

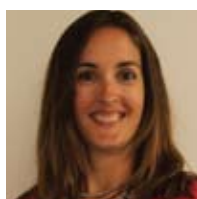
PHYSICAL ACTIVITY IN LUNG CANCER

Emerging data link physical activity with long-term benefits

Julia Devonish, PhD; Nicole Culos-Reed, PhD; Gwyn Bebb, MA, BMBCh, PhD, FRCPC



Julia Devonish, PhD is a second-year medical student at the Medical University of the Americas. *Email:* devonishjulia@gmail.com.



Nicole Culos-Reed, PhD is an Associate Professor in the Faculty of Kinesiology, University of Calgary, and Researcher with the Department of Psychosocial Resources, Tom Baker Cancer Centre. Dr. Culos-Reed examines the role of physical activity in cancer survivorship. *Email:* nculosre@ucalgary.ca

Gwyn Bebb, MA, BMBCh, PhD, FRCPC is a Medical Oncologist and Investigator, Translational Research Laboratory, and Director, Glans-Look Lung Cancer Database at the Tom Baker Cancer Centre, and an Associate Professor of Medicine at University of Calgary. *Email:* gwyn.bebb@albertahealthservices.ca

Interventions aimed at improving physical activity (PA) levels in cancer patients have been established as safe and generally well tolerated both during and after cancer treatments, providing numerous benefits, and perhaps extending survival.^{1,2} PA guidelines for exercise testing and prescription in adult survivors of breast, prostate, colon, hematologic and gynecologic cancers have been published.³

Although lung cancer (LC) is the second most common malignancy, guidelines do not include this patient population. Emerging data suggest PA benefits both as an exercise-based physiologic assessment during evaluation for resection and as a complementary approach to reproduce benefits observed in other cancer and chronic lung disease populations.^{1,4,5} PA interventions must be tailored to 3 distinct clinical settings: 1) resectable disease, 2) unresectable locally advanced disease and 3) metastatic disease.

RESECTABLE DISEASE

The majority of LC PA research has focused on the surgical population. Approximately two-thirds of patients report activity levels insufficient to meet guideline recommendations.⁶ Importantly, those meeting guidelines report better quality of life (QoL) than less active counterparts.⁷

Cardiopulmonary exercise testing (CPET) has become an integrated component of the preoperative risk assessment, as it replicates stressful conditions similar to those experienced during surgical procedures.⁸ Evidence of its safety and feasibility in LC has been documented.⁹ Exercise testing that assesses maximal oxygen consumption (VO_2 max) is preferred as it is a strong independent predictor of both survival and surgical complications as well as a key factor in determining candidacy in patients whose predicted postoperative forced expiratory volume in 1 second (FEV_1) or diffusing capacity of lung for carbon monoxide (D_{LCO}) are $<40\%$.^{4,8,10} Patients with a preoperative VO_2 max of $\geq 15 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, $10\text{--}15 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, and $<10 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ are at low,

increased, and very high risk of surgical complications respectively.^{8,11,12}

A compelling reason for PA intervention in LC is the possibility of increasing the number of candidates for curative intent treatments. Through improvements in VO_2 max via exercise training, potential surgical candidates may alter their risk category, potentially deeming themselves eligible. Feasibility was demonstrated in 8 patients who, despite favourable clinical stage, were denied surgery based on poor pulmonary functioning.¹³ Following 4 weeks of individualized aerobic and resistance training, each patient significantly improved exercise capacity and subsequently received surgery with no mortality and 25% morbidity. Another investigation provided aerobic training at 60–100% of baseline VO_2 max until surgical resection.¹⁴ Intention-to-treat analyses found a $2.4 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ improvement in VO_2 max prior to surgery. Per protocol analyses revealed greater improvement in those attending $\geq 80\%$ of the prescribed sessions ($3.3 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Despite small patient series and no level I evidence, some European bodies recommend early pre- and post-operative programs to surgical candidates.^{12,15} Improvements in peri- and post-operative recovery have also been noted with this approach.¹⁴

LOCALLY ADVANCED AND METASTATIC DISEASE

Advanced LC poses additional challenges. CPET feasibility in inoperable disease found 28% lower VO_2 max in patients than in sedentary age- and sex-matched controls.⁹ In unresectable or medically inoperable disease, sequential chemotherapy and radiation provides modest improvements in survival in Stage II and III disease, while concurrent radical chemoradiotherapy offers long-term control at the cost of increased toxicity (i.e. Grade 3–4 esophagitis).¹⁶ The systemic effects of chemotherapy on physical functioning, compounded by radiation-induced fatigue and fibrosis likely contribute to the observed

exercise intolerance.^{9,16} Significantly more physical symptoms, psychological problems and QoL declines in comparison to other populations of cancer survivors are reported.¹⁷

Only one intervention in this clinical subset (i.e. Stage IIIB or IV) exists within the literature.¹⁸ The program involved aerobic, resistance and flexibility exercise. No significant differences in QoL, fatigue, mood, muscular strength or functional capacity were observed from pre- to post-intervention, with the exception of improved LC symptoms. While this lone study does provide preliminary evidence of the feasibility of such interventions, it also suggests that maintaining the status quo for longer may be the main benefit. Within the general cancer literature, evidence suggests PA benefits in both metastatic disease and palliation, but extrapolating these conclusions to LC may not be an easy proposition.^{19,20}

FUTURE DIRECTIONS

Guidelines for exercise testing and prescription in cancer have been recently published, with general adult PA guidelines serving as a framework.³ Given the likelihood that a LC patient will be of an advanced age at presentation, guidelines for older adults may be a more appropriate framework.²¹ To further the LC PA evidence, researchers should employ these recommendations around the specificity, frequency, intensity and type of aerobic, resistance and flexibility exercise.

Clearly, there is a dearth of evidence to guide how PA can be incorporated into LC management. While the naysayers will tend to point to the dismal outlook associated with LC as a reason for not pursuing this line of research, there are compelling reasons to drive new research forward. The last decade has seen the acceptance of second- and third-line treatments which have extended LC survival even in the metastatic setting. The incorporation of targeted treatment for molecularly defined patients extends progression-free survival while creating minimal toxicity. It is also important to recognize that 15% of LC patients are never-smokers and are therefore not prone to the classic exercise limitation often associated with LC. There is a need for statistically powered randomized controlled trials within the 3 broad patient categories to examine and validate efficacious intervention, with adequate followup to assess long-term effects, so that the benefits of PA demonstrated in other cancers can potentially be extended to the LC patient.

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Disclosure:

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