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Low physical activity levels and functional decline in individuals with lung cancer

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ABSTRACT

Objectives: Physical activity has been infrequently measured objectively in non-small cell lung cancer (NSCLC). We aimed to investigate levels of physical activity, functional and patient reported outcomes at diagnosis and over six months in participants with recently diagnosed NSCLC and compare results with both physical activity guidelines and outcomes of similar-aged healthy individuals.
Methods: This prospective observational study assessed 50 individuals from three Australian tertiary hospitals with stage I–IIIB NSCLC at diagnosis, then 10 weeks and six months later. Thirty five healthy individuals without cancer were assessed once. Outcome measures included tri-axial accelerometery (number of steps per day), six minute walk distance (6MWD), muscle strength and questionnaires including health-related quality of life (HRQoL).
Results: Individuals with NSCLC were engaged in significantly less physical activity than similar-aged healthy individuals, with 60% not meeting physical activity guidelines. At diagnosis they had worse quadriceps strength, nutritional status and HRQoL. Over six months, participants with NSCLC experienced decline in self-reported physical activity, 6MWD and muscle strength, and worsening symptoms.
Conclusion: At diagnosis individuals with NSCLC engage in less physical activity, are weaker and more depressed than healthy individuals and their self-reported physical activity declines over six months. Future studies are required to investigate the efficacy of interventions to increase physical activity.

1. Introduction

Physical inactivity is a global pandemic [1]. The World Health Organisation (WHO) recommends that adults aged 65 years and above engage in 150 min of moderate intensity physical activity (PA) per week [2]. The same guidelines apply for individuals with cancer [3]. Increased PA in breast and colon cancer is associated with a trend towards survival benefit [4]. Exercise interventions are associated with benefits on cardiorespiratory fitness, health related quality of life (HRQoL), mood, symptoms and treatment side-effects in individuals with a range of cancer types [3,5,6]. Whilst there is a strong body of research regarding levels of PA of individuals with cancer, limited research has been undertaken in NSCLC, specifically using objective measures. Lung cancer is associated with significant disease burden, high symptom levels and impairment in HRQoL [7,8]; for these reasons we hypothesise that PA levels will be low in this patient group.

The primary aims of this study were, therefore, to: (1) measure the level of PA of individuals with newly diagnosed NSCLC in an Australian setting and compare this to (a) recommended WHO PA guidelines and (b) levels of PA in similar-aged healthy individuals; and (2) measure change in PA level of individuals with NSCLC (a) from time of diagnosis to 10 weeks (during treatment) and (b) from time of diagnosis to six months. Secondary aims were to: (1) compare functional and patient-reported outcomes of individuals with NSCLC at time of diagnosis with that of a group of similar-aged healthy individuals; and (2) measure the change in functional and patient-reported outcomes of individuals with NSCLC (a) from diagnosis to 10 weeks and (b) from diagnosis to six months. The Strengthening the Reporting of Observational Studies in

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Epidemiology (STROBE) guidelines were followed in reporting this study [9].

2. Methods

2.1. Participants and study design

A multicentre prospective cohort study was conducted at three tertiary hospitals in Melbourne, Australia from November 2010 to October 2012. All sites had ethical approval (AH H2010/03933; PMCC 10/123; MH 2010.236) and written consent was obtained from all patients. Two groups of participants were recruited. Group one were English speaking individuals with newly diagnosed stage I–IIIB NSCLC pre-treatment (surgery, chemotherapy and/or radiotherapy) and group two were similar-aged healthy individuals without cancer recruited from posters advertising the study.

Participants with NSCLC were assessed at three time-points: baseline (at diagnosis pre-treatment); 10 weeks following diagnosis (generally during chemotherapy/radiotherapy); and six months following diagnosis. Healthy participants were assessed once.

Standard care at the institutions was followed and not modified. Individuals with NSCLC were not offered any formal education regarding PA/exercise and referral to rehabilitation was not part of usual care at the centres.

2.2. Measurement of primary outcome: physical activity

Physical activity was measured as number of steps per day using a waist-mounted KinetaMap device (tri-axial accelerometer) (Sparkfun Electronics GPS-08725, Colorado) [10]. Participants were instructed to wear the device for five consecutive days during waking hours, including at least one weekend day, in their home environment. A minimum of three 'full days' (defined by device turned 'on' for ≥8 h/day) were required for participants' data to be included. Steps data were analysed with computer software programs custom-designed for this study. Data were averaged across the number of full days that the device was worn.

Self-reported PA was measured using the Physical Activity Scale for the Elderly (PASE) [11]. Higher scores represent higher levels of PA. The maximum score attainable is 400 and the average score for elderly individuals is 103 points [11]. Participants' levels of reported PA were compared with the recommended WHO PA guidelines [2] and classified as sufficient (≥150 min/week), insufficient (inactive) (1–149 min/week) or sedentary (0 min/week) [12].

2.3. Measurement of secondary outcomes

Functional capacity was measured using the six minute walk distance (6MWD) for individuals with NSCLC and cardiopulmonary exercise testing (CPET) for healthy individuals (given the ceiling effect on 6MWD in healthy populations) [13]. The 6MWD was conducted according to published recommendations, including with the use of a practice test [14] and predicted distances were also calculated [15]. CPET determined participants' peak oxygen consumption (VO_2peak) and was performed using Sensormedics Vmax Spectra (Sensormedics, Yorba lina, Ca, USA) and a cycle ergometer (Lode BV, Groningen, The Netherlands). Percentage predicted VO_2peak was calculated [16].

A Powertrack-II Commander1500 hand-held dynamometer was used to measure strength of quadriceps femoris, tibialis anterior and rotator cuff [17]. A Jamar hydraulic hand-grip dynamometer was used to measure hand-grip strength (NSCLC group only) [18]. An isometric maximal voluntary contraction was assessed for each muscle group and the highest force achieved over a five second duration was recorded [19]. Performance status was measured using the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) rated by the patient and physician [20]. Nutritional status was measured using the Mini-Nutritional Assessment (MNA) [21]. The European Organization for the Research and Treatment of Cancer questionnaire and lung cancer module (EORTC QLQ-C30-LC13) assessed HRQoL over the previous week (NSCLC group only) [22]. The Short Form 36 (SF-36v2) was used to assess health status [23]. Scores are presented as norm based T-scores compared to Australian data of mean (SD) 50(10). Psychological status was measured using the Hospital Anxiety and Depression Scale (HADS) [24]. Distress was assessed with the Distress Thermometer and cancer symptoms were assessed with the Memorial Symptom Assessment Scale (MSAS) [25].

Demographic and medical data were obtained. Comorbidities were scored with the simplified Colinet comorbidity score. Participants' residential location was recorded and those living >50 km from Melbourne city were classified as rural.

2.4. Sample size

For a moderate effect size ($d = 0.6$) and alpha 0.05, 35 participants per group were required to detect a difference in steps/day (calculated using *t*-tests) [26]. Accounting for a 30% drop-out rate, the number of participants with NSCLC was increased to 50. A moderate effect size was used to calculate sample size because there were no data available to calculate difference in steps at the time of designing the study.

2.5. Statistical analysis

All data were analysed through SPSS Windows Version 20.0 (SPSS, Chicago, IL, USA). Descriptive statistics and graphical displays were used to identify missing and out-of-range values and to assess distributional characteristics of test scores prior to formal analysis. Descriptive statistics were used to assess compliance with assessments and to summarise baseline characteristics and outcome data by group. Pearson's χ^2 for nominal variables, Mann–Whitney *U*-tests for ordinal variables and independent samples *t*-tests for continuous variables were used to compare demographic and clinical characteristics of consenters and study decliners [26]. Pearson's χ^2 was used to test for group differences in meeting PA guidelines and type of most frequent PA.

One-way analysis of covariance was used to assess group differences in continuous outcomes after adjusting for pre-existing differences associated with age, provided equal variances could be assumed [26]. If the Levene Statistic was significant, however, group differences were assessed with the Mann–Whitney *U*-test. Alpha was set at 0.05 (two-tailed) for these analyses. Standard effect size indexes (Cohen's *d* and *r* as appropriate) were used to quantify the size of between group differences [26].

Longitudinal outcome analyses for NSCLC patients were carried out by fitting a mixed-effects repeated measures model to all available data for each outcome separately. All models were estimated by maximum likelihood and an unstructured variance–covariance matrix was used to model the covariance structure among repeated measures [27]. For each outcome, a reference cell model was used to compute an estimate of the mean at baseline assessment, as well as estimates of the differences between baseline and follow-up assessments with tests of significance [28]. The Bonferroni correction was applied to adjust tests for multiple comparisons; in this case, alpha was set at 0.05/2 = 0.025 (two-tailed) [29]. Kazis effect size index was calculated to quantify the size of changes from baseline [30]. Pearson's correlation coefficient was used to assess bivariate relations between study outcomes [31].