Physical Activity as a Supportive Care Intervention in Palliative Cancer Patients: A Systematic Review

Sonya S. Lowe, MD, MSc, Sharon M. Watanabe, MD, and Kerry S. Courneya, PhD

Abstract Previous systematic reviews have concluded that physical activity improves supportive care outcomes in cancer patients, but the conclusions are based largely upon data from patients with early-stage cancer. The aim of this study was to systematically review the best available evidence of physical activity as a supportive care intervention in palliative cancer patients. All published studies examining the effect of physical activity interventions on quality of life, fatigue, and physical function outcomes in palliative cancer patients aged 18 years or older were included. Six studies were identified, with significant heterogeneity in terms of study design, participant characteristics, type of physical activity intervention, and outcomes. Although they generally reported positive preliminary findings, the overall methodologic quality of the studies was poor. There is insufficient evidence to evaluate the efficacy of physical activity as a supportive care intervention in palliative cancer patients; methodologically, rigorous studies with larger samples and appropriate comparison groups are warranted.

Palliative care is the interdisciplinary and holistic management of progressive, advanced disease wherein prognosis is limited and the primary goal is quality of life (QOL).[1] In the end stages of illness, overall QOL can encompass physical, psychosocial, and spiritual issues for both the patient and their family. The progression of disease is often accompanied by the escalation of symptoms, such as pain and fatigue, which can contribute greatly to total suffering. Alleviating suffering is a key aim of palliation, thus minimizing the symptomatic burden can apply throughout the illness trajectory, particularly at the end stages of disease.[2]

Palliative care is a key component of the management of cancer. In Canada, an estimated 159,900 new cancer diagnoses and 72,700 deaths from cancer occurred in 2007.[3] As both screening and treatment modalities for cancer improve, patients are living longer with cancer and its associated symptoms; disease and symptom burden are particularly compounded in those with progressive, incurable, and locally recurrent or metastatic cancer. Thus, the role of palliative care in targeting symptoms, and thereby improving overall QOL, becomes more crucial in cancer patients.

Among the most devastating and disruptive symptoms of cancer are cancer-related fatigue (CRF) and loss of physical function. CRF is defined as a constant, subjective sensation of exhaustion associated with cancer or its treatment that impedes normal functioning and that is out of proportion to recent activity; the prevalence of CRF among palliative cancer patients is estimated to be between 60% and 90%.[4] Loss of physical function can be attributed to CRF, as well as generalized muscle weakness and wasting due to anorexia-cachexia syndrome; this decline in physical function, and subsequent loss of mobility and independence, has been identified as one of the top distressing symptoms that negatively impacts QOL in palliative cancer patients.[5] Therefore, the need for supportive care interventions targeting CRF and loss of physical function is critical in palliative cancer care.

Physical activity is one potential intervention that can address this need in palliative cancer patients. Physical activity is defined as any bodily

Dr. Lowe is AHFMR Clinical Fellow, Division of Palliative Care Medicine, Department of Oncology, University of Alberta, and a member of the Department of Symptom Control and Palliative Care, Cross Cancer Institute, Edmonton, Alberta, Canada. Dr. Watanabe is Associate Professor, Division of Palliative Care Medicine, Department of Oncology, University of Alberta, and Director, Department of Symptom Control and Palliative Care, Cross Cancer Institute, Edmonton, Alberta, Canada. Dr. Courneya is Canada Research Chair in Physical Activity and Cancer; Professor, Faculty of Physical Education and Recreation; and Director, Behavioral Medicine Laboratory and Fitness Centre, Faculty of Physical Education & Recreation, University of Alberta, Edmonton, Alberta, Canada

Manuscript submitted July 31, 2008;
accepted January 13, 2009.

Correspondence to: Sonya S. Lowe, MD, MSc, Department of Oncology, University of Alberta, 11560 University Avenue, Edmonton, Alberta, Canada T6G 1Z2; telephone: (780) 432-8318; fax: (780) 432-8419; e-mail: sonyalow@cancerboard.ab.ca

J Support Oncol 2009;7:27–34

movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels.[6] In early-stage cancer survivors, recent meta-analyses have shown that physical activity can positively affect a wide variety of biopsychosocial outcomes, including cardiorespiratory fitness, mood, CRF, physical function, and overall QOL.[7] Given that CRF and loss of physical function become more disabling as cancer progresses, it is unclear whether the benefits of physical activity generalize from patients with early-stage cancer to those with progressive, incurable disease.

A recent review of CRF and palliative care highlighted the need to delineate the types of physical activity interventions that would be most beneficial for patients with end-stage cancer to improve QOL outcomes.[4] Although there are multiple prior reviews summarizing physical activity interventions in cancer survivors, none has focused on the end-of-life phase, where palliation is the primary goal. To date, there is no rigorous systematic review of physical activity interventions in palliative cancer patients. Here, we present the first systematic review of the available evidence of physical activity as a supportive care intervention in palliative cancer patients.

Methods

INCLUSION CRITERIA

To be included in this review, a study had to examine a physical activity intervention in palliative cancer patients, aged 18 years or older, regardless of gender, tumor type, or type of cancer treatment. For the purposes of this article, physical activity was defined as any bodily movement produced by the skeletal muscles that results in a substantial increase in energy expenditure over resting levels; exercise was defined as any form of physical activity undertaken by an individual during leisure time and performed repeatedly over an extended period with the goal of improving fitness or health.[6] Palliative cancer was defined as progressive, incurable, and locally recurrent or metastatic cancer, with a clinician-estimated life expectancy of less than 12 months.

All study designs were included. Studies were required to have at least one of the following primary outcomes: patient-reported QOL, patient-reported physical functioning, or patient-reported fatigue. Secondary outcomes of interest included objective measures of physical fitness, objective measures of physical functioning, and patient-reported palliative symptoms. A decision was made a priori to exclude studies that involved a mixed population of different stages of disease, including palliative cancer patients, if they did not report data or analyze data separately for advanced stage. Data were extracted on the frequency, intensity, and duration of physical activity, as well as recruitment, retention, and adherence rates.

STUDY SELECTION, DATA ABSTRACTION, AND QUALITY ASSESSMENT

Two independent reviewers (SSL, SMW) screened the titles and abstracts of the initial search of all databases to identify potentially relevant studies and excluded those that were clearly irrelevant. All potentially relevant studies were obtained, and the same reviewers evaluated full papers against the inclusion/exclusion criteria. Data extraction on participants, methods, interventions, outcomes, and adverse events was performed by the same reviewers onto forms designed and pilot-tested for this review. Disagreement regarding inclusion of studies was resolved by consensus, with arbitration by a third reviewer (KSC) if required. The original reviewers assessed the methodologic quality of each study using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies 2003 (Thomas Tool), rating each of the following study components as strong, moderate, or weak: selection bias, study design, confounders, blinding, data collection methods, and withdrawals/dropouts. Its individual component ratings were used to compare quality across studies.[8]

Upon inspection of eligible studies, there was a high degree of clinical heterogeneity in terms of participants, interventions, and outcomes, such that data pooling and quantitative analysis would not be appropriate. Therefore, data were reviewed qualitatively for each included study, presenting effect estimates and statistical significance as reported in the original articles.

Results

SEARCH AND SELECTION OF STUDIES

The initial screen from all electronic databases identified 6,036 studies, of which 154 were considered potentially relevant. Hand-searching of journals and conference proceedings yielded seven potentially relevant studies. Excluded were 85 duplicates and 22 reviews, leaving a total of 47 potentially relevant papers.[9–56] Study author contact yielded one potentially relevant unpublished study protocol.[57] Non–English language articles were obtained and translated.

Sixteen studies were excluded because they did not meet inclusion criteria for type of participant, and 20 studies were excluded because they did not meet inclusion criteria for type of intervention. Three studies were excluded because of inadequate description of either the population or the intervention administered, and two studies did not report outcomes of interest for the review. After a full text review, six studies were judged to meet the inclusion criteria.[22,23,28,30,45,46]

OVERVIEW OF INCLUDED STUDIES

The six included studies involved a total of 84 participants from five countries (Australia, Austria, Germany, Norway, and the United States), published over a 7-year period (2000–2006; Table 1). All six were pilot studies: three were case reports, two were single-group uncontrolled trials, and one was a randomized controlled trial (RCT). All six studies were English-language articles published in peer-reviewed journals. One of the included studies was described in two separate published articles,[44,45] so data extraction was performed on both articles to obtain complete information for the single study.

Half of the six studies examined aerobic exercise interventions, whereas the other half examined mixed interventions involving both aerobic and resistance training components (Table 1). Four of the six studies (67%) involved hospital-based

Table 1

Characteristics of Studies Examining Physical Activity Interventions in Palliative Cancer Patients

STUDY	FEATURES	PARTICIPANTS	DIAGNOSES	INTERVENTION	OUTCOME MEASURES	COMMENTS
Porock et al, 2000 (Australia)[46]	Unsupervised home-based physical activity program in home hospice care patients	9 patients: 3 male, 6 female; mean age ± SD: 59.87 ± 9.77 yr	Pancreas (n = 2) Melanoma (n = 1) Bowel (n = 4) Breast (n = 1) Oral (n = 1) Metastases (n = 7) Active RT (n = 1) Active chemotherapy (n = 2)	Individualized "Duke Energizing Exercise Plan" with range of physical activities throughout the day; frequency and duration set according to Winningham's half rule of thumb for 28 d	1. Fatigue via MFI 2. Anxiety and depression via HADS 3. Symptom distress via McCorkle and Young's SDS 4. QOL via Graham and Longman's QOL scale	Single group pre-post intervention study; no staging information available; incomplete data for HADS, adherence, and withdrawals
Crevenna et al, 2003 (Austria)[22]	Supervised aerobic exercise program during palliative thalidomide therapy	1 man, age 55	Advanced hepatocellular cancer with lung and brain metastases	Bicycle ergometer cycling with workload systematic increase to maintain training HR at 60% of maximum workload of first symptom-limited test; 60 min per session, 2 sessions per week, for 6 wk	1. Symptom-limited ergometric bicycle exercise test: peak work capacity, endurance capacity, and HR 2. Six-minute walk 3. Grimsby's self-reported physical performance questionnaire 4. QOL via SF-36 5. Self-reported benefit in physical performance, mental state, satisfaction, and QOL	Case report; partially reported baseline performance status; no adverse events reported; 100% compliance with training sessions; participant commented on "being persistently and positively motivated by the physicians"
Crevenna et al, 2003 (Austria)[23]	Supervised aerobic exercise program during palliative chemotherapy (gemcitabine, epirubicin, paclitaxel) and palliative radiotherapy	1 woman, age 48	Advanced breast cancer with lung, liver, and bone metastases	Bicycle ergometer cycling with workload increased to maintain training HR at 60% of maximum workload of first symptom-limited exercise test; 60 min per session, 3 sessions per week, for 52 wk	1. Symptom-limited ergometric bicycle exercise test: VO_2max, peak work capacity, and HR 2. Lung function via respiratory quotient 3. QOL via SF-36 4. Self-reported benefit in physical performance, mental state, fatigue, sleep, satisfaction, and QOL	Case report; baseline performance status not reported; no adverse events reported; participant attributed benefit to persistent and positive motivation by the physicians
Kelm et al, 2003 (Germany)[30]	Supervised whole-body strength and endurance training during postoperative intrahepatic chemotherapy	1 man, age 58	Rectal adenocarcinoma (pT3N0M1) with liver metastases	1. Strength training machines at 40%–60% of one repetition maximum, up to five series of 20 repetitions 2. Treadmill/bicycle/upper-body ergometer, 10 min each with resistance and speed controlled to maintain HR between 130 and 150 beats/min Six weeks postoperatively and every 2 wk between chemotherapy cycles, for total of 13 wk	1. Upper- and lower-extremity strength: one repetition maximum 2. Endurance by reduction in HR and lactate concentration 3. Lung function by FEV_1, FVC, and VC 4. QOL by GIQLI score 5. Immune function by natural killer cell count	Case report; unknown baseline performance status; unable to determine whether functional gains were secondary to postoperative recovery or intervention
Headley et al, 2004 (USA)[28]	Unsupervised home-based seated exercise program in stage IV breast cancer patients receiving chemotherapy	38 women; mean age ± SD: 51 ± 9.43 yr	Stage IV breast cancer (n = 38)	Seated exercise program using Armchair Fitness: Gentle Exercise video; 30 minutes per session, 3 sessions per week, for 12 wk	1. Fatigue and QOL via FACIT–F 2. Perceived intensity via Borg Rating of Perceived Exertion scale	Randomized, controlled, longitudinal trial; incomplete data for adherence, intensity, and frequency of activity

Table 1 continues on the following page.

Table 1 continued

Characteristics of Studies Examining Physical Activity Interventions in Palliative Cancer Patients

STUDY	FEATURES	PARTICIPANTS	DIAGNOSES	INTERVENTION	OUTCOME MEASURES	COMMENTS
Oldervoll et al, 2005, 2006 (Norway)[44,45]	Supervised group exercise program in palliative patients from outpatient clinic and hospice	34 patients: 15 male, 19 female; mean age ± SD: 65 ± 11.5 yr; mean KPS ± SD: 83 ± 13.2	Gastrointestinal (n = 16) Breast (n = 5) Genitourinary (n = 5) Lung (n = 1) Miscellaneous (n = 7) Metastases (n = 27) Active chemotherapy (n = 9) Active hormone therapy (n = 3)	Group exercise program (3–8 patients per group) with personalized circuit training stations focused on upper- and lower-extremity muscle strength, standing balance, and aerobic endurance, with 50 min per session, 2 sessions per week for 6 wk	1. Physical performance via 6-min walk, timed sit-to-stand, and functional reach 2. Fatigue via FQ 3. QOL via EORTC QLQ-C30	Single group pre-post intervention study; no progression of workload reported; adherence rate to exercise sessions, 10.6/12; 46% attrition rate

Abbreviations: SD = standard deviation; RT = radiotherapy; MFI = Multidimensional Fatigue Inventory; HADS = Hospital Anxiety and Depression Scale; SDS = Symptom Distress Scale; QOL = quality of life; HR = heart rate; SF-36 = Short Form 36 Survey; VO_2max = peak oxygen uptake; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; VC = vital capacity; GIQLI = Gastrointestinal Quality of Life Index; FACIT–F = Functional Assessment of Chronic Illness Therapy–Fatigue version IV; KPS = Karnofsky Performance Score; FQ = Fatigue Questionnaire; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire

exercise training programs, with the remaining two studies (33%) examining home-based physical activity interventions. Of the three included studies with more than one participant, one study examined a group exercise intervention. The frequency of interventions ranged from biweekly to daily physical activity sessions, with the duration of intervention programs ranging from 4 to 52 weeks.

Two of the included case reports were published in 2003 by Crevenna et al, who examined supervised ergometric bicycling interventions in two patients: a 6-week program in a 55-year-old man with metastatic hepatocellular carcinoma to the lungs and brain[22] and a 52-week program in a 48-year-old woman with metastatic breast cancer to the liver, lungs, and bone.[23] The former patient was undergoing concurrent thalidomide (Thalomid) treatment and participated in twice-weekly sessions with increasing workload to maintain his heart rate at 60% of maximum workload for 60-minute sessions.[22] The latter patient was undergoing concurrent palliative chemotherapy and radiotherapy and participated in 60-minute sessions three times per week while systematically increasing workload according to the same criteria.[23]

The third case report was published in 2003 by Kelm et al, who examined a 13-week whole-body strength and endurance training program in a 58-year-old man with metastatic rectal adenocarcinoma to the liver undergoing concurrent intrathecal chemotherapy.[30] The participant completed biweekly sessions involving both strength-training machines at 40%–60% of one-repetition maximum and treadmill walking or ergometric cycling, with resistance and speed controlled to maintain a heart rate of between 130 and 150 beats per minute.

One of the uncontrolled trials was conducted in 2000 by Porock et al, who examined an unsupervised home-based physical activity program in home hospice care patients in Australia.[46] Their study sample was composed of six women and three men, with a mean age of 60 ± 10 years. The most common cancer diagnosis was bowel cancer, with seven participants having metastases. Two participants reported undergoing concurrent chemotherapy, whereas one participant reported undergoing concurrent radiotherapy. The 4-week intervention consisted of an individualized "Duke Energizing Exercise Plan," wherein participants could choose among a range of physical activities throughout the day; the frequency and the duration of each session were determined by how much activity the participant could tolerate, beginning with half that much several times daily (Winningham's half rule of thumb).

The second uncontrolled trial was published in 2006 by Oldervoll et al, who examined a 6-week supervised group exercise program in outpatient clinic and hospice cancer patients with a clinician-estimated life expectancy of between 3 and 12 months.[45] Their study sample comprised 15 men and 19 women, with a mean age of 65 ± 12 years. The mean baseline Karnofsky Performance Score was 83 ± 13. The most common diagnosis was gastrointestinal cancer (n = 16), with 79% of participants having metastases. Twenty-six percent of participants were undergoing concurrent chemotherapy, and 9% of participants were undergoing concurrent hormonal therapy during the intervention period. Groups of between three and eight participants performed a series of personalized circuit training stations focused on whole-body muscle strength, standing balance, and aerobic endurance for 50-minute sessions twice per week.

The only RCT was published in 2004 by Headley et al, who conducted an unsupervised, home-based seated exercise program in patients with stage IV breast cancer receiving chemotherapy.[28] Their study sample was composed of 38 women, with a mean age of 51 ± 9 years. The participants performed a 30-minute seated exercise program using the Armchair Fitness: Gentle Exercise video in their own homes three times per week for a total of 12 weeks. Self-reported intensity was assessed using Borg Ratings of Perceived Exertion, however, no method of progression of intervention workload was reported.

Of the three included studies that had more than one participant, Headley et al's study did not report recruitment rates.[28] Porock et al reported that 46% of approached patients (11 of 24) agreed to participate,[46] whereas Oldervoll et al reported a

62% (63 of 101) recruitment rate.[44] Of the six studies, four did not report adherence rates; Crevenna et al reported 100% adherence from their participant with metastatic hepatocellular carcinoma,[22] and Oldervoll et al reported that an average of 10.6 of 12 (88%) prescribed sessions were completed.[45] Of the three included studies that had more than one participant, two studies did not report retention rates; Oldervoll et al reported that 34 of 47 participants (72%) completed the exercise intervention, with all completing follow-up assessments.[44,45]

In summary, there is significant clinical heterogeneity in terms of study designs, participants, and interventions among the six included studies (Table 1). There is a wide variety of cancer diagnoses, with differences in the presence of metastases and concurrent therapy. There is variable reporting of specifics of the physical activity interventions administered, including frequency, intensity, and duration. Despite this widespread diversity, there is promising evidence that at least some palliative cancer patients are able to tolerate and complete various physical activity interventions with few adverse events.

METHODOLOGIC QUALITY OF INCLUDED STUDIES

Given the infancy of research in this area, it is not unexpected that the overall methodologic quality of the six included studies was low, as assessed by the Thomas Tool.[8] As is often the case with pioneering studies in a new field, emphasis is placed on pilot and feasibility issues such as recruitment, adherence, and retention; categories such as selection bias, allocation bias, blinding, and confounding may not apply to the qualitative comparison of feasibility studies. There is no evidence to support the summation of the Thomas Tool category scores as a means of comparing interstudy quality; therefore, the individual studies were compared and described qualitatively.

PRIMARY AND SECONDARY OUTCOMES OF INCLUDED STUDIES

All six studies had either incomplete data reporting or missing data for one or more outcomes (Tables 2 and 3). Half of the studies reported an increase in patient-reported QOL scores; in Headley et al's study, the experimental group had a statistically significant slower decline in total well-being scores than the control group.[28] Two of the studies reported an increase in patient-reported physical function scores after their respective exercise interventions,[22,45] whereas Headley et al showed no significant difference between groups at any point.[28] With respect to patient-reported fatigue, Headley et al reported that the experimental group had a statistically significant slower rate of increase in fatigue than the control group,[28] whereas Oldervoll et al demonstrated a borderline significant decrease in total fatigue subscale scores.[45] Similarly, Oldervoll et al reported a statistically significant improvement in the dyspnea subscore before and after intervention.[45]

Only the three included case reports assessed objective measures of physical fitness, and only one of the remaining studies assessed objective measures of physical function (Table 3). All three case reports observed an increase in work capacity and physical fitness measures post exercise.[22,23,30] Oldervoll et al found a statistically significant improvement in the 6-minute walk and timed sit-to-stand before and after intervention, which was not reflected in their patient-reported physical functioning outcome.[45]

Discussion

This systematic review summarizes the available evidence of physical activity as a supportive care intervention in palliative cancer patients. There was a paucity of evidence of physical activity as a supportive care intervention in palliative cancer patients: of 6,036 studies identified in the initial screen, only 6 studies fulfilled all inclusion criteria. All six were pilot studies, and only one of the included studies had a control group. Although the ability to generalize findings across this patient population was precluded, the use of small sample sizes and the absence of control groups are inherent in gathering pilot data.

The predominance of pilot and feasibility studies is reflective of the emerging nature of this research area, and the current state of evidence appears to follow this natural evolution. The objective of these primary studies was not to establish efficacy but, rather, to determine whether palliative cancer patients were interested in, and able to tolerate, physical activity interventions and whether it was feasible to conduct these interventions in this frail population. Although methodologic quality assessment is generally a fundamental component of systematic reviews, current quality criteria have been developed for efficacy trials rather than pilot and feasibility studies.

Nevertheless, there are promising findings from these preliminary studies of physical activity interventions in palliative cancer patients. Throughout the six included studies, the majority of participants were able to tolerate various physical activity interventions. The sole RCT showed a statistically significant slower rate of decline in total well-being, as well as a statistically significant slower rate of increase in total fatigue, between treatment and control groups.[28] The two single-group pre- to post-intervention trials demonstrated trends of improvement in patient-reported QOL, fatigue, and physical functioning.[45,46] Three case reports showed improvement in selected outcomes.[22,23,30] Overall, these studies indicate that select palliative cancer patients are able to complete physical activity interventions and that at least some of these patients report improvement in supportive care outcomes post intervention.

It is clear, however, that more feasibility studies are required to advance this emerging field of research. Although it is encouraging that select palliative cancer patients are able to tolerate physical activity, which subgroups of this population would most benefit is still unknown. Moreover, the characteristics differentiating palliative cancer patients who are interested and able to participate in physical activity interventions from those who are not require further definition. The six included studies employed a broad range of both patient-reported and objective measures of supportive care outcomes, many of which have not been previously tested or validated in palliative cancer populations; further studies are needed to develop and refine standardized outcome assessments for these physical activity interventions to facilitate comparisons among different trials.

Table 2

Patient-Reported Outcomes of Studies Examining Physical Activity Interventions in Palliative Cancer Patients

STUDY	QUALITY OF LIFE (TOOL/SCORE)	PHYSICAL FUNCTION (TOOL/SCORE)	FATIGUE (TOOL/SCORE)	SYMPTOMS
Porock et al, 2000 (Australia)[46]	Graham and Longman's QOL scale; mean QOL rating: 5.3 (day 0); 6.1 (day 7); 6.6 (day 14)	None reported	Incomplete data for all time points	Incomplete data
Crevenna et al, 2003 (Austria)[22]	SF-36; general health perception subscale: pre-intervention, 65; post-intervention, 62	SF-36; physical functioning subscale: pre-intervention, 65; post-intervention, 85	SF-36; vitality/fatigue subscale: pre-intervention, 25; post-intervention, 50	SF-36; pain subscale: pre-intervention, 22; post-intervention, 41
Crevenna et al, 2003 (Austria)[23]	None reported	None reported	None reported	SF-36; incomplete data
Kelm et al, 2003 (Germany)[30]	GIQLI; pre-intervention: 106; post-intervention: 129 (+21.6% difference)	None reported	None reported	None reported
Headley et al, 2004 (USA)[28]	FACIT–F; total scores: t[49] = 2.31, $P = 0.0254$; decline in total well-being slower in experimental group than in control group	FACIT–F; functional well-being subscale: no significant difference between groups at any time point	FACIT–F; fatigue subscale; t[49] = 2.78, $P = 0.0078$; decline in fatigue slower in experimental group than in control group	None reported
Oldervoll et al, 2005, 2006 (Norway)[44,45]	EORTC QLQ-C30; global QOL subscale: pre-intervention, 61 (20); post-intervention, 64 (20); $P = 0.26$	EORTC QLQ-C30; physical functioning subscale: pre-intervention, 65 (20); post-intervention, 67 (22); $P = 0\ 62$	Fatigue Questionnaire; total fatigue subscale: pre-intervention, 17.5 (4.7); post-intervention, 15.5 (5.8); $P = 0.06$; mental fatigue subscale: pre-intervention, 5.3 (1.7); post-intervention, 5.1 (2.0); $P = 0.42$; physical fatiguesubscale: pre-intervention, 12.2 (3.6); post-intervention, 10.4 (4.1); $P = 0.04$	EORTC QLQ-C30; nausea/vomiting; pre-intervention, 18 (25), post-intervention, 14 (19); $P = 0.26$; pain: pre-intervention, 41 (35); post-intervention, 37(34; $P = 0.36$; dyspnea: pre-intervention, 42 (33); post-intervention, 30 (31); $P = 0.006$; appetite loss; pre-intervention, 37 (38); post-intervention, 28 (35); $P = 0.07$

Abbreviations: QOL = quality of life; SF-36 = Short Form 36 Survey; GIQLI = Gastrointestinal Quality of Life Index; FACIT–F = Functional Assessment of Chronic Illness Therapy–Fatigue version IV; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire

Table 3

Objective Outcomes of Studies Examining Physical Activity Interventions in Palliative Cancer Patients

STUDY	PHYSICAL FUNCTION (TOOL/SCORE)	PHYSICAL FITNESS (TOOL/SCORE)
Porock et al, 2000 (Australia)[46]	None reported	None reported
Crevenna et al, 2003 (Austria)[22]	None reported	Heart rate at submaximal workload: pre-intervention, 135 beats/min; post-intervention, 103 beats/min (–23.7%); peak work capacity: pre-intervention, 114; post-intervention, 137 (+20.2%); endurance capacity: pre-intervention, 69%; post-intervention, 84% (+20.3%)
Crevenna et al, 2003 (Austria)[23]	None reported	Heart rate at maximal workload: pre-intervention, 178 beats/min; post-intervention, 191 (+7.3%); peak oxygen uptake: pre-intervention, 20.3, post-intervention, 31 (+52.7%); peak work capacity: pre-intervention, 129; post-intervention, 175 (+35.7%)
Kelm et al, 2003 (Germany)[30]	Incomplete data	Heart rate: –10%; lactate concentration: –21.5%; forced expiratory volume in 1 second (FEV_1): pre-intervention, 2.48; post-intervention, 2.80 (+12.9%); forced vital capacity (FVC): pre-intervention, 3.27; post-intervention, 3.64 (+11.3%); inspiratory vital capacity: pre-intervention, 3.32; post-intervention, 3.61 (+9.0%)
Headley et al, 2004 (USA)[28]	None reported	None reported
Oldervoll et al, 2005, 2006 (Norway)[44,45]	Six-minute walk: pre-intervention, 481 (144); post-intervention, 510 (156); $P = 0.007$; timed sit-to-stand: pre-intervention, 5.1 (2.3); post-intervention, 4.1 (1.4) $P = 0.001$; functional reach: pre-intervention, 30.4 (6.9); post-intervention, 32.8 (8.3); $P = 0.07$	None reported

Most important, none of the studies reported assessing the physical activity needs, interests, and preferences of palliative cancer patients prior to developing their physical activity interventions. In addition, none of the studies reported assessing the underlying physical activity behavior or determinants of this population. The primary aim of palliative care is to maximize QOL; thus, identifying the unique priorities and preferences of palliative cancer patients is a critical first step toward this goal. Designing an intervention based on the patients' identified programming interests and needs may optimize recruitment and adherence rates and may potentially increase efficacy with respect to supportive care outcomes.[58] Clearly, future pilot studies that elicit the specific physical activity behavior, determinants, interests, and preferences of palliative cancer patients are warranted prior to developing physical activity interventions for this population.

Currently, ours is the first systematic review of the available evidence of physical activity as a supportive care intervention in palliative cancer patients. The initial screen of 14 electronic databases, hand-searching of three major palliative care journals and two major palliative care conference proceedings, including reference lists, yielded 6,036 studies, which attests to the comprehensiveness of the search strategy. Furthermore, field experts were contacted to identify unpublished studies, and non–English language articles were translated, thus increasing the potential yield of studies. Study selection, data abstraction, and quality assessment were performed independently by two reviewers, thus enhancing the rigor of the review.

A potential limitation of this review was the restriction of participant definition by clinician-estimated life expectancy. Defining a "palliative" population has been identified as one of the top methodologic challenges of conducting palliative care research; with respect to cancer, there is no standardized definition of a palliative patient, and multiple terms such as "advanced cancer," "end-stage cancer," and "terminal cancer" have been used without uniform consensus as to the description of the eligible population.[59] By narrowing our systematic review inclusion criteria to studies of cancer patients with a clinician-estimated prognosis of 12 months or less, our overall yield of included studies was restricted: 5% of potentially relevant studies (7 of 154) were excluded based upon this criterion. The majority of excluded studies did not report on participant life expectancy or actual survival; therefore, the reviewers estimated life expectancy of the participants based upon the reported medical data. Prognostication by clinicians, however, has been found to be inaccurate, and current tools for survival prediction require further refinement and validation in the terminally ill population.[60]

Another potential limitation was the a priori decision to exclude studies that involved a mixed population of different stages of disease if they did not report data or analyze data separately by disease stage. Six percent of potentially relevant studies (9 of 154) were excluded based on this decision; nearly all of these studies reported the number of participants in each stage I to IV, but the outcome data were presented cumulatively for the entire cohort. This decision may have restricted our yield of included studies and hence impacted the overall quality of the review.

Conclusion

Few studies have examined physical activity in palliative cancer patients, and the current evidence is limited largely to case reports and uncontrolled trials. Nevertheless, these preliminary studies provide some evidence that at least some palliative cancer patients are willing and able to tolerate physical activity interventions, with some patients demonstrating improvement in some supportive care outcomes post intervention. The potential role for physical activity as a supportive care intervention is promising, and further feasibility studies are needed to substantiate preliminary findings and further advance this emerging area of research. Consensus is required to develop common definitions for palliative cancer populations, interventions, and outcomes to validate findings, justify interpretations, and make meaningful recommendations to patients and their families.

ACKNOWLEDGMENTS

Dr. Lowe is supported by a full-time clinical fellowship award from the Alberta Heritage Foundation for Medical Research. Dr. Courneya is supported by the Canada Research Chairs program, as well as a Research Team Grant from the National Cancer Institute of Canada, with funds from the Canadian Cancer Society and the Sociobehavioral Cancer Research Network.

The authors would like to thank Ms. Marlene Dorgan, Head of the John W. Scott Health Sciences Library at the University of Alberta, for her assistance with the development of the search strategy.

References

PubMed ID in brackets

1. Ventafridda V. According to the 2002 WHO definition of palliative care…. Palliat Med 2006;20:159. [16764219]

2. Kaasa S, Loge JH. Quality-of-life assessment in palliative care. Lancet Oncol 2002;3:175–182. [11902505]

3. Canadian Cancer Society/National Cancer Institute of Canada: Canadian Cancer Statistics 2008. Toronto, Canada, 2007.

4. Del Fabbro E, Dalal S, Bruera E. Symptom control in palliative care, part II: cachexia/anorexia and fatigue. J Palliat Med 2006;9:409–421. [16629571]

5. Strömgren AS, Sjogren P, Goldschmidt D, Petersen MA, Pedersen L, Groenvold M. Symptom priority and course of symptomatology in specialized palliative care. J Pain Symptom Manage 2006;31:199–206. [16563314]

6. Bouchard C, Shephard RJ. Physical activity, fitness, and health: the model and key concepts. In: Bouchard C, Shephard RJ, Stephens T, eds. Physical Activity, Fitness, and Health. International Proceedings and Consensus Statement. Champaign, Ill: Human Kinetics Publishers; 1994:77–88.

7. Conn VS, Hafdahl AR, Porock DC, McDaniel R, Nielsen PJ. A meta-analysis of exercise interventions among people treated for cancer. Support Care Cancer 2006;14:699–712. [16447036]

8. Thomas H. Quality assessment tool for quantitative studies—effective public health practice project. Hamilton, Ont: McMaster University; 2003.

9. Adamsen L, Midtgaard J, Rorth M, et al. Feasibility, physical capacity, and health benefits of a multidimensional exercise program for cancer patients undergoing chemotherapy. Support Care Cancer 2003;11:707–716. [12898370]

10. Adamsen L, Midtgaard J, Andersen C, Quist M, Moeller T, Roerth M. Transforming the nature of fatigue through exercise: qualitative findings from a multidimensional exercise programme in cancer

patients undergoing chemotherapy. Eur J Cancer Care (Engl) 2004;13:362–370. [15305905]

11. Adamsen L, Quist M, Midtgaard J, et al. The effect of a multidimensional exercise intervention on physical capacity, well-being and quality of life in cancer patients undergoing chemotherapy. Support Care Cancer 2006;14:116–127. [16096771]

12. Andersen C, Adamsen L, Moeller T, et al. The effect of a multidimensional exercise programme on symptoms and side-effects in cancer patients undergoing chemotherapy—the use of semi-structured diaries. Eur J Oncol Nurs 2006;10:247–262. [16476570]

13. Booth S, Adams L. The shuttle walking test: a reproducible method for evaluating the impact of shortness of breath on functional capacity in patients with advanced cancer. Thorax 2001;56:146–150. [11209105]

14. Brown DJ, McMillan DC, Milroy R. The correlation between fatigue, physical function, the systemic inflammatory response, and psychological distress in patients with advanced lung cancer. Cancer 2005;103:377–382. [15558809]

15. Buaiz J, Van Strien P, Lill M, Bauer T, Wyler L, Lim S. Measurable benefits to therapeutic exercise and fatigue management in post-hematopoietic stem cell transplant (HSCT) patients. Support Care Cancer 2002;10:365.

16. Carson JW, Carson KM, Porter LS, Keefe FJ, Shaw H, Miller JM. Yoga for women with metastatic breast cancer: results from a pilot study. J Pain Symptom Manage 2007;33:331–341. [17349503]

17. Christopher KA, Morrow LL. Evaluating a community-based exercise program for women cancer survivors. Appl Nurs Res 2004;17:100–108. [15154122]

18. Coleman EA, Coon S, Hall-Barrow J, Richards K, Gaylor D, Stewart B. Feasibility of exercise during treatment of multiple myeloma. Cancer Nurs 2003;26:410–419. [14710804]

19. Coleman EA, Hall-Barrow J, Coon S, Stewart CB. Facilitating exercise adherence for patients with multiple myeloma. Clin J Oncol Nurs 2003;7:529–534, 540. [14603549]

20. Coyne B, Rosenzweig M. Functional status and physical activity in women with metastatic breast cancer. Oncol Nurs Forum 2006;33:465–466.

21. Crevenna R, Marosi C, Schmidinger M, Fialka-Moser V. Neuromuscular electrical stimulation for a patient with metastatic lung cancer—a case report. Support Care Cancer 2006;14:970–973. [16523264]

22. Crevenna R, Schmidinger M, Keilani M, et al. Aerobic exercise as an additive palliative treatment for a patient with advanced hepatocellular cancer. Wien Med Wochenschr 2003;153:237–240. [12836463]

23. Crevenna R, Schmidinger M, Keilani M, et al. Aerobic exercise for a patient suffering from metastatic bone disease. Support Care Cancer 2003;11:120–122. [12560941]

24. Crevenna R, Fialka-Moser V, Keilani MY, Schmidinger M, Marosi C, Quittan M. Aerobic physical traning in a breast cancer patient with inflammatory recurrence. Wien Med Wochenschr 2002;152:581–584. [12506684]

25. Dahele M, Skipworth RJ, Wall L, Voss A, Preston T, Fearon KC. Objective physical activity and self-reported quality of life in patients receiving palliative chemotherapy. J Pain Symptom Manage 2007;33:676–685. [17360150]

26. Dunn V, Gordon J, Craven S, Lennard R. Low-intensity physical exercise in palliative day therapy patients: a pilot study. Palliat Med 2006;20:252.

27. Eriks IE, Angenot EL, Lankhorst GJ. Epidural metastatic spinal cord compression: functional outcome and survival after inpatient rehabilitation. Spinal Cord 2004;42:235–239. [15060521]

28. Headley JA, Ownby KK, John LD. The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. Oncol Nurs Forum 2004;31:977–983. [15378098]

29. Jones LW, Eves ND, Mackey JR, et al. Safety and feasibility of cardiopulmonary exercise testing in patients with advanced cancer. Lung Cancer 2007;55:225–232. [17113185]

30. Kelm J, Ahlhelm R, Weissenbach P, et al. Physical training during intrahepatic chemotherapy. Arch Phys Med Rehabil 2003;84:687–690. [12736882]

31. Korstjens I, Mesters I, van der Peet E, Gijsen B, van den Borne B. Quality of life of cancer survivors after physical and psychosocial rehabilitation. Eur J Cancer Prev 2006;15:541–547. [17106335]

32. Lee MS, Yang SH, Lee KK, Moon SR. Effects of Qi therapy (external Qigong) on symptoms of advanced cancer: a single case study. Eur J Cancer Care (Engl) 2005;14:457–462. [16274468]

33. Lee MS, Jang HS. Two case reports of the acute effects of Qi therapy (external Qigong) on symptoms of cancer: short report. Complement Ther Clin Pract 2005;11:211–213. [16005839]

34. Mackey KM, Sparling JW. Experiences of older women with cancer receiving hospice care: significance for physical therapy. Phys Ther 2000;80:459–468. [10792856]

35. Makridis C, Ekbom A, Bring J, et al. Survival and daily physical activity in patients treated for advanced midgut carcinoid tumors. Surgery 1997;122:1075–1082. [9426422]

36. McDonald A, Burjan E, Martin S. Yoga for patients and carers in a palliative day care setting. Int J Palliat Nurs 2006;12:519–523. [17170669]

37. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 2006;24:3535–3541. [16822843]

38. Midtgaard J, Rørth M, Stelter R, et al. The impact of a multidimensional exercise program on self-reported anxiety and depression in cancer patients undergoing chemotherapy: a phase II study. Palliat Support Care 2005;3:197–208. [16594459]

39. Midtgaard J, Tveteràs A, Rørth M, Stelter R, Adamsen L. The impact of a supervised exercise intervention on short-term postprogram leisure time physical activity level in cancer patients undergoing chemotherapy: 1- and 3-month follow-up on the body & cancer project. Palliat Support Care 2006;4:25–35. [16889321]

40. Montagnini M, Lodhi M, Born W. The utilization of physical therapy in a palliative care unit. J Palliat Med 2003;6:11–17. [12710571]

41. Montoya M, Fossella F, Palmer JL, et al. Objective evaluation of physical function in patients with advanced lung cancer: a preliminary report. J Palliat Med 2006;9:309–316. [16629561]

42. Morita Y, Yamakawa T, Koyama S. A case of terminal cancer which underwent visiting rehabilitation. Med J Minami Osaka Hosp 2003;51:245–252.

43. Mustian KM, Katula JA, Gill DL, Roscoe JA, Lang D, Murphy K. Tai Chi Chuan, health-related quality of life and self-esteem: a randomized trial with breast cancer survivors. Support Care Cancer 2004;12:871–876. [15599776]

44. Oldervoll LM, Loge JH, Paltiel H, et al. Are palliative cancer patients willing and able to participate in a physical exercise program? Palliat Support Care 2005;3:281–287. [17039983]

45. Oldervoll LM, Loge JH, Paltiel H, et al. The effect of a physical exercise program in palliative care: a phase II study. J Pain Symptom Manage 2006;31:421–430. [16716872]

46. Porock D, Kristjanson LJ, Tinnelly K, Duke T, Blight J. An exercise intervention for advanced cancer patients experiencing fatigue: a pilot study. J Palliat Care 2000;16:30–36. [11019505]

47. Sarna L. Fluctuations in physical function: adults with non-small cell lung cancer. J Adv Nurs 1993;18:714–724. [8390495]

48. Segal RJ, Reid RD, Courneya KS, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003;21:1653–1659. [12721238]

49. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Impact of dyspnea, pain, and fatigue on daily life activities in ambulatory patients with advanced lung cancer. J Pain Symptom Manage 2002;23:417–423. [12007759]

50. van Weert E, Hoekstra-Weebers J, Grol B, et al. A multidimensional cancer rehabilitation program for cancer survivors: effectiveness on health-related quality of life. J Psychosom Res 2005;58:485–496. [16125515]

51. Wood CA, Anderson J, Yates JW. Physical function assessment in patients with advanced cancer. Med Pediatr Oncol 1981;9:129–132. [7231359]

52. Woods TE, Kolden GG, Yang D, Mullen EA, Holland JC. Exercise across the breast cancer continuum: risk reduction, rehabilitation and palliative care. Psychooncology 2005;14(suppl):S2.

53. Yoshioka H. Rehabilitation for the terminal cancer patient. Am J Phys Med Rehabil 1994;73:199–206. [7515247]

54. Dimeo F, Thomas F, Raabe-Menssen C, Pröpper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery: a randomised controlled trial. Support Care Cancer 2004;12:774–779. [15338385]

55. Laakso L, McAuliffe AJ, Cantlay A. The impact of physiotherapy intervention on functional independence and quality of life in palliative patients. Cancer Forum 2003;27:15–20.

56. Loh SH. Qigong therapy in the treatment of metastatic colon cancer. Altern Ther Health Med 1999;5:111–112. [10394680]

57. Oldervoll LM, Loge JH, Kaasa S, et al. Physical activity and physical function in palliative patients. Trondheim: St. Olav's Hospital; 2006.

58. Jones LW, Courneya KS. Exercise counseling and programming preferences of cancer survivors. Cancer Pract 2002;10:208–215. [12100105]

59. Borgsteede SD, Deliens L, Francke AL, et al. Defining the patient population: one of the problems of palliative care research. Palliat Med 2006;20:63–68. [16613401]

60. Lau F, Cloutier-Fisher D, Kuziemsky C, et al. A systematic review of prognostic tools for estimating survival time in palliative care. J Palliat Care 2007;23:93–112. [17853845]