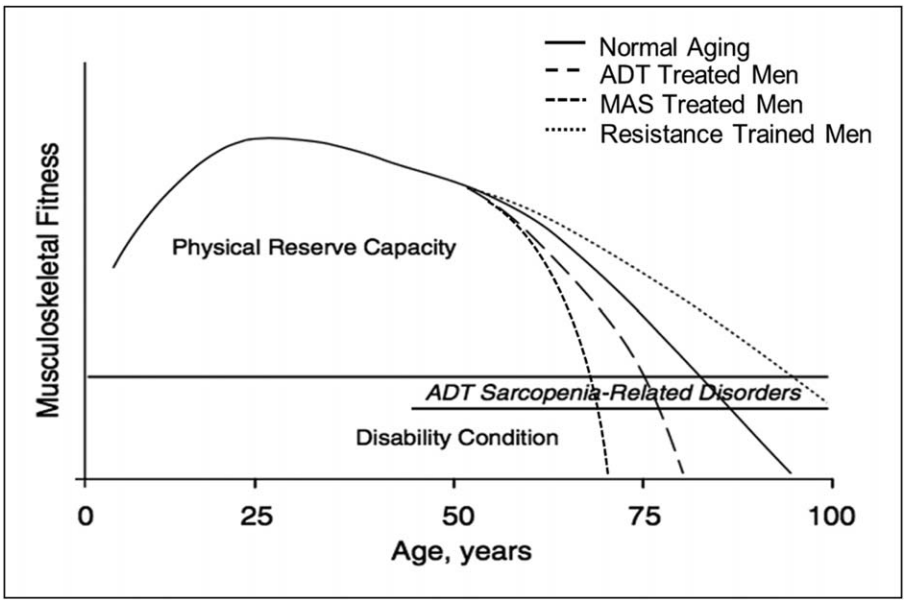

FIGURE 3. Theoretical model illustrating musculoskeletal fitness reduction during normal aging, androgen deprivation therapy and maximal androgen suppression, highlighting the potential role of exercise to increase musculoskeletal fitness and improve physical reserve capacity. Adapted with permission [46].

beneficial for patients receiving ADT to prevent, preserve or reverse treatment-related side-effects [45,46], this has yet to be demonstrated in patients receiving maximal antiandrogen suppression. Indeed, exercise is very likely to mitigate fatigue commonly reported by patients on novel antiandrogen therapies [41▪,81], and may synergistically assist in the mitigation of resistance to enzalutamide, with natural killer cells recently implicated in the suppression of androgen receptor splicing variant 7 (ARv7) (i.e. an androgen receptor splicing variant linked to the development of resistance) [87▪▪]. As natural killer cell production and mobilization increases following exercise [68▪▪], by extension, this may aid in the suppression of ARv7; however, further research is required.

Exercise and chemotherapy

Chemotherapies provided to patients with advanced prostate cancer aim to provide symptom control, delay disease progression and increase survival; however, often present with their own clinical challenges and side-effects. Docetaxel remains the mainstay of first-line taxanes, with cabazitaxel established as a second-line taxane in eligible patients (i.e. consideration of bone marrow reserves, bone marrow quality, hepatic function and patient presentation) in favour of mitoxantrone; with cabazitaxel also available as a first-line taxane for patients resistant to docetaxel [10,74]. Owing to the side-effects of cytotoxic therapies, coupled with side-effects of other therapies (i.e. ADT in hormone-sensitive patients), patients may not tolerate full dosages across all cycles of treatment, and in some cases may be ineligible for further chemotherapy treatments if bone marrow and organ function is compromised [88–90]. Further, patients commonly present with high levels of fatigue, physical impairment and develop neutropenia following chemotherapy [91–94] which may lead to patients electing to refuse further chemotherapy dosages or undergo additional courses. Strategies to alleviate treatment toxicities and maintain hepatic and physical function are thus required.

Exercise is well established as a therapy to mitigate cancer-related fatigue [22,41▪], restore physical function and enhance physical fitness [23,42,44,95]; however, exercise may have broader clinical benefits for prostate cancer patients receiving chemotherapy. For example, neoadjuvant exercise may improve patient preparation and physical tolerance of first-line chemotherapy, inclusive of posttherapy recovery, with body composition established as a predictor of chemotherapeutic toxicity [96▪▪]. Furthermore, adjuvant exercise may synergistically increase cytotoxic circulation and intratumoural delivery of chemotherapy, thus increasing therapeutic potency [49▪▪,50▪▪], and may mitigate, restore or reverse side-effects associated with chemotherapy, inclusive of reductions in neutropenia onset, duration and severity of nadir (Fig. 4) following proposed improvements in immune function [97–99]. Neoadjuvant and adjuvant exercise therefore has the potential

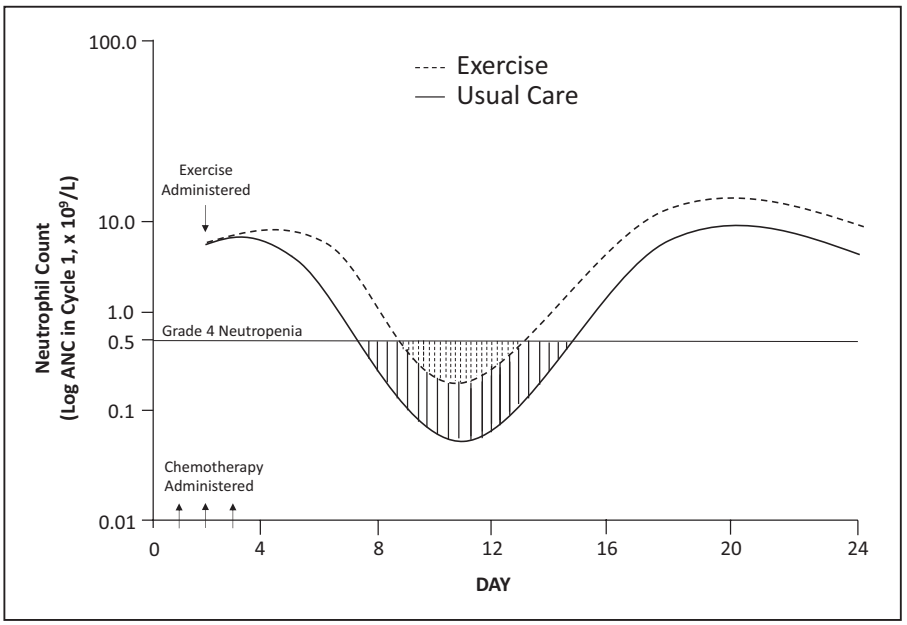

FIGURE 4. Theoretical model illustrating the potential acute and aggregate neutrophil response to exercise (dashed line) versus usual care (solid line) during chemotherapy cycles, highlighting a potentially reduced severity and duration of nadir (i.e. region of lowest neutrophils during neutropenia, where infection risk is at its highest).

to assist patients to receive their full individual and aggregate doses of chemotherapy, and coupled with posttherapy exercise, may promote bone marrow quality [97] and improve patient physical condition to heighten clinical eligibility to receive and tolerate second-line chemotherapy; two clinically meaningful outcomes for advanced prostate cancer patients that are worthy of exploration.

EXERCISE PROGRAMMING

Clinical considerations

Owing to their variable treatment histories, lifestyle-related and disease-related comorbidities and age-related decline, advanced prostate cancer patients will present with complex clinical cases that will influence the modality, volume, frequency, duration and intensity of exercise prescribed, and the manner in which their exercise programme progresses. Commonly amongst them is bone metastases, a historical barrier to exercise observed in over 80% of advanced cancer patients [100,101]. For patients with bone metastases, it is currently recommended to use exercises that avoid directly loading skeletal regions where metastatic lesions exist (Table 1) [102]. Current studies exploring the safety, feasibility and preliminary efficacy of targeted loading of skeletal sites with bone metastases are currently underway [69▪], with results soon to be released.

Autoregulation, periodization and exercise selection

Advanced prostate cancer patients may present with numerous treatment side-effects of varying magnitudes at a given exercise session, or across multiple exercise sessions. To accommodate for transient changes and fluctuations in a patient's wellbeing through-out courses of treatment and through-out their disease progression, all exercise programmes should be individualized (i.e. based on a needs analysis and physical assessment) and progressive using autoregulation (i.e. a method in which cancer patients progress at their own pace based on daily and weekly variations in their health, performance capability, recovery capacity or scheduling commitments) [103,104]. Autoregulation is an important concept, allowing patients to consultatively self-determine their capabilities at each session collaboratively with the supervising clinical exercise physiologist, thereby lowering intensity or volume if the patient is fatigued or unwell, or raising intensity or volume if the patient is energetic and motivated. Commensurate with other standard exercise principles, exercise programmes should be periodized (i.e. the systematic planning and phasic organization of exercise volume and intensity, including deloading periods to promote patient recovery), commence conservatively, and include a variety of exercise types and modalities.

Advanced cancer patients should receive medical clearances from either their oncologist (i.e. cancer-specific medications and clearances), cardiologist (i.e. cardiac-specific medication and clearances) and/or general practitioner (i.e. other medications and comorbidity clearances) prior to engaging in an exercise programme, which may limit the modality of exercise permitted. Nevertheless, exercise programmes should ideally involve a multimodal approach with aerobic and resistance exercise of varying intensities and volumes to target the cardiorespiratory and musculoskeletal systems, respectively (Table 2), and to promote various biochemical, hormonal (endocrine–paracrine) and immune responses to disparate modalities. Current clinical exercise guidelines [105–107] recommend achieving a combination of 150 min of moderate, or 75 min of vigorous aerobic exercise coupled with 2–3 resistance exercise sessions

Table 1. Modular multimodal exercise programme for patients with bone metastases

	Resistance			Aerobic		Flexibility
Metastases site	Upper	Trunk	Lower	WB	NWB	Static
Pelvis	√	√	√**		√	√
Lumbar spine	√		√		√	√***
Thoracic spine/ribs	√*		√	√	√	√***
Proximal femur	√	√	√**		√	√
All regions	√*		√**		√	√***

√, target exercise region; *, exclusion of shoulder flexion/extension/abduction/adduction – inclusion of elbow flexion/extension; **, exclusion of hip extension/flexion – inclusion of knee extension/flexion; ***, exclusion of spine/flexion/extension/rotation; NWB, nonweight bearing (e.g. cycling); WB, weight bearing (e.g. walking). Reproduced from [102].

Table 2. Exercise programming across modalities: definitions and recommendations

Exercise modality	Description and recommendation
Aerobic exercise	Exercise that provides stress to the cardiorespiratory system (heart, blood vessels and lungs), and targets cardiometabolic health. This can be performed at moderate-to-high intensities, under continuous or intermittent/interval conditions (MICT/HIIT)
	Examples: cycle ergometers, treadmills, cross-trainer ergometers
MICT (moderate intensity continuous training)	Constant moderate intensity work at a level that can be maintained for an extended period of time without fatigue. Patients may require MICT sessions to be split into discrete bouts at the earlier stages of their programme, until fitness and endurance develops
	Intensity: RPE 5–6, (~60–70% HRmax); RPE 4 during deload
	Work durations: 20–40 min
	Rest durations: 0–2 min
	Number of sets: 1–2 sets
HIIT (high-intensity interval training)	Short bouts of high-intensity work, separated by periods of active or passive recovery. Patients may have a transient increased in risk of fall for 10 min following the completion of a HIIT session. Monitoring patient response during and following work bouts is required
	Intensity: RPE 8–9, (~80–90% HRmax); RPE 7 during deload
	Work durations: 30–60 s
	Rest durations: 90–120 s
	Number of sets: 4–6 sets
Resistance exercise	Exercise that is performed against resistance (bodyweight or external load) and aims to stress the musculoskeletal system (muscle-bone), with muscle a key secretory and endocrine organ. Dynamic, compound, whole-body movements should be performed first, prior to isolated single-joint activities. Trunk flexion and extension exercises can be incorporated into the cool-down portion of the programme, along with flexibility exercises for the exercised muscle
	Examples: weight machines, free weights (dumbbells and barbells), body-weight exercises, weighted objects (gym sticks and power bags)
	Intensity: 6–12 RM
	Number of sets: 2–4 sets
	Number of Exercises: 6–8 involving large muscle groups
Impact exercise	Exercise that involves impact, putatively thought to target the skeletal system and bone health. Patients with bone metastases are currently contraindicated for impact exercise, as safety has yet to be demonstrated in these patients. Patients with no known bone metastases can perform impact exercises as tolerated. Start conservatively, from a foundation of 12–36 resistance exercise sessions, and build into programme for volume and difficulty
	Examples: marching, two-legged jumps, hopping, skipping, bounding
	Repetitions: 10–15 repetitions
	Number of sets: 2–3 sets
	Number of exercises: 2–4 exercises involving upper and lower body

HIIT, high-intensity interval training; HRmax, heart rate maximum; MICT, moderate-intensity continuous training; RM, repetition maximum; RPE, rating of perceived exertion using the BORG10 scale.

for cancer patients and survivors. However, owing to heightened clinical concerns and patient fear of skeletal and other adverse events [69▪], only ~30% of advanced prostate cancer patients with bone metastases reported meeting aerobic exercise guidelines; with the remaining ~70% either insufficiently or completely inactive (i.e. performing no aerobic exercise at all) [14▪]. Given the historical safety concerns surrounding resistance exercise in this population (with safety and feasibility recently demonstrated [100,101]), resistance exercise participation would be even lower than those reported for aerobic exercise. Although any activity is better than no activity, it is incumbent upon clinicians to promote patient engagement with exercise physiologists and treat exercise as a medicine for advanced prostate cancer, one which all patients should participate.

CONCLUSION

Exercise medicine is rapidly evolving as an emerging and provocative therapy in oncology, with excellent promise to meet the broad and magnified needs of advanced prostate cancer patients. This review highlights established clinical evidence, developing preclinical evidence and potential future avenues of novel research pertaining to the role of exercise as an adjuvant, synergistic and targeted therapy. In

particular, we highlight the powerful potential of exercise to enhance chemotherapeutic and radiotherapeutic effectiveness, interfere with tumour-driven dysregulation of angiogenesis and osteogenesis and delay disease progression and extend survival. Importantly, due to the complex clinical presentations of advanced prostate cancer patients, this review provides exercise prescription and programming recommendations to ensure that exercise participation is flexible and effective, yet safe and well tolerated by patients. Lastly, we assert the need for future research to focus on translating impressive preclinical outcomes, to patient-focused human clinical trials, to continue to establish exercise as an essential therapy for inclusion into standard of care practices in oncology.

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Conflicts of interest

There are no conflicts of interest.

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