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Invited Topical Review

Physiotherapy management of blood cancers

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Introduction

Physiotherapy is an important part of the management of people with blood cancer. Blood cancer is associated with significant physical and psychological burden. The goals of physiotherapy include facilitating the individual to prepare physically for medical treatment, maintain health during treatment, recover after treatment, and maximise health and wellbeing in the survivorship and palliative stages of disease. Exercise training and physical activity are critical components of physiotherapy management, and this is supported by growing evidence of the benefit of exercise for people with blood cancer. This review summarises the clinical presentation of blood cancer, the disease burden, the management of blood cancer with a focus on physiotherapy treatment, and future directions for research and clinical practice. Whilst blood cancers affect people of all ages, this review focuses on the management of adults with blood cancer.

What is blood cancer?

Blood cancer, also known as haematological cancer or haematological malignancy, is a term used to describe cancers that originate in blood-forming tissues such as bone marrow and the immune system.[1] There are five main classifications of blood cancer (Box 1), although there are numerous subtypes within these classifications, including over 40 subtypes of leukaemia and 50 subtypes of lymphoma.[2,3] The prognosis and medical treatment vary between subtypes.[2–4]

Blood cancer is the third most common cancer diagnosed in Australia after breast cancer and colorectal cancer,[1,5] and represents approximately 10% of all cancers diagnosed worldwide.[4] The incidence is rising and this is predominately due to the ageing population and improvements in diagnosis.[1,5] It is more common in males than females (age-standardised incidence rate 75 cases per 100,000 males and 48 cases per 100,000 females in Australia)[5] and is diagnosed in people of all ages, although the highest incidence is in people in their 70s and 80s.[1] Blood cancer is the leading cause of non-preventable cancer death in Australia.[1] The 5-year survival rate is 68%[5] and this has improved rapidly due to advances in medical treatment[4] (5-year survival in the early 1990s was 52%).[5]

With increasing cases and improved survival rates, the prevalence of blood cancer is rising.[1] There were approximately 112,000 people with blood cancer in Australia in 2018 and this is expected to reach 275,000 people by 2035.[1] Survivors of blood cancer commonly experience persistent symptoms and complications from the medical treatment, resulting in ongoing physical and psychological impairments.[6] Therefore, there is a growing number of people in the community with unmet supportive care needs related to blood cancer, some of which can be addressed by physiotherapy treatment, as discussed in this paper. However, access to supportive care and physiotherapy is limited:[1] a recent Australian survey of 3,227 people with blood cancer found that 25% of them wished they had access to physiotherapy or occupational therapy for their blood cancer – but they did not.[1] One factor contributing to the practice gap is lack of knowledge of clinicians related to this clinical area;[7] therefore, upskilling to be informed about blood cancer, the common impairments that patients experience and the evidence about physiotherapy treatments is critical.

Medical treatments of blood cancer

The medical treatments for blood cancer have improved dramatically over recent times. The treatment is specific to the cancer type and dependent on factors including age, comorbidities, performance status and cancer stage.[8] Treatments are given in combination and can include chemotherapy, radiotherapy, oral drug therapy such as tyrosine kinase inhibitors, immunotherapy, blood transfusions and stem cell transplantation. Stem cell transplantation, also known as haematopoietic cell transplantation or bone marrow transplantation, is a common form of treatment for blood cancer, and a potentially curative treatment option for some patients.[8] The rates of stem cell transplantation are rising in Australia and it is used more frequently in older individuals who previously would have been considered ineligible due to their age.[9] Due to the aggressive nature of stem cell transplantation, patients are required to have good functional status

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Box 1. Common classifications of blood cancer.

Leukaemia
- cancer that develops in the blood and bone marrow usually affecting white blood cells (lymphocytes or myeloid cells)

Lymphoma
- cancer that develops in the lymphatic system

Myeloma
- cancer that develops in the bone marrow in plasma cells

Myeloproliferative neoplasm
- cancer that originates from a mutation in stem cells in the bone marrow and causes overproduction of blood cells

Myelodysplastic syndrome
- cancer that originates from an acquired mutation of stem cells in the bone marrow and causes a reduction in healthy blood cells

pre-transplant to be eligible for the procedure.[8] Physiological age, rather than chronological age, is an important consideration for suitability.[8]

In allogeneic stem cell transplantation, donor cells from a 'healthy' person who is human leukocyte antigen-compatible are used. This type of transplantation is commonly used to treat acute myeloid leukaemia and acute lymphoblastic leukaemia.[8] Prior to allogeneic stem cell transplantation, the patient must undergo conditioning, which involves chemotherapy, serotherapy and/or whole body radiotherapy, with the aim of destroying malignant cells in the bone marrow and triggering immunosuppression.[8] Stem cell transplantation then occurs, during which donor stem cells from bone marrow, peripheral blood or cord blood are intravenously infused into the body.[9] A major complication of allogeneic stem cell transplantation is graft-versus-host disease (GVHD),[8] which results in chronic inflammation and fibrosis and can affect multiple organs of the body.[10] Chronic GVHD requires prolonged systemic immunosuppressive treatment[11] and is discussed in greater detail in subsequent sections.

In autologous stem cell transplantation, the individual's own stem cells are used. This type of transplant is commonly used to treat multiple myeloma and non-Hodgkin lymphoma.[8] The individual's stem cells are harvested, they then undergo a period of high-dose chemotherapy and then the stem cells are reinfused back into the body.[8] Autologous stem cell transplantations are associated with less severe side effects than allogeneic transplantations.[8] There is a risk of complications following both types of transplants, although autologous stem cell transplantation does not have the added risk of GVHD and prolonged immunosuppression.[8]

The medical treatments for blood cancer are often intense and prolonged, and patients can be hospitalised for extended periods (Figure 1). The planned and prolonged period of inpatient medical treatment makes this patient population somewhat unique compared with many other patient groups that physiotherapists manage. For some types of blood cancer, treatment protocols can continue in the outpatient setting for up to 3 years; such is the case for acute lymphoblastic leukaemia, where patients undergo chemotherapy in three phases: induction, consolidation and then maintenance treatments.[1] The medical treatments used in blood cancer are associated with toxicities and significant side effects and complications, some of which can be long-standing. A summary of potential early and late complications from stem cell transplantation is provided in Table 1.

In Australia, patients are usually hospitalised for 3 to 6 weeks to receive treatments such as chemotherapy and a stem cell transplantation, and then stay close to the hospital to be able to attend regular outpatient medical appointments for assessment and ongoing medical treatments until 100 days post-transplant. Stem cell transplantations are only conducted at a few hospitals in Australia;[12] therefore, there is a significant burden associated with the potential requirement for many patients to temporarily relocate for treatment. Accommodation and travel support is offered by charities such as the Leukaemia Foundation.[13] However, from a physiotherapy perspective, this means that patients are likely to be staying in, or close to, major transplant hospitals for months at a time and, on a practical level, should be more easily able to participate in physiotherapy and exercise programs during this acute phase of treatment (Figure 1).[14,15]

	PRE-TREATMENT (months)	DURING TREATMENT (weeks to months)	POST-TREATMENT (months to years)	SURVIVORSHIP	PALLIATIVE CARE
Medical	**Home with frequent outpatient appointments ± day admission/s** Work-up for treatments, extensive investigations ± commencement medical treatment as outpatient or day oncology	**Inpatient hospital admission/s** Inpatient medical treatments such as chemotherapy, radiotherapy, immunotherapy, blood transfusions and/or stem cell transplantation	**Accommodation near hospital with frequent outpatient appointments** Close monitoring; ongoing outpatient medical treatments such as transfusions or oral therapies	**Home with infrequent outpatient appointments** Surveillance and monitoring	**Inpatient admission/s or in community** Support with end-of-life and palliative care
Physiotherapy treatment options	**Outpatient physiotherapy** Initial Ax: moderate- to high-intensity exercise program (outpatient or home-based); education on physical activity	**Inpatient physiotherapy** Ax: mobilisation; low- to moderate-intensity exercise program; range of motion/stretching; balance training; ADL training; discharge planning/support three to five times per week, once or twice a day	**Outpatient physiotherapy** Post-treatment Ax: screening for medical treatment complications; physiotherapy treatment targeting impairments; moderate- to high-intensity exercise program (outpatient or home); education on return to physical activity and work/hobbies; education on healthy lifestyle behaviours	**Outpatient physiotherapy** Ax: screening for complications and late effects; physiotherapy to target impairments; moderate- to high-intensity exercise program; education on physical activity and healthy lifestyle behaviours	**Inpatient or home-based physiotherapy** Ax: treatment directed by patient goals: gentle exercise, provision of gait aids, ADL support, symptom management, relaxation or breathing exercises

Figure 1. Physiotherapy management across the disease and treatment pathway for blood cancers. The medical treatment pathway varies between the different types of blood cancer and is individualised to the patient. This is a simplistic representation of a common treatment pathway and a summary of physiotherapy treatments that may be appropriate at each timepoint.
ADL = activities of daily living, Ax = assessment.

Table 1
Complications after stem cell transplantation. Adapted from Saad et al.[8]

Early complications (occurring within 100 days)	Late complications (occurring after 100 days)
• Acute GVHD*	• Chronic GVHD[a]
• Infection	• Infection
• Prolonged cytopenia and graft failure	• Organ dysfunction
• Organ toxicities	• Late radiation-related toxicities including cataracts and hypothyroidism
• Sinusoidal obstruction syndrome	• Late chemotherapy-related toxicities including heart failure
	• Secondary malignancies including myelodysplastic syndromes

GVHD = graft-versus-host disease.
[a] allogeneic stem cell transplantation only.

The burden of blood cancer

Blood cancer is associated with a high number of symptoms, side effects (Box 2) and complications (Table 1) caused by the underlying cancer and medical treatments. Symptoms and side effects vary across the disease and treatment journey; however, people consistently report the presence of a high number of co-occurring symptoms. This is on average 10 symptoms at the time of diagnosis, eight symptoms in stable disease, 12 symptoms in refractory disease and eight symptoms during relapse.[16] Many symptoms are seen in people undergoing medical treatment, in inpatients and those with advanced disease.[16] Cancer-related fatigue and feeling worried are the most common physical and psychological symptoms (Box 2).[16]

Cancer-related fatigue is 'a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and treatment that is not proportional to recent activity and interferes with usual functioning'.[17] It can be persistent in blood cancer survivors years after diagnosis/treatment.[18] It is the most common ongoing concern of survivors,[19] a key barrier to exercise[20] and is associated with poorer health-related quality of life (HRQoL).[21]

Distress in blood cancer is high across the domains of physical, psychological and global health.[16] Younger adults with blood cancer are more likely to experience distress.[22] Psychological distress is most common in patients with a new diagnosis and those who are hospitalised.[16] Distress associated with physical symptoms is more common in patients with refractory or progressive disease.[16] Following completion of treatment, patients describe distress associated with their ongoing physical impairments and loss of physical health compared with pre-diagnosis.[23]

Box 2. Physical and psychological symptoms in people with blood cancer.[a] Adapted from Manitta et al.[16]

Cancer-related fatigue 69%	Changes in skin 24%
Feeling worried 50%	Feeling bloated 23%
Difficulty sleeping 41%	Sweats 23%
Drowsiness 41%	Nausea and vomiting 22% and 8%
Feeling sad 41%	Itching 21%
Drowsiness 41%	Constipation 20%
Dry mouth 40%	Weight loss 19%
Pain 39%	Difficulty swallowing 18%
Numbness 38%	Changes in food taste 18%
Breathlessness 36%	Problems with urination 18%
Irritable 36%	Loss of sexual interest 18%
Difficult concentrating 34%	Diarrhoea 17%
Cough 33%	Lymphoedema 17%
Feeling nervous 33%	Don't look like self 16%
Lack of appetite 27%	Mouth sores 15%
Dizziness 24%	Hair loss 14%

[a] Listed in order of prevalence from a broad range of patients with blood cancer (type, stage, treatment and time since diagnosis) as described by Manitta et al.[16]

In the longer term, approximately 50% of survivors report at least one moderate-to-high level of unmet need, with physical aspects of daily living and psychological needs being the most commonly reported.[19] Within 5 years of treatment, about 35% of blood cancer survivors report ongoing problems with mobility and activities of daily living.[6] Poor HRQoL is an ongoing problem; treatment-related side effects and fear of recurrence contribute to this.[6] Worse HRQoL is seen in survivors of blood cancer who are younger, women or unemployed.[6]

Graft-versus-host disease

Graft-versus-host disease is a major complication of allogeneic stem cell transplantation (Table 1). It can be mild, affecting single organs, or it can be more severe, affecting multiple organs. Acute GVHD is seen in 20 to 80% of patients, typically affects the skin, liver and gastrointestinal tract, and clinically presents as a rash, gastrointestinal complications and hyperbilirubinaemia.[8] Chronic GVHD occurs in approximately 42% of patients within 3 years of transplantation,[10] although it usually develops within the first 100 to 200 days.[10] Chronic GVHD is associated with significant morbidity and mortality. It requires prolonged systemic immunosuppressive treatment[11] and infection is the main cause of death.[11]

The clinical manifestations of GVHD vary depending on the organs involved. This can range from the skin, mouth and oral cavity, eyes, genitalia, gastrointestinal tract, liver, lungs, haematopoietic, neurological, immune and/or musculoskeletal systems.[11] In the lungs, GVHD can cause bronchiolitis obliterans syndrome, airflow obstruction and recurrent infections,[11] clinically presenting as dyspnoea, wheeze and cough.[11] Neurologically, polyneuropathy, myositis and myasthenia can develop, clinically presenting as muscle weakness, wasting and pain.[11] Musculoskeletal manifestations from chronic GVHD and the ongoing use of systemic corticosteroid treatments include osteoporosis, steroid-induced myopathy, fasciitis and sclerotic contractures,[11] clinically presenting as joint contractures, restricted range of motion, limb swelling, muscle weakness and wasting.[11] There is significant heterogeneity in the clinical presentation of patients with chronic GVHD; therefore, physiotherapists working with patients who have developed GVHD must perform a thorough whole body assessment to identify impairments.

The National Institutes of Health have published a consensus paper on supportive care recommendations for the prevention and treatment of complications related to chronic GVHD.[11] The recommendations in their entirety are important for physiotherapists to be aware of; however, several aspects are worth highlighting due to their direct relevance to physiotherapists.[11] These are summarised in Table 2. Recommended treatments within physiotherapy scope of practice include pulmonary rehabilitation,[24] bronchodilators and supplemental oxygen therapy for lung complications; rehabilitation, falls prevention and bracing/splints for neurological complications; and exercise training for musculoskeletal complications (Table 2).[11]

Physical impairments

Patients with blood cancer can experience a multitude of physical impairments. There is a complex pattern of fatigue, reduced physical activity and deconditioning, combined with the impact of the cancer and medical treatments, which contribute to the development and worsening of physical impairments.[21] At diagnosis, in the months before treatment, individuals have been found to have reduced functional exercise capacity and muscle strength compared with expected values.[21,26] In 29 patients with lymphoma undergoing chemotherapy, pre-treatment 6-minute walk distance and quadriceps force were 89% predicted (IQR 38 to 111) and 82% predicted (SD 16) of normative values, respectively.[21] Reductions in muscle force before treatment may be due to a combination of tumour-related factors stimulating enhanced protein catabolism and decline in protein synthesis, and increased levels of tumour necrosis factor resulting in muscle wasting and contractile dysfunction.[21,27] There is also the influence of lack of physical activity.[21] In a sample of 71 hospitalised

Table 2
Recommendations within physiotherapy scope of practice for the prevention and treatment of complications from chronic graft-versus-host disease. Adapted from Carpenter et al[11] and Majhail et al.[25]

Organ affected	Prevention strategy	Treatments
Skin	Strict sun protection including avoidance of sun exposure 10 am to 4 pm, use of sunscreen and protective clothes	• Deep muscle massage for treatment of stiffness or contractures • Stretches to improve ROM
Lung	Education against smoking	• Pulmonary rehabilitation • Supplemental oxygen
Neurological system	Falls prevention	• Neurological rehabilitation • Resistance training • Orthotics
Musculoskeletal	• Monitor for reduced limb ROM every 3 to 12 months whilst on immunosuppressive therapy • Daily stretching at home • Stretching by a physiotherapist two to three times/week for severe cases • Follow general physical activity guidelines	• Frequent assessments of muscle strength and function (sit to stand ability) • Resistance training (isometric, isotonic, isokinetic) • Aerobic training • Weight-bearing exercise for osteoporosis
Cardiac and vascular	Education on healthy lifestyle: exercise, healthy weight, no smoking and diet	
Psychological	• Education on important return to regular exercise and sexual activities • Education on management of sexual functioning, body image, sleep, fatigue and musculoskeletal symptoms • Regular assessment of carer psychological adjustment and functioning	

ROM = range of motion.

patients undergoing chemotherapy for a range of blood cancers compared with healthy controls, there were reductions in: skeletal muscle mass index (whole body) of 4.1 (SD 0.9) versus 4.6 (SD 0.7) kg/m^2; quadriceps strength of 44 (SD 17) versus 52 (SD 17) % body weight ratio; and hand-grip strength of 39 (SD 12) versus 53 (SD 13) % body weight ratio.[26] During treatment patients experience further reductions in functional exercise capacity, muscle strength and mass,[21] potentially stimulated by the cytotoxic effects of chemotherapy more so than reduced physical activity.[21]

Sarcopenia and cachexia are common disorders in blood cancer. Sarcopenia is the age-related loss of muscle mass.[28] It is seen in approximately 51% of patients with blood cancer before treatment, confirmed with either bioimpedance analysis[29] or computed tomography.[30] Sarcopenia is a major concern in cancer as it contributes to poor tolerance to chemotherapy.[31] In blood cancer, sarcopenia is associated with worse outcomes including lower muscle strength, worse physical function, higher fatigue, greater pain, poorer HRQoL and worse overall survival.[29,32,33] Cancer-associated cachexia is the cytokine-mediated degradation of muscle and adipose deposits.[28] It is a complex metabolic syndrome, multifactorial and driven through an inflammatory response, resulting in it being a common complication in cancer.[34] It affects approximately 25% of patients with blood cancer,[26] although rates are lower than for many other solid tumours.[35] Cancer-associated cachexia leads to muscle wasting, weight loss and progressive functional impairment and is a common cause of cancer death.[28,34]

The optimal treatments for sarcopenia and cachexia for patients with cancer are unknown.[31,35] Exercise is recommended and may diminish the effects of sarcopenia and cachexia through stimulation of muscle protein synthesis and modulation of inflammation and insulin sensitivity.[36,37] However, there are limited data on exercise for cancer cachexia and scant data specifically for blood cancers.[36] A recent Cochrane review concluded that the effectiveness, acceptability and safety of exercise for cancer cachexia (in any cancer type) is uncertain and further research is required.[36] Clinically, at present for patients with cancer, a multimodal treatment approach is recommended including nutritional therapy, exercise training and or anti-inflammatory interventions.[31,35] Given the common occurrence of sarcopenia and cachexia in blood cancer, it is important that physiotherapists include an assessment of muscle strength as well as consideration of the nutritional status of their patient prior to, and alongside, exercise prescription. In the case of sarcopenia or cachexia, establishing adequate nutrition is critical; many centres have an automatic referral process to dieticians for nutritional assessment and management; however, if this is not the case, referral on from the physiotherapist is likely warranted.

Table 3
American College of Sports Medicine physical activity recommendations for the prevention and treatment of cancer in general.[38]

Recommendations for prevention of cancer[a]	Recommendations for cancer survivors
Participate in 150 to 300 minutes/wk of moderate aerobic exercise, or 75 to 150 minutes/wk of vigorous aerobic exercise	• Avoid inactivity • Increase to three 30-minute sessions per week of moderate intensity aerobic exercise and 20 to 30 minutes, two sessions per week of resistance training • Physical activity is associated with improvements in common cancer-related health outcomes including physical function, fatigue, anxiety and depression

[a] Data for the prevention of bladder, breast, colon, endometrial, oesophageal, kidney and stomach cancers.

Physical activity recommendations and barriers to compliance in blood cancer

The role of physical activity in the prevention and treatment of cancer is well established.[38,39] There is substantial and strong evidence for the prevention of many cancers, predominately solid tumours.[39] There is less evidence in blood cancer, although this is growing and the recent recommendations concluded that there is now 'limited' evidence for the protective effect of physical activity in blood cancer.[39–41] A systematic review with 27 trials demonstrated that higher physical activity levels were protective against lymphomas (non-Hodgkin lymphoma and Hodgkin lymphoma combined) (RR 0.89, 95% CI 0.81 to 0.98).[40] Data from seven trials demonstrated a dose response with a 1% reduction in lymphoma incidence per 3 metabolic equivalent of task (MET) hours/week of physical activity increase (RR 0.99, 95% CI 0.98 to 1.00, 6,019 participants).[40] Further research on physical activity and blood cancer prevention is warranted.

The recommendations for physical activity for people with cancer (Table 3) are predominately drawn from solid tumours or mixed

cancer types.[38] Research in blood cancer is less advanced,[42,43] partly due to the field being slower to adopt exercise due to safety concerns of an increased risk of infection and bleeding.[42] Concern has diminished with consistent data from trials in blood cancer showing that exercise is safe when conducted within safe parameters.[42,43] The current public message about physical activity for blood cancer is to avoid inactivity and return to usual activities when able after diagnosis.[44]

Survivors of blood cancer are poorly compliant with the physical activity guidelines. In a large population-based Canadian study with 606 blood cancer survivors, only 22% met the physical activity guidelines and these individuals were more likely to be younger and university educated.[45] Another 22% met the aerobic component only ($\geq$ 150 minutes/week) and 10% met the resistance component only (two or more sessions).[45] Yet intentions to exercise were high and 77% of participants intended to meet part of or the complete guideline.[45] People with blood cancer value the importance of exercise.[46,47] It is viewed as: a positive contribution that they can make toward their physical and mental wellbeing; providing a sense of empowerment and control; associated with hope for the future; helping to prepare for treatment, manage symptoms; and reducing the risk of recurrence and progression.[46,47]

Barriers to physical activity with blood cancer are numerous and include: symptoms and side effects, including fatigue, pain, shortness of breath and lack of strength; comorbidities and age-related inactivity; injuries; and lack of self-confidence and motivation.[20,46,47] Fatigue is the most commonly reported barrier,[20] whereas social barriers such as time and cost are less frequent.[20] Activity levels are lowest during treatment[48,49] and consistently do not return back to pre-diagnosis levels.[20,48] The leading predictor of post-diagnosis physical activity is pre-diagnosis physical activity.[20] This suggests that physiotherapy assessment of physical activity history is vital, and those individuals who have been less active may need additional support. Reassurance and early education that exercise will improve and not worsen fatigue are important for patients and families.[20]

Physiotherapy management of blood cancer

Physiotherapy management in blood cancer is centred around physical activity and exercise training. Figure 1 depicts the common timepoints at which physiotherapists can intervene during the treatment pathway and Figure 2 summarises the level of evidence for physiotherapy interventions. Exercise training is safe and generally feasible across these timepoints;[50] however, the rationale and prescription vary considerably. Prescription can range from assisted mobilisation or gentle chair-based exercises at times during inpatient treatment when blood counts are low, up to moderate- to high-intensity aerobic and resistance exercise training before or after treatment in outpatient settings. At each timepoint a unique exercise plan should be developed for the patient[50] and be frequently reviewed and adjusted based on symptom profile and safety parameters. This section describes the ideal scenario of evidence-based physiotherapy management; however, in some hospitals and centres this may not yet be reflected in current clinical practice.

Assessment

An initial physiotherapy assessment is recommended for patients being worked-up for treatment (Figure 1), ideally as part of a clinical pathway[51] and alongside other disciplines including dieticians. The purpose is to assess physical fitness and identify impairments, to be able to target physiotherapy treatments, and monitor deterioration or complications with treatment.[51] Suggested components of an initial assessment are provided in Table 4.[51] Physiotherapists may also be able to access results of respiratory function tests. Physiotherapy assessment prior to treatment is not always part of standard care. Often, the first time that a physiotherapist sees the patient it is as an inpatient, once treatment has commenced or following referral from medical or nursing colleagues if the patient has mobility, functional or respiratory issues. Assessment during hospitalisation should occur prior to each physiotherapy encounter[50] (see next section), and after treatment should occur on initial contact with the therapist and then at regular intervals (recommended to be monthly)[51] (Figure 1). After treatment, physiotherapists should screen for signs of complications such as GVHD and target treatment accordingly (Table 2).[11]

Acute physiotherapy during medical treatment

Acute physiotherapy is typically delivered in the inpatient hospital setting whilst patients are hospitalised for medical treatment. The goals of physiotherapy treatment are maintenance of strength and function during this period of time when patients usually experience significant deconditioning.[50] Physiotherapy routinely includes mobilisation and exercise training;[51] however, other treatments including

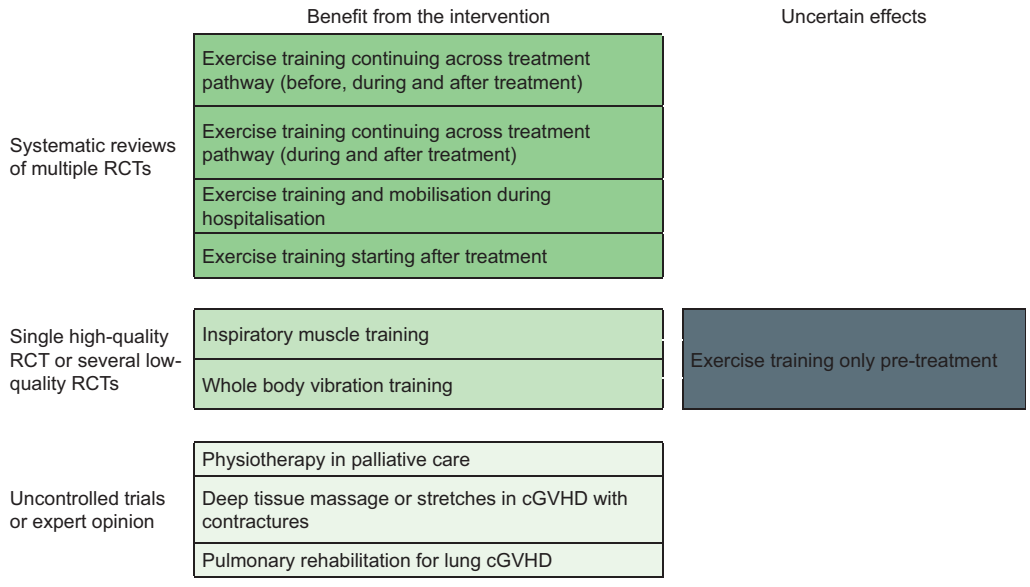

Figure 2. Interventions for the management of blood cancer with associated levels of evidence. 'Exercise training only pre-treatment' refers to data from studies that only included exercise at this time point and did not continue with an exercise program during or after treatment.
cGVHD = chronic graft-versus-host disease, RCTs = randomised controlled trials.

Table 4
Physiotherapy assessment pre-treatment in blood cancer. Adapted from Mohammed et al.[51]

Outcome/component	Example measures
Subject assessment/history	Comprehensive physiotherapy subjective assessment including: medications existing musculoskeletal and comorbid conditions occupation and return to work or study goals physical activity levels[a] – current and past functional impairments symptoms[a] anxiety, depression or distress[a]
Functional exercise capacity	6-minute walk test or incremental shuttle walk test
Physical function	30-second chair stand test, Short Physical Performance Battery or Timed Up and Go
Self-reported function	Lower Extremity Functional Scale or Disabilities of the Arm, Shoulder and Hand Questionnaire
Peripheral muscle and hand-grip strength	Hand-held and hand-grip dynamometers
Peripheral muscle mass	Ultrasound
Frailty	Clinical frailty scale
Upper and lower limb range of motion	Range measured with a goniometer
HRQoL	EORTC QLQ-C30

EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life questionnaire, HRQoL = health-related quality of life.
[a] Can also be assessed using self-reported questionnaires.

range of motion, balance training and activities of daily living training may be required (Figure 1). The exercise programs tested in the literature to date vary, although they are most commonly individualised, supervised, low- to moderate-intensity aerobic exercises,[50,51] sometimes supplemented with resistance exercises and unsupervised exercise on non-physiotherapy days.[50,51] Physiotherapy is often delivered on a 1:1 basis either in the patient's single room or on a pressure-filtered ward to minimise infection risk;[43] however, emerging data suggest that group-based exercise on a pressure-filtered ward is safe[14] and potentially adds the psychological benefit of peer support.[48]

The evidence to date suggests that exercise during treatment is safe and feasible, with very few adverse events reported. The evidence for efficacy of exercise during treatment is inconsistent. Results of recent systematic reviews[42,43] show neutral or positive benefits of exercise on patient outcomes of muscle strength, endurance and fatigue compared with decline in control groups,[43,50] although the results are inconsistent, trials are small and the risk of bias is high.[43,50] Many studies have been unable to attenuate deconditioning experienced during treatment.[14,43] There may be earlier recovery of blood counts,[52] but other studies have not demonstrated between-group differences.[43] Commonly, exercise is tested as part of a broader pre-to-post exercise program. The meta-analysis by Abo et al[43] of seven trials commencing exercise either before or during stem cell transplantation demonstrated a reduced hospital length of stay in favour of exercise training (MD 2.1 days, 95% CI 0.4 to 3.7, 379 participants, low-certainty evidence).[43] Cost-effectiveness of such programs is unknown.

Daily assessment before physiotherapy treatment is important and should include symptom levels, vital signs and blood counts (haemoglobin, platelets and white blood cells).[50] Clinical decision-making is required to tailor an appropriate mobilisation or exercise treatment that takes the patient to their highest functional level within safety limits. Discussion with the treating medical team is recommended regarding the planned physiotherapy treatment and specific precautions or contraindications for the patient at that time. Wiskemann et al[53] and Abo et al[14] utilised models where patients self-rated their wellbeing prior to each session and this rating was used by therapists to adjust the exercise plan (Figure 3).

Patients are likely to have anaemia, thrombocytopenia and neutropenia, which impact the appropriateness of physiotherapy treatments. There is a balance between bed rest to prevent bleeding, infection or clinical compromise versus the risk of functional decline and deconditioning associated with prolonged sedentary time. Several publications have reported haematological safety criteria for physiotherapy or exercise during blood cancer treatment.[15,50,51,54] Table 5 provides an example of a safety protocol based on the consensus-based recommendations for acute physiotherapy for patients with multiple myeloma undergoing chemotherapy and stem cell transplantation,[50] which is endorsed by the Canadian Physiotherapy Association. Physiotherapists should also refer to their local hospital policies and work in consultation with the medical team.

Other emerging physiotherapy treatments investigated in studies to date include inspiratory muscle training, whole body vibration[55] and mindful breathing.[56] In the trial by Almeida et al,[57] 57 inpatients undergoing stem cell transplantation received standard care physiotherapy (early mobilisation, breathing exercises and aerobic training). The intervention group additionally performed inspiratory muscle training, 5 days/week, at 40% baseline maximal inspiratory pressure, through an inspiratory pressure threshold loading device and supervised by a physiotherapist.[57] The inspiratory muscle training group had improved maximal inspiratory pressure at hospital discharge (+17%) compared with a reduction in the control group (−20%) from admission.[57] Both groups maintained muscle strength, functional exercise capacity and physical function from admission to hospital discharge (median 21 days) attributed to the standard care physiotherapy.[57]

Self-rating	Score of out 10[a]	Health status	Exercise prescription
Green	8 to 10	Good or normal health No symptoms No concerns	Moderate-intensity aerobic (Borg 3 to 5 out of 10) and resistance (RPE 12 to 14 out of 20) exercises
Orange	5 to 7	Medium health Mild symptoms of fatigue and nausea Very mild pain	Low- to moderate-intensity aerobic (Borg 1 to 3 out of 10) and resistance (RPE 9 to 11 out of 20) exercises
Red	0 to 5	Low health Fatigue, nausea or pain Borderline blood counts	Low-intensity aerobic exercises usually chair based (Borg 1 to 3 out of 10) and functional exercises (RPE 9 to 11 out of 20) without resistance

Figure 3. Traffic light system (patient-self rating) used to assess patient wellbeing and inform daily adjustments to inpatient exercise prescription, as utilised by Abo et al.[14]
Borg = Modified Borg Dyspnoea scale, RPE = Rating of Perceived Exertion scale.
[a] Rating from 0 (feeling very unwell, significant symptoms, difficult to get out of bed) to 10 (feeling well, normal health status, no issues).

Table 5
Safety considerations for acute physiotherapy (mobilisation and exercise prescription) for blood cancer. Adapted from Jeevanantham et al.[50]

Condition	Precautions and contraindications[50]
Anaemia	If haemoglobin < 80 g/L • Exercise training generally contraindicated • Consult with physician before commencement • Physiotherapy intervention with caution • Mobilisation with caution and monitor closely for vital signs and adverse events including chest pain, pallor, leg cramps, dizziness, arrhythmias, shortness of breath, respiratory distress, SBP > 200 mmHg, DBP > 110 mmHg, drop in SBP > 10 mmHg from baseline, HR > 120 bpm, SpO_2 < 88% on activity, positive orthostatic response During red blood cell transfusion • Mobilisation with caution and monitor closely for abnormal vital signs and adverse events including dislodgment of intravenous site, syncope or reaction to blood products
Thrombocytopenia	Monitor for signs of bleeding Educate patients about signs of bleeding and precautions Caution with equipment and clothing to prevent bleeding Consult with physician about appropriateness of physiotherapy, weighing up the balance for bed rest to prevent bleeding versus functional decline with inactivity If platelet count < 10,000/μL • Only essential ambulation such as to bathroom, with assistance or supervision to prevent falls • Gentle ROM in sitting or lying If platelet count 10,000 to 20,000 μL • Gentle ROM and exercises without resistance or strain • Exercise in standing or mobilisation only if patient ambulates unassisted, independently and has no signs of bleeding If platelet count 20,000 to 40,000/μL • Low-intensity (gentle) aerobic exercise permitted • Light resistance exercises using elastic bands without strain and only if no signs of bleeding If platelet count > 40,000/μL • Low-intensity (gentle) aerobic exercise including stationary cycling permitted If platelet count < 50,000/μL • Avoid high-intensity exercise
Leukopenia and neutropenia	Patient to wear a face mask when ambulating outside of room Patient to perform regular hand hygiene, including before and after physiotherapy Equipment to be cleaned before and after use Physiotherapy intervention delivered in patient's room
Bony lesions or skeletal issues	Exercise under supervision Modify exercise program to patient situation Avoid high-impact activities and end range of motion. Exercises should avoid twisting, bending, overhead reaching, pushing, pulling and lifting weights. Ensure correct technique, including back care, and use gait aids and braces as needed

DBP = diastolic blood pressure, HR = heart rate, ROM = range of motion, SBP = systolic blood pressure, μL = microlitre.

Exercise training before and after treatment

Physiotherapy before and after treatment is mainly focused on exercise training (Figure 1). Variations in clinical practice exist in terms of the degree of physiotherapy input available; however, prehabilitation and rehabilitation programs are more commonly becoming standard care for this patient group in line with growing evidence. For patients after transplantation, if there is not a hospital/outpatient program available, home-based exercise is encouraged and it is recommended to avoid exercising with the public, such as in a gym, until there has been full recovery of the immune system.[38] Before treatment, exercise aims to maximise muscle strength and exercise capacity in order to attenuate the decline with treatment. Higher strength and exercise capacity going into treatment are associated with better performance in these measures after treatment.[58] After hospitalisation and treatment, exercise aims to target residual impairments, symptoms and side effects. At this point, symptoms and wellbeing fluctuate, and exercise volume and intensity should be reviewed and adapted daily depending on patient presentation.[38]

Knips et al recently updated their Cochrane review of aerobic exercise for patients with blood cancer.[42] The update includes 18 randomised controlled trials (RCTs) and 1,892 participants with blood cancer exercising at different points across the treatment pathway. The earliest trial started recruitment in 2002[59] and patients received a stem cell transplant in half of the trials.[42] The exercise programs tested in trials varied considerably: home, inpatient or outpatient based; consisting of either aerobic, resistance or mixed training. The timing of programs varied across before, during and after treatment. The longest program was 30 weeks[60] and shortest program commenced 6 days before transplant and finished the day before hospital discharge after treatment.[59] Meta-analyses demonstrated significant benefit on fatigue (SMD 0.31, 95% CI 0.13 to 0.48, 826 participants, moderate-certainty evidence) and a small effect for reduction in the depression subscale of HRQoL (SMD 0.19, 95% CI 0.0 to 0.38, 445 participants, low-certainty evidence). No clear between-group differences were observed for mortality (RR 1.10, 95% CI 0.79 to 1.52, 1,172 participants, low-certainty evidence), global HRQoL, physical function HRQoL or anxiety-domain HRQoL. The HRQoL results did not change in sub-analyses of patients receiving chemotherapy only or stem cell transplantation. Meta-analyses were unable to be completed for exercise capacity or strength, due to heterogeneity in measurement of these outcomes; individual trials report conflicting results (eight RCTs benefit and five RCTs no difference).[42] The authors suggest that variations in the exercise programs, medical treatments and standard care may have influenced their outcomes.[42]

The systematic review by Abo et al[43] focused specifically on patients with blood cancers undergoing stem cell transplantation and included 27 studies (24 RCTs), with one-third of studies published in the last 5 years. Only two studies focused entirely on pre-transplant exercise;[61,62] both were small feasibility studies. Neither study demonstrated significant changes in patient outcomes before and after the program, and both reported low to moderate feasibility.[61,62] Abo et al[43] included 10 studies with exercise entirely during treatment, six entirely after treatment/hospitalisation, and 10 with exercise across the pre-, during and or post-treatment settings. The mean PEDro score of RCTs was 5 (SD 1), which is illustrative of the high risk of bias within the RCTs published to date. Meta-analyses demonstrated positive effects of exercise compared with no exercise on functional exercise capacity (6-minute walk distance MD 29 m, 95% CI 13 to 45, 542 participants, moderate-certainty evidence) and upper and lower body muscle strength (lower body strength SMD 0.39, 95% CI 0.20 to 0.58, 431 participants, low-certainty evidence).[43] The difference between these results and Knips et al[42] may be due to the narrower inclusion (only stem cell transplantation recipients) and

addition of several new trials. Meta-analysis results concurred with the findings by Knips et al[42] in terms of positive effects on global HRQoL and fatigue.[43] Effects on functional exercise capacity and fatigue were larger in patients undergoing allogeneic stem cell transplant than autologous, although certainty for these sub-analyses was low.[43]

The feasibility of pre- and post-treatment exercise programs varies in the literature. For example, in patients undergoing a transplant, consent varies from 23 to 99% and adherence from 24 to 92%.[43] In the pre-treatment setting, home-based and outpatient-based programs have been tested, but both appear to have problems related to feasibility. Van Haren et al[61] included 29 patients of mixed blood cancer types undergoing either allogeneic or autologous stem cell transplant. The intervention was a physiotherapist-supervised, moderate-to high-intensity aerobic and resistance training program, twice/week, for 4 to 6 weeks pre-transplant. Adherence to the program was 69% but the median number of sessions attended was only six. Wood et al[62] included 34 patients who were awaiting allogeneic stem cell transplantation. The intervention was an unsupervised, home-based, high-intensity interval aerobic exercise program supported by weekly motivational phone calls and provision of an activity tracking device. Recruitment was ceased early due to challenges, and intervention adherence was poor. The authors recommended that future trials maintain high frequency of patient contact (such as through remote monitoring) and focus on exercise close to and during the transplantation period, as most other trials have done. The largest RCT in exercise and blood cancer was a four-arm RCT (self-directed exercise, self-administered relaxation, both and neither) with 711 patients.[63] This trial demonstrated no difference in outcomes, including HRQoL at 100 days, distress, sleep or survival, and suggested that a hands-off, self-directed approach may not be effective in this population.[63] Early after discharge from hospital, patients routinely attended outpatient medical appointments up to three times/week for the first 100 days. This provides an opportunity for outpatient hospital-based physiotherapy input including exercise programs (Figure 1). Local experience is that there is good feasibility of offering an exercise program for patients to join at the hospital when attending their medical appointments during this time.[15]

Education forms an important part of physiotherapy treatment for people with blood cancer. This includes advice to keep active and safely return to physical activity when able; physical activity guidelines; barriers to being active; symptom management; healthy lifestyle behaviours including diet; infection control; and safety considerations related to exercise. For patients who do not have access to physiotherapy or an exercise program at their treating hospital, referral to a community oncology rehabilitation or pulmonary rehabilitation program is recommended.[64]

Physiotherapy in palliative care

Physiotherapy for patients in palliative or end-of-life care is typically focused on supporting the individual to maintain their independence, comfort and HRQoL, as well as reduce carer burden. Physiotherapists work closely with the palliative care multidisciplinary team in this setting. Treatment should relate directly to the goals of the patient; it may focus on alleviating symptoms, maintaining physical function and ability to perform activities of daily living.[65] Treatments are individualised to the patient and can include mobilisation, less intensive exercise, provision of gait aids, activities of daily living training/support, symptom management, and relaxation or breathing exercises (Figure 1).

Future directions for research and practice

Physiotherapy plays an important role in the management of blood cancer across the disease and treatment pathway. There has been significant growth in the evidence, especially in the last 5 years, mainly focused on the efficacy of exercise training. Early concerns related to exercise and safety are now lessened. Given the significant disease burden and residual complications experienced by patients well after treatment has concluded, there is a strong rationale for physiotherapy and exercise training to address these impairments. With prevalence of blood cancer increasing, there is urgency for high-quality evidence to inform clinical practice. Questions remain around: the optimal type, timing and setting of exercise training; the cost-effectiveness of programs; the impact on overall survival; and longer-term patient outcomes beyond 1 year post-treatment. Additionally, many of the trials conducted to date are limited by high risk of bias and most conclusions from recent meta-analyses are low certainty. Future trials are still needed and should avoid prior limitations, including lack of assessor blinding, incomplete outcome data and selective reporting of outcomes without prior trial registration.

There is a huge interest in this field and numerous trials in progress, which will soon significantly improve understanding (there are currently 25 open exercise studies registered on ClinicalTrials.gov). Several of these trials include multi-modal interventions offering exercise combined with nutritional support, relaxation strategies, mindfulness, cognitive behavioural therapy, psychology, and/or input from other allied health disciplines as both a multidisciplinary prehabilitation or rehabilitation program.

Due to the COVID-19 pandemic, clinical practice in the field was forced to adapt rapidly and, in many centres, exercise programs for patients with blood cancer delivered by telehealth (such as videoconferencing) are now part of standard care. In this situation, clinical practice moved forward by implementing telehealth-delivered programs before evidence was generated. A major emphasis of the current trials is investigating the efficacy of exercise delivered via telehealth. Lee et al[66] are investigating the benefit of a home-based exercise program, supervised by a clinical exercise physiologist, via telehealth for 60 participants with multiple myeloma 30 to 180 days after stem cell transplantation. The 8-week individualised exercise program includes 24 videoconferencing exercise sessions, run for at least 30 minutes on 3 days/week. The primary outcome is physical function measured by the Short Physical Performance Battery. The trial is currently recruiting and estimated to be completed at the end of 2024. Given the issues of feasibility described by some prior trials, telehealth is an appealing model so this is likely to inform ongoing use of this model in clinical practice if the efficacy data are favourable.

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References

1. Leukaemia Foundation. *State of the Nation: Blood Cancer in Australia.* 2019.
2. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia*. 2022;36:1703–1719.
3. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IB, Berti E, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. *Leukemia*. 2022;36:1720–1748.
4. Siegel R, Miller K, Wagle N, Jemal A. Cancer statistics, 2023. *CA*. 2023;73:17–48.
5. Australian Institute of Health Welfare. *Cancer data in Australia*. Canberra: AIHW; 2022.
6. Immanuel A, Hunt J, McCarthy H, van Teijlingen E, Sheppard ZA. Quality of life in survivors of adult haematological malignancy. *Eur J Cancer*. 2019;28:e13067.
7. McCourt O, Yong K, Ramdharry G, Fisher A. Physical Activity During and After Haematological Cancer Treatment: A Cross-Sectional Survey of Haematology Healthcare Professionals in the United Kingdom. *J Multidiscip Healthc*. 2021;14:1659.
8. Saad A, de Lima M, Anand S, Bhatt VR, Bookout R, Chen G, et al. Hematopoietic Cell Transplantation, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. *JNCCN*. 2020;18:599–634.
9. Nivison-Smith I, Bardy P, Dodds AJ, Ma DD, Aarons D, Tran S, et al. A Review of Hematopoietic Cell Transplantation in Australia and New Zealand, 2005 to 2013. *Biol Blood Marrow Transplant*. 2016;22:284–291.

10. Bachier CR, Aggarwal SK, Hennegan K, Milgroom A, Francis K, Dehipawala S, et al. Epidemiology and Treatment of Chronic Graft-versus-Host Disease Post-Allogeneic Hematopoietic Cell Transplantation: A US Claims Analysis. *Transplant Cell Ther*. 2021;27:504.e501–504.
11. Carpenter PA, Kitko CL, Elad S, Flowers ME, Gea-Banacloche JC, Halter JP, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: V. The 2014 Ancillary Therapy and Supportive Care Working Group Report. *Biol Blood Marrow Transplant*. 2015;21:1167–1187.
12. Australian Bone Marrow Donor Registry. Information for Patients: Adult transplant centres. https://www.abmdr.org.au/patients/adult-transplant-centres/. Published 2023. [Accessed 27/01/2023].
13. Leukaemia Foundation. About Leukaemia Foundation accommodation services. https://www.leukaemia.org.au/how-we-can-help/accommodation-services/about-accommodation-services/. Published 2023. [Accessed 27/01/2023].
14. Abo S, Ritchie D, Denehy L, Panek-Hudson Y, Irving L, Granger CL. Feasibility of early-commencing group-based exercise in allogeneic bone marrow transplantation: the BOOST study. *Bone Marrow Transplant*. 2021.
15. Abo S, Ritchie D, Denehy L, Panek-Hudson Y, Irving L, Granger CL. A hospital and home-based exercise program to address functional decline in people following allogeneic stem cell transplantation. *Support Care Cancer*. 2018;26:1727–1736.
16. Manitta V, Zordan R, Cole-Sinclair M, Nandurkar H, Philip J. The symptom burden of patients with hematological malignancy: a cross-sectional observational study. *J Pain Symptom Manage*. 2011;42:432–442.
17. Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation. *J Clin Oncol*. 2014;32:1840–1850.
18. Hjermstad MJ, Fosså SD, Oldervoll L, Holte H, Jacobsen AB, Loge JH. Fatigue in Long-Term Hodgkin's Disease Survivors: A Follow-Up Study. *J Clin Oncol*. 2005;23:6587–6595.
19. Barata A, Wood WA, Choi SW, Jim HSL. Unmet Needs for Psychosocial Care in Hematologic Malignancies and Hematopoietic Cell Transplant. *Curr Hematol Malig Rep*. 2016;11:280–287.
20. Craike M, Hose K, Livingston PM. Physical activity participation and barriers for people with multiple myeloma. *Support Care Cancer*. 2013;21:927–934.
21. Vermaete N, Wolter P, Verhoef G, Gosselink R. Physical activity and physical fitness in lymphoma patients before, during, and after chemotherapy: a prospective longitudinal study. *Ann Hematol*. 2014;93:411–424.
22. Raphael D, Frey R, Gott M. Psychosocial distress in haematological cancer survivors: An integrative review. *Eur J Cancer*. 2017;26:e12640.
23. Raphael D, Frey R, Gott M. The nature and timing of distress among post-treatment haematological cancer survivors. *Eur J Cancer Care*. 2019;28:e12951.
24. Tran J, Norder EE, Diaz PT, Phillips GS, Elder P, Devine SM, et al. Pulmonary rehabilitation for bronchiolitis obliterans syndrome after hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant*. 2012;18:1250–1254.
25. Majhail NS, Rizzo JD, Lee SJ, Aljurf M, Atsuta Y, Bonfim C, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2012;18:348–371.
26. Fukushima T, Nakano J, Ishii S, Natsuzako A, Hirase T, Sakamoto J, et al. Characteristics of muscle function and the effect of cachexia in patients with haematological malignancy. *Eur J Cancer*. 2019;28:e12956.
27. Reid MB, Lännergren J, Westerblad H. Respiratory and Limb Muscle Weakness Induced by Tumor Necrosis Factor-α. *Am J Respir Crit Care Med*. 2002;166:479–484.
28. Peterson SJ, Mozer M. Differentiating Sarcopenia and Cachexia Among Patients With Cancer. *Nutr Clin Pract*. 2017;32:30–39.
29. Morishita S, Kaida K, Tanaka T, Itani Y, Ikegame K, Okada M, et al. Prevalence of sarcopenia and relevance of body composition, physiological function, fatigue, and health-related quality of life in patients before allogeneic hematopoietic stem cell transplantation. *Support Care Cancer*. 2012;20:3161–3168.
30. Xiao DY, Luo S, O'Brian K, Ganti A, Riedell P, Sanfilippo KM, et al. Impact of sarcopenia on treatment tolerance in United States veterans with diffuse large B-cell lymphoma treated with CHOP-based chemotherapy. *Am J Hematol*. 2016;91:1002–1007.
31. Bozzetti F. Forcing the vicious circle: sarcopenia increases toxicity, decreases response to chemotherapy and worsens with chemotherapy. *Ann Oncol*. 2017;28:2107–2118.
32. Go S, Park M, Song H, Kim HG, Kang MH, Kang JH, et al. A comparison of pectoralis versus lumbar skeletal muscle indices for defining sarcopenia in diffuse large B-cell lymphoma - two are better than one. *Oncotarget*. 2017;8:47007–47019.
33. Sun Q, Cui J, Liu W, Li J, Hong M, Qian S. The Prognostic Value of Sarcopenia in Acute Myeloid Leukemia Patients and the Development and Validation of a Novel Nomogram for Predicting Survival. *Front Oncol*. 2022;12:828939.
34. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011;12:489–495.
35. Baracos V, Martin L, Korc M, Guttridge DC, Fearon KC. Cancer-associated cachexia. *Nat Rev Dis Primers*. 2018;4:17105.
36. Grande AJ, Silva V, Sawaris Neto L, Teixeira Basmage JP, Peccin MS, Maddocks M. Exercise for cancer cachexia in adults. *Cochrane Database Syst Rev*. 2021;3:Cd010804.
37. Maddocks M, Murton AJ, Wilcock A. Therapeutic exercise in cancer cachexia. *Crit Rev Oncog*. 2012;17:285–292.
38. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. *Med Sci Sports Exerc*. 2019;51:2375–2390.
39. Patel AV, Friedenreich CM, Moore SC, Hayes SC, Silver JK, Campbell KL, et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. *Med Sci Sports Exerc*. 2019;51:2391–2402.
40. Davies GA, Strader C, Chibbar R, Papatheodorou S, Dmytriw AA. The relationship between physical activity and lymphoma: a systematic review and meta analysis. *BMC cancer*. 2020;20:962.
41. Jochem C, Leitzmann MF, Keimling M, Schmid D, Behrens G. Physical Activity in Relation to Risk of Hematologic Cancers: A Systematic Review and Meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2014;23:833–846.
42. Knips L, Bergenthal N, Streckmann F, Monsef I, Elter T, Skoetz N. Aerobic physical exercise for adult patients with haematological malignancies. *Cochrane Database Syst Rev*. 2019;2019:undefined-undefined.
43. Abo S, Denehy L, Ritchie D, Lin KY, Edbrooke L, McDonald C, et al. People With Hematological Malignancies Treated With Bone Marrow Transplantation Have Improved Function, Quality of Life, and Fatigue Following Exercise Intervention: A Systematic Review and Meta-Analysis. *Phys Ther*. 2021;101.
44. Cormie P, Atkinson M, Bucci L, Cust A, Eakin E, Hayes S, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust*. 2018;209:184–187.
45. Vallerand JR, Rhodes RE, Walker GJ, Courneya KS. Correlates of meeting the combined and independent aerobic and strength exercise guidelines in hematologic cancer survivors. *IJBNPA*. 2017;14:44.
46. Colton A, Smith M, Broadbent S, Rune K, Wright H. Perceptions of Older Adults with Hematological Cancer on Diet and Exercise Behavior and Its Role in Navigating Daily Tasks. In. Int J Environ Res Public Health. Vol 19: MDPI AG; 2022: 15044–15044.
47. Abo S, Parry SM, Ritchie D, Sgro G, Truong D, Denehy L, et al. Exercise in allogeneic bone marrow transplantation: a qualitative representation of the patient perspective. *Support Care Cancer*. 2022;30:5389–5399.
48. Vallance JKH, Courneya KS, Jones LW, Reiman T. Differences in quality of life between non-Hodgkin's lymphoma survivors meeting and not meeting public health exercise guidelines. *Psycho-Oncol*. 2005;14:979–991.
49. Danaher EH, Ferrans C, Verlen E, Ravandi F, van Besien K, Gelms J, et al. Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncol Nurs Forum*. 2006;33:614–624.
50. Jeevanantham D, Rajendran V, McGillis Z, Tremblay L, Larivière C, Knight A. Mobilization and Exercise Intervention for Patients With Multiple Myeloma: Clinical Practice Guidelines Endorsed by the Canadian Physiotherapy Association. *Phys Ther*. 2021;101.
51. Mohammed J, Aljurf M, Althumayri A, Almansour M, Alghamdi A, Hamidieh AA, et al. Physical therapy pathway and protocol for patients undergoing hematopoietic stem cell transplantation: Recommendations from The Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) Group. *Hematol Oncol Stem Cell Res*. 2019;12:127–132.
52. Kim SD, Kim HS. A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. *Eur J Cancer Care*. 2006;15:453–457.
53. Wiskemann J, Dreger P, Schwerdtfeger R, Bondong A, Huber G, Kleindienst N, et al. Effects of a partly self-administered exercise program before, during, and after allogeneic stem cell transplantation. *Blood*. 2011;117:2604–2613.
54. Mina DS, Langelier D, Adams SC, Alibhai SM, Chasen M, Campbell KL, et al. Exercise as part of routine cancer care. *Lancet Oncol*. 2018;19:e433–e436.
55. Pahl A, Wehrle A, Kneis S, Gollhofer A, Bertz H. Whole body vibration training during allogeneic hematopoietic cell transplantation-the effects on patients' physical capacity. *Ann Hematol*. 2020;99:635–648.
56. Ng DL, Gan GG, Anuar NA, Tung YZ, Lai NZ, Tan YW, et al. The effect of a single session of 30-min mindful breathing in reducing fatigue among patients with haematological cancer – a randomised controlled trial. *BMC Palliative Care*. 2021;20:1–9.
57. Almeida LB, Laterza MC, Rondon M, de Matos LD, Granger CL, Denehy L, et al. Inspiratory muscle training in addition to conventional physical rehabilitation in hospitalized patients undergoing hematopoietic stem cell transplantation: a randomized controlled trial. *Support Care Cancer*. 2022;30:9393–9402.
58. Ishikawa A, Otaka Y, Kamisako M, Suzuki T, Miyata C, Tsuji T, et al. Factors affecting lower limb muscle strength and cardiopulmonary fitness after allogeneic hematopoietic stem cell transplantation. *Support Care Cancer*. 2019;27:1793–1800.
59. Baumann F, Kraut L, Schüle K, Bloch W, Fauser A. A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplant*. 2010;45:355–362.
60. Coleman EA, Coon SK, Kennedy RL, Lockhart KD, Stewart CB, Anaissie EJ, et al. Effects of exercise in combination with epoetin alfa during high-dose chemotherapy and autologous peripheral blood stem cell transplantation for multiple myeloma. *Oncol Nurs Forum*. 2008;35:E53–E61.
61. van Haren I, Staal JB, Potting CM, Blijlevens NM, Staal JB, Nijhuis-van der Sanden MW. Physical exercise prior to hematopoietic stem cell transplantation: A feasibility study. *Physiother Theory Pract*. 2018;34:747–756.
62. Wood WA, Weaver M, Smith-Ryan AE, Hanson ED, Shea TC, Battaglini CL. Lessons learned from a pilot randomized clinical trial of home-based exercise prescription before allogeneic hematopoietic cell transplantation. *Support Care Cancer*. 2020;28:5291–5298.
63. Jacobsen PB, Le-Rademacher J, Jim H, Syrjala K, Wingard JR, Logan B, et al. Exercise and stress management training prior to hematopoietic cell transplantation: Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0902. *Biol Blood Marrow Transplant*. 2014;20:1530–1536.
64. Dennett A, Sarkies M, Shields N, Peiris CL, Williams C, Taylor NF. Multidisciplinary, exercise-based oncology rehabilitation programs improve patient outcomes but their effects on healthcare service-level outcomes remain uncertain: a systematic review. *J Physiother*. 2021;67:12–26.
65. Chowdhury R, Brennan F, Gardiner M. Cancer Rehabilitation and Palliative Care-Exploring the Synergies. *J Pain Symptom Manag*. 2020;60:1239–1252.
66. Lee K, Nathwani N, Shamunee J, Lindenfeld L, Wong FL, Krishnan A, et al. Telehealth exercise to Improve Physical function and frailty in patients with multiple myeloma treated with autologous hematopoietic Stem cell transplantation (TIPS): protocol of a randomized controlled trial. *Trials*. 2022;23:921.