

Rehabilitation for patients with advanced cancer

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Physicians embrace the concept of rehabilitation, but may think of it only as it relates to restoring function through exercise. We use a broader definition that applies to patients with advanced cancer. Cancer rehabilitation is a process that assists a person with a cancer diagnosis to obtain optimal physical, social, psychological and vocational functioning within the limits created by the disease and its treatment.¹

This article describes the rationale for combining exercise, nutritional counselling and symptom control in articulated programs for patients with advanced cancer and their families. We present results of prospective single-institution studies (Box 1) and discuss the role of these studies in cancer research and treatment. Initially, all research reports were included, regardless of study design. Many either describe outcomes for single-modality programs or are descriptive accounts of issues faced by patients and their families. Some reports discuss the need for multimodal therapy or recommendations, or both, but do not include outcome data.²⁻⁴ We identified one randomized and five nonrandomized trials that studied the outcomes of a combined exercise, nutritional counselling and symptom-control program.

Why is rehabilitation for patients with advanced cancer important?

Patients with advanced cancer and their families highly value control of symptoms, maintenance of function and nutrition, and improvement in quality of life, as do physicians.⁵⁻⁷ Yet, although drug protocols for cancer are clearly outlined, formal programs addressing symptoms and function are not common. To achieve these goals, a multimodal approach that includes the full spectrum of rehabilitation from the onset of advanced cancer is essential.^{2,8}

There is clear evidence that certain dietary patterns, exercise and a healthy psychosocial status influence cancer incidence and early progression.⁹⁻¹⁴ "Survivorship" programs that embrace

these entities are well accepted.¹⁵ However, few centres provide comprehensive care models that include patients with advanced cancer.

What are the components of an effective rehabilitation program?

Exercise

Physiologic changes associated with exercise provide a rationale for its use throughout the progression of cancer, both to alleviate symptoms and possibly to prolong life.¹⁶⁻¹⁸ These include a reduction in the chronic inflammatory state associated with a poor prognosis, a reduction in insulin-like growth factor and insulin resistance, a reduction in muscle proteolysis and an improvement in muscle synthesis, thus reducing cancer cachexia.¹⁶

Few studies on the benefits of exercise in patients with advanced cancer have been pub-

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Box 1: Evidence for this review

We searched PubMed, CancerLit, The Cochrane Collaboration, the library catalogues of Bruyère Continuing Care and The Ottawa Hospital Library, the grey literature and CINAHL (Cumulative Index to Nursing and Allied Health Literature) from 2008 to 2013. Search terms included the following: "advanced cancer," "stage III cancer," "stage IV cancer," "incurable cancer or late stage cancer," "rehabilitation," multidisciplinary, interdisciplinary or interprofessional," "nutrition or diet," "cachexia or anorexia or loss of appetite," "weight loss or loss of weight," "psychosocial aspects," "physical aspect," "physiotherapy," "physical therapy" and "exercise or occupational therapy." Articles were screened for relevance using a PICO (population, intervention, context, outcome) framework (population: all adult patients with stage III and IV cancer; intervention: rehabilitation delivered by the following professionals: medical oncologists/palliative care physicians, dietitians, physiotherapists, occupational therapists, nurses, psychologists and social workers; context: hospital, hospice, cancer centre and palliative care unit).

KEY POINTS

- Palliative care programs should be expanded to include formal exercise and nutrition components.
- From diagnosis, patients with advanced cancer should have access to palliative care.
- Further research is needed to determine whether rehabilitation will improve survival in patients with advanced cancer.

lished. A systematic review⁹ of exercise in a palliative care population found six clearly interpretable studies, one a randomized controlled trial (RCT).¹⁰ Only 84 patients were enrolled in the six trials. The authors concluded that there was evidence that at least some patients in palliative care are willing and able to tolerate physical activity interventions, and that the modest but promising reported outcomes should encourage more feasibility studies.⁹ In an RCT on exercise in a mixed population of 231 patients with an estimated survival of two years or less, fatigue did not improve but performance on two functional tests did; the authors concluded that exercise may sustain function in patients with advanced cancer.¹⁰

Nutritional interventions

Participation in nutrition programs has not brought about global benefits in patients with advanced cancer. Weight and energy intake may stabilize or increase for a period, and quality of life may improve, but there is no evidence that function, fatigue or survival improve.¹¹ It is difficult to interpret nutrition studies. A plethora of nutritional guidelines exist, with conflicting rec-

ommendations,¹² and degree of dietitian input and compliance of patients and families are not usually quantified.

A recent review found no studies combining nutrition and exercise therapies in patients with lung cancer.¹³ This is surprising, because geriatric studies show that nutrition will not usually improve function unless muscles are exercised.^{19,20}

Optimizing symptom control

Palliative care leads to substantial improvements in both quality of life and mood.⁵ Among patients with lung cancer, those receiving early palliative care had less aggressive care at the end of life but longer survival.²¹

Combined interventions

A randomized trial evaluated the clinical and cost effectiveness of a mixed rehabilitation intervention for patients with advanced cancer.²² Forty-one participants were enrolled; 36 completed the trial. The primary outcome was the psychological subscale of the Supportive Care Needs Survey (SCNS). Secondary outcomes were other domains of the SCNS, psychological status, continuity of care, quality of life and re-

Variable	Glare et al. ²³	Del Fabbro et al. ²⁴	Chasen et al. ²⁵	Gagnon et al. ²⁶
General symptom burden				
ESAS*	NR			
Anxiety	NR		Improved§	Improved§
Depression	NR		Improved§	Improved§
Well-being	Improved§		Improved§	Improved§
Tiredness	Improved§		Improved§	Improved§
Nutrition				
Appetite	Improved¶	Improved¶	Improved¶	Improved¶
Weight change	Improved¶	Improved¶	Improved¶	Improved¶
Quality of life†	Improved§	NR	Improved§	Improved§
Fatigue‡				
General fatigue	Improved§	NR	Improved§	Improved§
Function				
Six-minute walk test	Improved§		Improved§	Improved§
Patients assessed at 2-mo follow-up, %	58	NR	58	70
Note: ESAS = Edmonton Symptom Assessment System, NR = not reported. *Measured by the modified ESAS, which ranges from 0 (symptom is absent) to 10 (worst possible symptom severity). †Measured by the modified ESAS, which ranges from 0 (excellent quality of life) to 10 (very bad quality of life). ‡Measured by the Multidimensional Fatigue Inventory, whereby each fatigue dimension receives a score out of 20 with a higher score indicating greater fatigue. §Effect size ≥ 0.35; p ≤ 0.01. ¶Stable weight or increased weight at 2 mo.				

source use. Services were selected according to patient need; it is therefore unclear whether all 36 received nutritional and exercise counselling. The intervention arm showed significant improvement in the SCNS psychological, physical and patient care subscales and self-reported health state.²²

Table 1 summarizes results from four studies of rehabilitation interventions for patients with advanced cancer.^{23–26} In an Australian nonrandomized study, 25 of 41 enrolled patients with advanced cancer who remained in the combined program for two months showed improved nutritional and functional status, endurance and strength, with a decrease in reported symptoms.²³ The team in this study included a palliative care physician, dietitian and physical therapist. After baseline assessment, patients received individualized nutritional interventions, exercise programs and symptom management and were followed prospectively for up to six months. The exercise program was undertaken either in the physical therapy gym at the hospital or at home with monthly reviews. Patients performed a combination of endurance and strengthening exercises. Measures were determined at baseline and on reviews at one, two, three and six months. The two-month follow-up visit was the principal end point of the study.²³

Researchers at the MD Anderson Cancer Center reported on 151 participants assessed at a cachexia clinic.²⁴ Fifty-nine patients did not return for follow-up. All patients with cancer received dietary counselling by a dietician and standard exercise recommendations. A combination of simple pharmacological and nonpharmacological interventions significantly improved appetite and increased weight in one-third of patients who were able to return for follow-up. No functional outcomes were reported.

In 2003, a multidisciplinary program was launched at McGill University and the Jewish General Hospital in Montréal based on the premise that nutritional counselling together with an exercise program and detailed symptom control could improve quality of life for patients and families, and slow loss of function.^{27–31} The program was conceived as a model for the application of palliative care early in the course of a predictably fatal cancer. Core team members include the patient and family, a nurse specialist, a dietitian, an allied health professional, palliative care physicians, a social worker and a clinic coordinator. Patients manage their own nutritional, exercise and symptom therapies with guidance from team members. Later, similar programs were launched at the Royal Victo-

ria Hospital in Montréal and the Élisabeth Bruyère Hospital in Ottawa.

Reviews of results achieved at the Royal Victoria Hospital have been published in a number of reports.^{27–31} Recently, outcome data from programs at the Royal Victoria Hospital and the Élisabeth Bruyère Hospital have been published (Appendices 1 and 2, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.131402/-/DC1).^{25,26}

Among 67 patients who completed the two-month program at the Élisabeth Bruyère Hospital, significant improvements with moderate effect sizes were seen in physiologic performance, nutrition (0.46), symptom severity (0.39–0.46), symptom interference in functioning (0.38–0.48), fatigue and physical endurance, mobility, and balance/function (0.45–0.61).²⁵ Patients who completed the program at the Royal Victoria Hospital experienced strong improvements in the physical and activity dimensions of fatigue (effect size 0.8–1.1).²⁶ They also had moderate reductions in the severity of weakness, depression, nervousness, shortness of breath and distress (effect size 0.5–0.7) and moderate improvements in six-minute walk distance, maximal gait speed, coping ability and quality of life (effect size 0.5–0.7). Furthermore, 77% of patients either maintained or increased their body weight.²⁶

In a recent report on the program at the Jewish General Hospital, Parmar and colleagues³² concluded that weight gains are associated with subjective improvements in physical functioning and that changes in perceived physical strength are consistently correlated with quality of life.

How do rehabilitation services complement palliative care services?

The tenets of rehabilitation intersect with those of palliative care, stressing symptom control melded with emotional and spiritual care and accompanied by formal exercise and nutrition protocols. The principles apply to all patients and families confronting a lethal disease from its onset. In practice, most palliative care programs emphasize end-of-life care. Whereas expert oncology panels laud the virtues of palliative care application early in the trajectory of advanced cancer,⁶ relatively few programs meet this standard.³³ The mindset that oncology represents cure whereas palliative care represents care may change if further evidence emerges that not only quality of life but also survival may improve when palliative care and rehabilitation are melded with conventional oncology therapy.³⁴

What further research is needed?

When caring for patients, we may limit our horizons if we fail to recognize the influence of their psychological state, nutrition, physical activity, symptoms and functional status on their disease and response to therapy. A truly comprehensive care program will incorporate elements that address each of these aspects. Evidence from nonrandomized studies indicates that full-service programs can ameliorate the symptomatic course of cancer. Data on survival are lacking; however, there is consistent evidence supporting the adoption of early palliative care that includes formal nutrition counselling and exercise.

Exercise and nutritional counselling are integral to “survivorship” models (i.e., rehabilitation designed for patients receiving treatment for cure) during and after treatment. Adding exercise and nutrition to a palliative care program creates a logical model for introducing early palliative care. Evidence of the success of conventional palliative care programs exists.³⁴ Could further improvements in quantity and quality of life be effected with a more complete team approach to early palliative care?

All programs report high patient “dropout” rates, most notably among patients with a high C-reactive protein level, which denotes the presence of a chronic inflammatory state. Patients with a chronic inflammatory state have a poor prognosis and a higher burden of symptoms.^{35–37} Refinement of future programs should include early patient access and more specific anti-inflammatory approaches. The MENAC study (<http://clinicaltrials.gov/show/NCT01419145>) is a multicentre RCT that is currently enlisting patients with cachexia to compare a multimodal intervention (including oral nutritional supplements, celecoxib and exercise) with standard care.

Conclusion

Early evidence suggests that a comprehensive cancer care program should incorporate rehabilitation services with drug and radiotherapy treatment throughout the span of care. Numerous pronouncements and consensus statements call on physicians to treat the “whole person,” and to introduce palliative care principles early.^{5–7}

We can learn from geriatricians, cardiologists and pulmonologists, who have incorporated successful rehabilitation programs in their disciplines. The pathophysiology of distress in patients with advanced cancer is not dissimilar from mechanisms affecting frail elderly patients, and patients with congestive heart failure and chronic obstructive pulmonary disease.

We propose that current evidence and community expectations are sufficient to encourage Canadian cancer centres to consider establishing full rehabilitation research models for patients with advanced cancer.

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