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Feasibility and preliminary efficacy of progressive resistance exercise training in lung cancer survivors☆

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ABSTRACT

Lung cancer survivors exhibit poor functional capacity, physical functioning, and quality of life (QoL). Here, we report the feasibility and preliminary efficacy of a progressive resistance exercise training (PRET) intervention in post-treatment lung cancer survivors. Seventeen post-treatment lung cancer survivors (10 female), with a mean age of 67 (range 50–85), mean BMI of 25, and diagnosed with non-small cell lung cancer (94%) were recruited in Edmonton, Canada between August 2009 and August 2010 to undergo PRET. The primary outcomes focused on feasibility including eligibility and recruitment rate, loss to follow-up, measurement completion, exercise adherence, and program evaluation. Secondary outcomes addressed preliminary efficacy and included changes in muscular strength (1 repetition maximum), muscular endurance (repetitions at 70% of 1 repetition maximum), body composition (DXA scan), physical functioning (6-minute-walk-test, up-and-go, sit-to-stand, arm curls), and patient-reported outcomes including QoL (SF-36, FACT-L), fatigue (FACT-F), dyspnea (MRCD), and patient-rated function (LLFI). Forty of 389 lung cancer survivors were eligible (10%) and 17 of the 40 (43%) were recruited. Over 80% of participants were able to complete all testing; two participants were lost to follow-up, and the median adherence rate was 96% (range: 25–100%). Ratings of testing burden were low (i.e., less than two out of seven for all items), and trial evaluation was high (i.e., greater than six out of seven for all measures). Paired *t*-tests showed significant increases in muscular strength ($p < .001$), muscular endurance ($p < .001$), six-minute walk distance ($p < .001$), up-and-go time ($p < .05$), number of arm curls ($p < .001$), and number of chair stands ($p < .001$). There were no significant changes in body composition or patient-reported outcomes. PRET is a feasible intervention with potential health benefits for a small proportion of lung cancer survivors in the post-treatment setting.

1. Introduction

Lung cancer accounts for 15% of all new cancer diagnoses and the most cancer deaths in North America [1]. Overall five year relative survival is only about 16%, however, if detected early the survival rate is 53% [2]. Lung cancer survivors, defined as anyone previously diagnosed with lung cancer [3], often exhibit poor functional capacity [4,5], poor patient-reported physical functioning, and compromised quality of life (QoL) [6,7]. In addition to the expected age-related losses in physical function, lung cancer survivors often present with comorbidities and disease burden which can lead to disability, loss of function and decreased QoL [8,9]. Few interventions have been developed to attenuate functional declines in lung cancer survivors [4,10–12].

Progressive resistance exercise training (PRET) is a well tolerated intervention for improving muscular strength, body composition, physical fitness, physical functioning, and QoL in clinical and older adult populations, including some cancer survivor groups [13–16]. No studies to date, however, have focused exclusively on PRET in lung cancer survivors. Consequently, there is a need for feasibility studies to address a series of questions regarding the interest, acceptability, and preliminary efficacy of PRET for improving strength, physical function, and QoL in post-treatment lung cancer survivors [15,17,18]. Here, we present the results of a prospective single-group study designed to evaluate the feasibility and preliminary efficacy of a PRET program in lung cancer survivors following treatment. We hypothesized that the training program would be feasible and result in improvements in objective health-related fitness as well as patient-reported outcomes.

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2. Materials and methods

2.1. Setting and participants

The study was conducted at the Cross Cancer Institute and the University of Alberta in Edmonton, Canada. Ethical approval was obtained from the Alberta Cancer Research Ethics Committee and the Health Research Ethics Board at the University of Alberta. Informed consent was obtained from all participants. Eligibility criteria were: (1) histologically confirmed stage I-IIIB non-small cell lung cancer (NSCLC) and limited stage small-cell lung cancer; (2) approval of treating physician; (3) not currently receiving treatment and none planned within the next three months; (4) ≥18 years old; (5) Karnofsky Performance Status ≥50; and (6) life expectancy of at least six-months. Individuals were excluded if they demonstrated: (1) uncontrolled co-morbidities (e.g. uncontrolled type II diabetes, hypertension above 160/100); (2) evidence or suspicion of bone metastasis; (3) any medical condition contraindicated for PRET (e.g. Marfan's syndrome), or (4) did not speak English.

2.2. Design and recruitment

The study was a prospective single group feasibility study. Two methods were used to recruit participants. Lung cancer clinics were screened weekly for potentially eligible participants. Additionally, the provincial cancer registry identified potentially eligible lung cancer survivors who were mailed a recruitment package. Interested participants who received the package were instructed to contact the project coordinator by mail (pre-paid envelope) or telephone. Potential participants were then screened for eligibility and scheduled for baseline testing.

2.3. Exercise training intervention

The exercise training was designed as a 28 session intervention to improve muscular strength. Prior to each training session participants had heart rate and blood pressure taken and performed a five-minute warm up of low intensity aerobic activity. Exercises performed were the leg press, chest press, seated row, leg extension, leg curl, shoulder press, lat pull down, and an abdominal exercise. Resistive training of the chest wall muscle groups was done with a PowerLung® training apparatus. Participants took 90–120 s of rest between exercises.

Stretches were performed on major muscle groups following training sessions.

The goal of the program was to complete exercise training three-times per week, on non-consecutive days, for 28 sessions over approximately 10-weeks. Participants were allowed to make up sessions with the goal of reaching 28 training sessions. Exercise sessions were supervised by a qualified exercise physiologist.

The exercise prescription was based upon the results of the baseline strength testing. Training began at approximately 60% of one repetition-maximum (1RM) for leg press and chest press as determined at baseline testing. For all other exercises, 1RM was estimated via a prediction equation [19] from an eight-to-ten RM determined prior to training. The goal of the training program was to progress to 85% of 1RM by week nine. The program progressed through three phases. In phase one, sessions one to nine, training began at a high volume and low intensity (i.e., 10 to 12 repetitions for two to three sets). In phase two, sessions 10 to 16, the volume decreased and the intensity increased by increasing the weight lifted (i.e., repetition goal decreased to six to eight, for two to three sets). In phase three, sessions 19 to 25, volume decreased and the intensity increased (i.e., repetition goal was four to six, for two to four sets). Sessions 26 to 28 were a progressive taper prior to follow-up testing.

Participants were progressed using a modified 'two for two rule' within a prescribed repetition goal, such that when participants could perform two or more repetitions over the assigned repetition goal in the last set for consecutive workouts for a certain exercise, then weight was increased by ~10%. If for any reason the specified training objective could not be reached, adjustments were made and the participant was asked to work to tolerance.

Participants performed chest wall training in a seated position on a power lung trainer. These trainers allow for control of inspiratory (resistance from one to six) and expiratory (resistance from one to three) flow at the mouth. The flow characteristics of this device have been previously investigated by Wells et al. [20]. The initial load was determined for each participant by the research coordinator (CJPM). During sessions one through nine, participants were asked to complete two sets of eight-to-twelve repetitions. From session 10 and beyond, participants were asked to complete three sets of eight-to-ten repetitions each training day for inspiration and expiration separately. The intensity was increased, via resistance settings, when participants were able to inhale or exhale deeply and forcefully in less than three seconds per breath for the majority of the repetitions in any one set for two training sessions in a row.

2.4. Feasibility outcomes

The primary feasibility outcomes included eligibility rate, recruitment rate, measurement completion rate, loss-to-follow-up, adherence, adverse events, and ratings of burden and acceptability. Eligibility rate was defined as the total number of survivors screened, divided by the total number eligible. Nonresponse to the registry mailout was considered ineligible. Recruitment rate was defined as the number of survivors recruited from those eligible. Measurement completion rate was defined as the number of participants able to complete each outcome measure at baseline and follow-up. Loss to follow-up was defined as participants who were withdrawn or dropped out.

Adherence to the exercise intervention was measured by the number of sessions attended out of 28. Adherence to the PRET prescription was tracked by the number of exercises (out of a possible 10) where participants met the repetition goal, averaged weekly. Ability to reach the intensity training goal was defined as the ability to reach 85% of baseline 1RM by week nine of training. Adverse events during or following exercise testing and training were tracked. Acceptability was measured via a program satisfaction survey completed post-training that assessed the burden of testing, as well as how participants felt about participating in the trial. These scales were scored from one (not at all) to seven (very much).

2.5. Preliminary efficacy outcomes

Preliminary efficacy was assessed by objective outcomes of muscular strength and endurance, physical functioning, and body composition. Patient-reported outcomes included QoL, fatigue, sleep quality, anxiety, depression, patient-reported functioning, and dyspnea. All objective and patient-reported measures were assessed at baseline and post-training.

Muscular strength was assessed by 1RM for upper body (chest press) and lower body (leg press) according to American College of Sports Medicine guidelines [21]. Absolute 1RM was recorded as the maximum weight lifted one time for the chest press and leg press. Absolute 1RM divided by body weight was recorded as the relative 1RM [21]. Relative muscular endurance was assessed for upper body (chest press) and lower body (leg press) as num-

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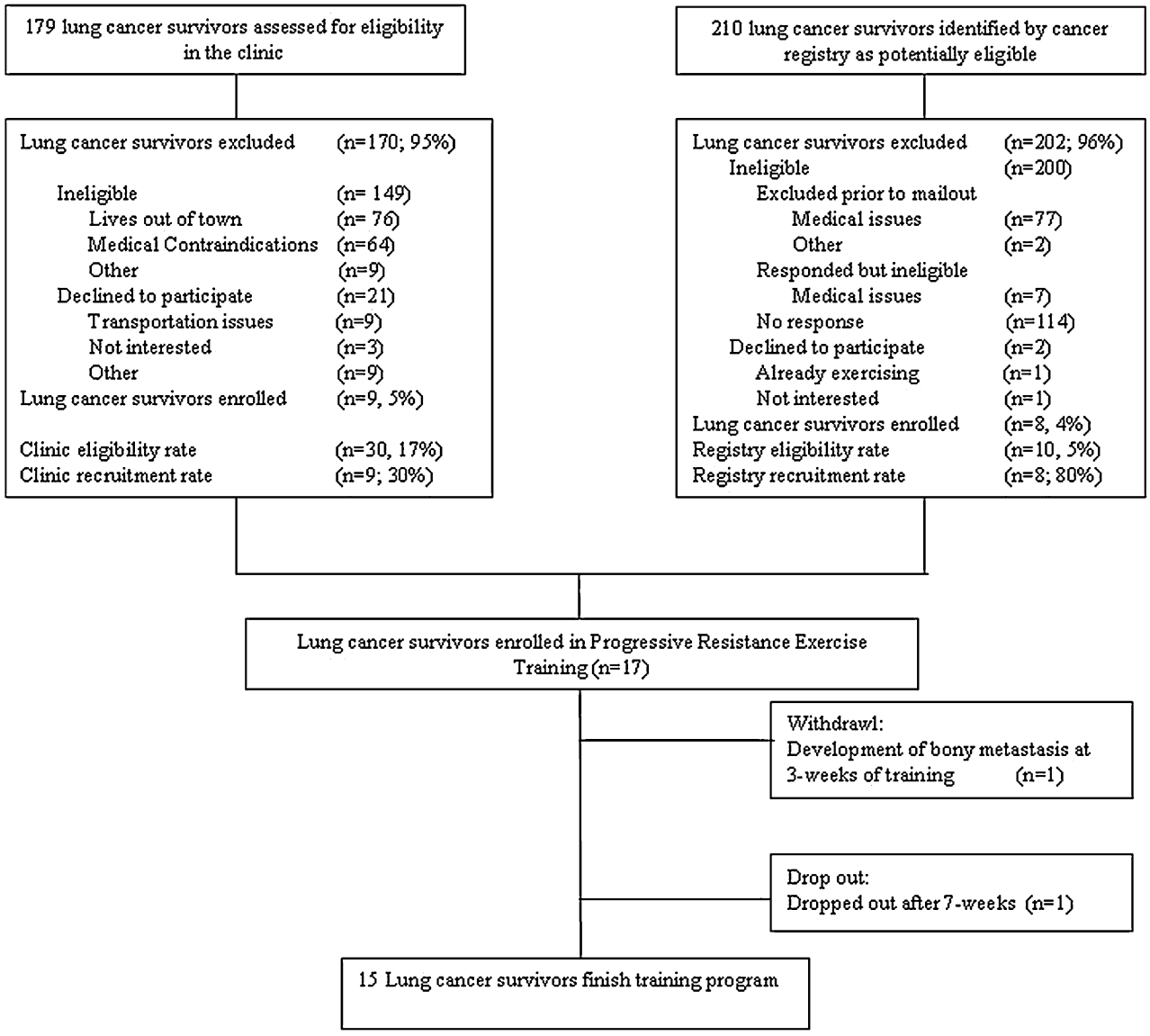

Fig. 1. Flow of participants through the trial.

ber of repetitions to exhaustion of 70% of 1RM at baseline [21]. Maximum inspiratory pressure (PI_{max}) and maximum expiratory pressure (PE_{max}; cm/H_2O) were measured on a Micro Medical respiratory pressure meter (Chatham, UK) as the pressure that could be maintained during a three-second inspiratory/expiratory maximal effort from functional residual capacity/total lung capacity respectively.

At baseline each participant was given instructions on resistance training technique, safety and spotting as outlined by Phillips et al. [22]. Before training, each muscular performance and inspiratory/expiratory pressure tests were performed three times, with five to seven days rest in-between. Three test trials with adequate familiarization have been shown to be sufficient for establishing a stable 1RM in older adults [22]. At follow-up a minimum of two tests were performed, with five to seven rest days in-between. The highest values obtained from these testing sessions for each variable was used in data analysis.

Objective physical functioning was assessed by the eight-foot get-up-and-go (time in seconds to get out of chair, walk eight-feet, round a pylon, and return to seated in chair), the sit-to-stand test (number of unassisted chair stands performed in 30 s), arm curl (number of arm curls performed with standard weight in 30 s; five lbs for women, eight lbs for men) [23], six-minute walk test (distance covered in meters in six-minutes on a 50 m straight course) [24]. The six-minute walk test was performed twice at baseline and post-testing in accordance with the American Thoracic Society guidelines [25]. Age and sex predicted six-minute walk distance (6MWD) was calculated according to Gibbons et al. [26]. To assess body composition, DXA was performed (General Electric LUNAR Prodigy High Speed Digital Fan Beam X-Ray-Based Bone Densitometer) [27].

The Short-form-36 (SF-36) was used to assess generic QoL [28,29]. The Functional Assessment of Cancer Therapy – Lung (FACT-L) scale was used to assess disease specific QoL [30]. FACT-Fatigue was used to assess fatigue [31]. Items from the Pittsburgh Sleep Quality Index (PSQI) were used to measure sleep quality [32]. Anxiety was assessed by the 10-item Spielberger State Anxiety Scale [33]. Depression was assessed by the Center for Epidemiologic Studies Short Depression (CES-D 10) Scale [34]. Dyspnea was assessed using the Oxygen Cost Diagram and the Medical Research Council Dysponea Scale [35]. The Late Life – Function Disability

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Table 1
Baseline demographic, medical, and behavioral profile of lung cancer survivors undergoing resistance training in Edmonton, Alberta, Canada, 2009–2010 ($n = 17$).

Variable	No.		%
Age, mean (range), y		66.7 (50–85)	
Sex, female	10		58.8
BMI, mean ± SD, kg/m^2		25.1 ± 3.5	
No. of medications, mean ± SD		2.1 ± 1.3	
No. of comorbidities, mean ± SD		2.5 ± 1.2	
Self-rated heath, mean ± SD		2.8 ± 0.6	
MRCD score, mean ± SD		1.8 ± 0.8	
FEV1 predicted (%), mean ± SD, L		77.4 ± 16.3	
FEV1/FVC predicted (%), mean ± SD		84.9 ± 12.4	
6MWD, mean ± SD, m, predicted (%)		445 ± 70.63%	
PGSGA, well-nourished	14		82.4
Post-secondary education	10		58.8
Married	13		76.5
Employed full time	4		23.5
Ethnicity, Caucasian	14		82.4
Previous cancer (>five y ago)	6		35.3
Behavioral profile			
Current smoker	2		11.8
Current drinker[a]	1		5.9
Current exerciser[b]	3		17.6
Time since diagnosis, mean (range), y		3.5 (0.3–6)	
Diagnosis NSCLC	16		94.1
LS SCLC	1		5.9
Stage of disease I/II	11		64.7
III	5		29.4
Surgery	14		82.4
Extent of resection			
Lobectomy	12		70.6
Pneumonectomy	2		11.8
Treatment			
Adjuvant chemotherapy	5		29.4
Chemo/RT	1		5.9
Chemo alone	1		5.9
RT alone (palliative)	1		5.9
RT alone (radical)	2		11.8
Treatment intent curative	13		76.5

NSCLC, non-small cell lung cancer; LS SCC, Limited stage small cell lung cancer; FEV1, forced expiratory volume in 1-second; FVC, forced vital capacity; PGSGA, Patient-Generated Subjective Global Assessment; MRCD, Medical Research Council Dyspnea Scale; 6MWD, six-minute walk distance RT, radiation therapy.

[a] Regular drinker, drinks every day.

[b] Current exerciser, ≥150 min of moderate strenuous exercise per week.

Index (LL-FI) was used to assess patient-reported physical functioning [36].

2.6. Analyses

Based on previous studies and expert opinion the goal was to recruit 30 participants in this feasibility trial over a one year period. All analyses were conducted using PASW Statistics 18 (IBM Inc., Somers, NY). Normality was assessed using Kolmogorov–Smirnov statistic. Paired *t*-tests were used to assess changes in objective and patient-reported outcomes. All tests were two-tailed with significance set at $\alpha = .05$. Given that this was a feasibility study with a small sample size we did not adjust for multiple testing and the efficacy results were interpreted for both statistical and clinical significance.

3. Results

Participant flow through the trial is outlined in Fig. 1. The demographic, medical, and behavioral profile of the participants is reported in Table 1. Participants had a mean age of 67, the majority were early stage (64.6%) NSCLC survivors (94.1%), had received surgery (82.4%), and were on average three and a half years post-diagnosis. Participants had a mean 6MWD of 445 ± 70, equivalent to 63% of age and sex predicted.

3.1. Feasibility outcomes

Between August 2009 and August 2010, 389 survivors were assessed for eligibility, 40 (10%) were eligible, and 17 (43%) were recruited. Measurement completion rates were between 82% and 94% for all measures. Two participants were lost-to-follow-up (12%). One participant dropped out after seven-weeks for personal reasons, in this case we carried forward the mid-point test results for muscular strength.

The mean and median adherence rate for all 17 participants was 87% and 96% respectively (range 25–100%), with 76% of participants achieving greater than 80% adherence. The mean time to complete the training program was 12.4 weeks (SD = 3.9). For weeks one to ten, the average number of exercises performed where participants met the repetition goal was 8.8 (SD = 0.9) out of ten. On average, an intensity of at least 85% of baseline 1RM was achieved for all exercises by week nine. Specifically, as a percent of baseline 1RM, participants were lifting 94–129% by week nine. Five participants did not reach the 85% of baseline 1RM goal for chest press. The goal was reached for all participants on all other exercises. The average testing burden scores were low (i.e., below two for all tests). Post-training the mean scores for acceptability were high; above six for positively worded phrases (e.g. something I would recommend to other lung cancer patients), and below one for the negatively worded phrase (i.e., waste of my time).

There were three adverse events during the trial: (1) a participant experienced an exacerbation of shoulder arthritis and was unable to continue with the chest press and shoulder press exercises but completed a modified training program, (2) a participant experienced lower back pain the day after session 13, and (3) a participant experienced shoulder pain following post-testing. All adverse events were successfully resolved.

3.2. Preliminary efficacy outcomes

Objective measures of preliminary efficacy are presented in Table 2. Muscular strength significantly improved by 32 kg (52%) and 15 kg (42%) for the leg press and chest press, respectively. Relative muscular endurance improved significantly for both chest press (150%; $p = .001$) and leg press (173%, $p < .001$). Peak inspiratory pressure increased significantly ($p < .001$), while improvements in expiratory pressure reached borderline significance ($p = .082$). For objective physical functioning, there were significant improvements in 6MWD ($p < .001$), number of chairs stands ($p < .001$), number of arm curls ($p < .001$), and up-and-go time ($p = 0.015$). There were no significant changes in body composition.

Patient-reported outcomes are presented in Table 3. There were borderline significant improvements in role-physical ($p = .072$), bodily pain ($p = .101$) and physical health component score ($p = .092$). No other patient-reported outcomes approached statistical significance but most changed in a favorable direction.

4. Discussion

To our knowledge, this is the first study to pilot PRET with a sample of lung cancer survivors. The eligibility rate in our study was low at 10%. In exercise training studies in post-treatment cancer survivors, reported eligibility rates are between 27 and 34% [37–39]. The main reasons for ineligibility in our study were medical contraindications and living outside the intervention area. Our recruitment rate of 42.5% however is similar to that of previous supervised exercise interventions in post-treatment lung cancer survivors and other cancer survivor groups [4,37–39]. There is a subset of this population who is interested in an exercise program.

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Table 2
Effects of resistance exercise training on health-related fitness outcomes in lung cancer survivors in Edmonton, Alberta, Canada, 2009–2010.

Measure	Baseline Mean ± SD	Post-training Mean ± SD	Mean change M [95% CI]; *p*
Muscular strength, 1RM, kg			
Chest press (*n* = 15)	36.3 ± 14.7	51.1 ± 16.2	14.9 [12.3 to 17.5]; *p* < .001
Leg press (*n* = 16)	62.9 ± 27.6	94.6 ± 35.3	31.7 [23.5 to 39.8]; *p* < .001
Relative muscular strength			
Chest press (*n* = 15)	0.53 ± 0.19	0.74 ± 0.21	0.22 [.18 to 0.25]; *p* < .001
Leg press (*n* = 16)	0.89 ± 0.31	1.35 ± 0.40	0.46 [.34 to 0.57]; *p* < .001
Muscular endurance (repetitions)			
Chest press			
70% of baseline 1RM (*n* = 14)	10.1 ± 3.2	25.2 ± 13.4	15.2 [7.5 to 23.0]; *p* = .001
Leg press			
70% of baseline 1RM (*n* = 15)	23.4 ± 10.6	64.0 ± 37.1	40.6 [23.1 to 58.1]; *p* < .001
Peak pressures (cm/water)			
Inspiratory (*n* = 15)	82.9 ± 23.2	95.3 ± 27.1	12.4 [7.1 to 17.7]; *p* < .001
Expiratory (*n* = 15)	109.2 ± 33.3	120.5 ± 40.5	11.3 [−1.6 to 24.3]; *p* = .082
Functional performance measure (*n* = 15)			
6MWD, m	452 ± 65	538 ± 118	86 [48 to 124]; *p* < .001
No. chair stands in 30 s	11.2 ± 3.1	15.4 ± 3.8	4.2 [2.3 to 6.1]; *p* < .001
No. arm curls in 30 s (R)	14.6 ± 3.1	18.2 ± 3.2	3.6 [2.1 to 5.1]; *p* < .001
Get-up-and-go, time, s	6.3 ± 1.6	5.5 ± 1.1	−0.8 [−1.4 to −0.2]; *p* = .015
DXA body composition scan (*n* = 14)			
Lean mass, kg			
Total body	43.0 ± 9.7	43.1 ± 9.2	0.1 [−0.4 to 0.6]; *p* = .678
Upper limb	4.4 ± 1.8	4.8 ± 1.3	0.4 [−0.3 to 1.1]; *p* = .206
Lower limb	13.9 ± 3.3	14.0 ± 3.3	0.1 [−0.1 to 0.3]; *p* = .188
Trunk	21.2 ± 47.4	21.1 ± 43.4	−0.2 [−0.5 to 0.2]; *p* = .419
ALM	18.2 ± 4.8	18.8 ± 4.5	0.5 [−0.2 to 1.3]; *p* = .134
Fat mass, kg			
Upper limb	2.2 ± 0.97	2.1 ± 0.96	−0.02 [−0.1 to 0.07]; *p* = .670
Lower limb	6.97 ± 2.7	6.95 ± 2.7	−0.03 [−0.2 to 0.2]; *p* = .786
Trunk	12.7 ± 4.9	12.9 ± 5.21	0.3 [−0.2 to 0.7]; *p* = .243
Body fat (%)	34.1 ± 9.1	34.1 ± 9.1	0.04 [−0.7 to 0.8]; *p* = .921
Whole weight, kg	69.0 ± 13.1	69.3 ± 13.1	0.3 [−0.3 to 0.9]; *p* = .355

Relative muscular strength = 1RM (kg)/body weight (kg); 6MWD, six-minute-walk-distance; (R), right hand; DXA, dual-energy X-ray absorptiometry; ALM, appendicular lean mass.

Table 3
Effects of progressive resistance exercise training on patient-reported outcomes in lung cancer survivors in Edmonton, Alberta, Canada, 2009–2010.

Measure (*n* = 15)	Baseline Mean ± SD	Post-training Mean ± SD	Mean change M [95% CI]; *p*
QoL, SF-36 (norm based scoring)			
Physical functioning	48.7 ± 6.4	50.4 ± 7.2	1.7 [−1.4 to 4.7]; *p* = .258
Role-physical	47.7 ± 8.1	51.1 ± 7.4	3.4 [−0.4 to 7.2]; *p* = .072
Bodily pain	51.4 ± 8.0	54.3 ± 7.8	2.9 [−0.1 to 6.4]; *p* = .101
General health	51.0 ± 8.1	52.7 ± 8.8	1.7 [−1.1 to 4.6]; *p* = .204
Vitality	55.2 ± 7.6	52.9 ± 8.9	−2.3 [−7.3 to 2.7]; *p* = .347
Social functioning	45.2 ± 4.0	45.7 ± 4.0	0.5 [−1.0 to 2.0]; *p* = .502
Role-emotional	41.7 ± 7.5	43.2 ± 6.3	1.6 [−0.8 to 3.9]; *p* = .168
Mental health	53.7 ± 9.3	53.6 ± 11.5	−0.1 [−7.7 to 7.5]; *p* = .972
Physical health component	50.3 ± 7.9	53.2 ± 8.1	2.9 [−0.5 to 6.4]; *p* = .092
Mental health component	48.5 ± 8.1	47.6 ± 9.3	−0.9 [−5.4 to 3.6]; *p* = .675
QoL, FACT			
FACT-G	94.9 ± 12.6	96.4 ± 12.7	1.5 [−0.9 to 3.8]; *p* = .196
FACT-L	123.7 ± 15.1	124.7 ± 15.5	1.0 [−2.2 to 4.3]; *p* = .507
TOI-L	78.6 ± 8.4	79.2 ± 9.2	0.6 [−2.4 to 3.7]; *p* = .658
Fatigue	45.6 ± 5.2	46.1 ± 7.0	0.5 [−3.5 to 2.5]; *p* = .715
Late life function index (0–100)			
Advanced lower extremity	70.5 ± 22.2	73.3 ± 24.3	2.8 [−4.4 to 9.9]; *p* = .422
Basic lower extremity	95.9 ± 8.1	97.6 ± 2.8	1.7 [−2.1 to 5.5]; *p* = .356
Upper extremity	91.5 ± 11.4	93.1 ± 8.0	1.6 [−2.3 to 5.5]; *p* = .400
Total	86.2 ± 12.4	88.3 ± 10.7	2.0 [−2.6 to 6.7]; *p* = .366
Depression (CES-D)	3.8 ± 4.2	4.4 ± 5.6	0.7 [−1.8 to 3.1]; *p* = .573
Anxiety (SSAS)	15.1 ± 3.0	14.5 ± 3.0	−0.5 [−2.5 to 1.5]; *p* = .715
Dyspnea			
Oxygen cost (0–100)	78.0 ± 12.9	80.1 ± 14.4	2.7 [−5.8 to 11.1]; *p* = .508
Medical Research Council dyspnea scale (1–5)	1.6 ± 0.6	1.4 ± 0.8	−0.2 [−0.6 to 0.2]; *p* = .334
Sleep quality			
How long to fall asleep each night, min	12.5 ± 11.5	12.6 ± 14.8	0.0 [−2.6 to 2.7]; *p* = 1.00
Hours of actual sleep, h	7.2 ± 2.0	7.3 ± 1.2	0.1 [−0.8 to 0.9]; *p* = .906
Overall sleep quality (1 very good to 4 very bad)	1.5 ± 0.5	1.5 ± 0.5	0.0 [−0.3 to 0.3]; *p* = 1.00

CES-D 10, Center for Epidemiologic Studies Short Depression Scale; SSAS, Spielberger State Anxiety Scale.

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Measurement completion rate for this intervention was very good. This, coupled with the low participant ratings of testing burden indicates the feasibility of maximal testing in this survivor population. Our 12% loss to follow-up compares favourably with a mean attrition of 21% reported in a systematic review for resistance training interventions in patients with COPD [40]. The adherence rate to the exercise intervention was very high, and compares favourably to other cancer survivor groups [4,15,39,41]. This may have resulted from the flexibility to make up missed sessions.

Throughout the trial there were three adverse events but all participants were able to continue training, and at post-testing exhibited improvements in strength and function. This result emphasizes the need for multidisciplinary teams to adequately address underlying conditions that may require attention during exercise training for this population.

Study participants demonstrated poor functional capacity at baseline, with an average of only 63% age and sex predicted 6MWD. The deconditioned nature of these survivors is also highlighted by the poor baseline muscular strength of participants, particularly when adjusted for body weight (i.e., relative 1RM). When men and women were considered separately, the average relative 1RM for leg press ranked in <10th percentile for the 60+ age categories [42].

This relatively short-term PRET program resulted in significant improvements in muscular strength and endurance. Participants exhibited an impressive increase in muscular strength of 42% and 51% for upper and lower body muscular strength, respectively which compares favourably to PRET training results in other post-treatment cancer survivor populations [15,39]. Participants were also successful in improving strength of the chest wall muscles using a novel training approach in this population. Additionally, relative muscular endurance for the upper and lower body improved 150% and 180% respectively which should enable participants to complete more demanding physical tasks for longer periods of time. These changes in muscular strength were likely attributable to neuromuscular adaptations that occur in the early stages of resistance training (e.g. increased in motor unit recruitment and firing rate, decreased antagonist muscle activation).

The six-minute walk test has been examined as a prognostic measure in chronic disease and disability. An initial 6MWD of greater than 400 m has been identified as a potentially useful prognostic marker in advanced NSCLC [43]. The inability to walk 400 m has also been associated with a higher risk of cardiovascular disease, mobility limitations, and mortality [44]. We demonstrated a statistically and clinically meaningful improvement in 6MWD of 86 m which is likely important for preserving function and delaying onset of mobility limitations. Several additional measures of objective physical functioning improved significantly following the intervention, namely chair stands, up-and-go time, and arm curls. Resistance training in patients with COPD has also been shown to elicit significant improvements in these objective measures of physical functioning training [40]. Improvements in these measures of functional ability indicate that the training program could increase participant competence in performing everyday physical tasks.

Body composition measures did not significantly change in our study. This result corresponds to findings from other cancer populations following resistance training [15]. Changes in hormonal profile and muscle physiology, as well as increased inflammation associated with the aging process has been shown to attenuate hypertrophy response to resistance training [45–48]. In this study, age could have moderated the hypertrophy response to resistance training; however, our sample was too small to perform any subgroup analysis. Future research should consider employing a randomized controlled design to investigate a longer intervention with modifications to target body composition (i.e., diet intervention). Additionally, alternative measures, such as muscle biopsy could be useful for assessing other important changes such as muscle fiber type composition, or cross sectional area.

This study was underpowered to detect changes in patient-reported outcomes such as QoL. However, it remains important to pilot test these measures to assess their potential utility. Following the PRET intervention, there were no statistically significant changes in QoL. Previous research suggests that QoL changes following PRET are typically modest in cancer survivors and patients with COPD [40,49]. The underpowered sample size and lack of control group make interpretation of these results tenuous; however, there could be several explanations for the lack of response observed here. In a recent systematic review, Granger and Denehy found that exercise interventions for NSCLC patients in the post-treatment setting had mixed results regarding the impact of the intervention on QoL [50]. One reason proposed for the lack of response of QoL following an exercise intervention was a ceiling effect. Participants in this study had mean score of 27 on the lung cancer subscale score at baseline, which is above the cut point of 24 which indicates clinical symptoms [51,52]. This indicates that individuals taking part in this study had relatively high QoL at baseline, likely resulting from a bias of enrolling participants with good performance status. However, this limits the ability to detect improvements in these parameters [50,53]. Additionally, there is recent evidence that QoL and self-reported function decline over time for older overweight cancer survivors, and sedentary older women [54,55]. In the current study the physical health component score of the SF-36 improved by three points, which is considered a meaningful, although not statistically significant, difference [56]. Preservation or small improvements in QoL and other patient-rated outcomes could be important. Ultimately, future adequately powered research with appropriate comparison groups is required to better understand the QoL response to exercise in lung cancer survivors.

There are several important strengths and limitations to this study. Firstly, this is an understudied patient population and an intervention that has not, to date, been tested exclusively in this population. Secondly, we used a comprehensive set of valid and reliable measures to examine feasibility and preliminary efficacy in this population. Our main limitations were the small sample size and the uncontrolled trial design. Single-group trials are subject to biased interpretation of results, and can overestimates treatment effects [57]. Additional limitations include limited power to detect differences in all outcomes, 47 statistical tests that increase the probability of chance findings, a heterogeneous survivor population and a relatively short-term intervention with limited follow-up.

5. Conclusion

In conclusion, PRET appears to be a feasible intervention with potential for health benefits in a small portion of lung cancer survivors. Therefore, additional feasibility research is warranted to focus on improving eligibility rates by testing less intense or medically supervised exercise, or offering home-based programs to facilitate training for those unable to access supervised centres.

Conflict of interest statement

None declared.

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