Title

Effects of pre- and post-operative resistance exercise interventions on recovery of physical function in patients undergoing abdominal surgery for cancer: A systematic review of randomised controlled trials

Authors

Stephensen D[1], Hashem F[2], Corbett K[3], Bates A[2], George M[4], Hobbs N[4], Hopkins M[4], Hutchins I[4], Lowery D[2], Pellatt-Higgins T[2], Stavropoulou C[5], Swaine IL[6], Tomlinson L[4], Woodward H[4],and Ali H.[4]

Author Affiliations:

1. Physiotherapy Department, East Kent Hospitals University Foundation NHS Trust, Canterbury UK
2. Centre for Health Service Studies, University of Kent, Canterbury, UK.
3. Centre for Critical Research in Nursing & Midwifery, Middlesex University, London, UK
4. Research and Development, Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK.
5. School of Health Sciences, City University London, London UK
6. Centre for Science and Medicine in Sport and Exercise, University of Greenwich, Chatham, UK.

Key Words

Exercise training, cancer, abdomen, surgery, physical fitness

Word count 2610

Contact details for corresponding author

Dr David Stephensen

Physiotherapy Department

East Kent Hospitals University NHS Foundation Trust

Ethelbert Road

Canterbury, UK

CT1 3NG

david.stephensen@nhs.net

01227 866481

ABSTRACT

Objective

To systematically review the effects of pre- and post-operative resistance exercise training on the recovery of physical function in patients undergoing abdominal surgery for cancer

Data sources

A systematic review of English articles using Medline, PEDro, Cinahl and The Cochrane Library electronic databases was undertaken.

Eligibility criteria for selecting studies

Studies were included if they used a randomised, quasi-randomised, or controlled trial study design and compared the effects of a muscle-strengthening exercise intervention (+/- other therapy) with a comparative non-exercise group; involved adult participants (≥18 years) who had elected to undergo abdominal surgery for cancer; and used muscle strength, physical function, self-reported functional ability, range of motion and/or a performance-based test as an outcome measure.

Results

Following screening of titles and abstracts of the 588 publications retrieved from the initial search, 24 studies met the inclusion criteria and were accessed for review of the full-text version of the article and 2 eligible met the inclusion criteria and were included in the review. One exercise programme was undertaken pre-operatively and the other post-operatively, until discharge from hospital. There were no differences between groups in either study.

Conclusion

The only two studies designed to determine whether pre- or post-operative resistance muscle-strengthening exercise programmes improved or negatively affected physical function outcomes in patients undergoing abdominal surgery for cancer provide inconclusive

results. The exercise interventions of the included studies were performed for 5 and 8 session respectively.

INTRODUCTION

Background:

Abdominal and thoracic cancers cause affect about 12,000 people annually in the UK. Many of these patients will undergo surgery, after which there is a high risk of post-operative complications and significant decline in physical functional. A systematic review of exercise for people with cancer by Stevinson and colleagues found some evidence that those that exercised had better physical function compared to those who didn't exercise, but there was insufficient evidence to demonstrate improvement in quality of life[1]. In addition, they were not able to determine which type of exercise intervention was best or if any had long-term benefit. A more recent Cochrane review of exercise for people with cancer by Mishra and colleagues found that exercise initiated after completion of active cancer treatment (i.e. surgery, chemotherapy, radiation therapy, or hormone therapy) has a beneficial effect on health-related quality of life, although no parallel improvement in self-reported physical function was found[2]. The exercise interventions included in this review varied greatly and included strength training, yoga, walking, cycling, Tai Chi, and Qigong. However, due to the small number of studies available, these authors were not able to evaluate the effect of different modes and intensities of exercise. Furthermore, studies of exercise in the pre-operative and early post-operative stage were not included in the review. Therefore, it is not known whether exercise, when commenced before the end of active cancer treatment, would have additional benefit on physical function for those undergoing surgery.

Whilst there is growing evidence for the beneficial effects of aerobic exercise, resistance exercise training has received much less attention[3-6]. It is thought that resistance exercise training could act to aid recovery of muscle function[7]. It has long been established that resistance exercise training is effective in stimulating muscle anabolic processes and increasing muscle strength[8]. It may even counteract some of the metabolic pathophysiology associated with cachexia[9]. Furthermore, it can be performed with very little equipment and

space and whilst patients are bed-bound in hospital or at home. Although there have been previous systematic reviews of the effects of exercise training, there have not been any that have specifically focussed on resistance training.

Previous reviews, relating to exercise training for cancer patients, have mostly focused on specific outcomes such as fatigue and quality of life[4-5] and most have centred on specific types of cancer[10-17]. Galvão et al published a review of exercise intervention studies for all cancers and a meta-analyses of exercise training interventions[18]. However, their review included a heterogeneous group of studies including some that were not randomised or had no control group. Quality systematic reviews requires critical appraisal of the quality of the reviewed studies and share accurate descriptions of the design, delivery, and interpretation of what was done in the study. In some instances detailed description of these aspects are not available.

One of the main challenges in studying the effects of a resistance exercise programme on physical function in cancer surgery patients, is in identifying an appropriate outcome measure. The review by Mishra and colleagues found no significant improvement in physical function as evaluated using self-report questionnaires but they did not measure any index of physical performance[1]. Therefore, the aim of our systematic review study was to undertake a systematic review of the literature on interventional studies investigating the effects of pre- and post-operative resistance exercise training on recovery of physical function in patients undergoing abdominal surgery for cancer. The findings will provide clinicians and investigators a basis to choose exercise interventions for use in clinical practice, or for future research.

METHODS

The PRISMA guidelines on systematic reviews were followed for this review[19]. Figure 1 summarises the review process.

Search Strategy

The Cochrane library, EBSCO (SPORTDiscus and CINAHL), Plos, Pubmed (Medline) and Elsevier (Scopus) electronic database were searched up to and including December 2014. The search strategy used was exercise OR training OR isometric OR static OR isotonic OR concentric OR eccentric OR resistance OR strengthening exercise OR exercise therapy OR circuit training OR rehabilitation OR physiotherapy; AND neoplasm OR abdominal cancer OR stomach cancer OR gastric cancer OR bowel cancer OR pancreatic cancer OR colorectal cancer OR colon cancer OR rectal cancer OR gastrointestinal cancer OR ovarian cancer OR endometrial cancer OR cervical cancer OR renal cancer OR kidney cancer OR bladder cancer OR uterine cancer OR gynaecological cancer OR urological cancer; AND abdominal surgery OR laparotomy OR laparoscopy OR laparoscopic OR anterior resection OR colectomy OR hemicolectomy; AND clinical trial OR random controlled trial OR quasi-randomised controlled trial OR controlled trial OR comparative trial.

All titles and abstracts generated by the search were independently screened for inclusion by three authors (DS, FH and KC). Disagreement between authors was discussed and consensus reached. The search was restricted to English language and were included if the following criteria were met: (i) randomised, quasi-randomised, or controlled trial study design comparing a muscle-strengthening exercise intervention (i.e. exercise using resistance to induce muscular contraction) +/- other therapy with a comparative group; and (ii) included adult participants (≥18 years) who underwent abdominal surgery (i.e. surgery pertaining to the contents of the abdominal cavity, its walls and orifices) for cancer; and (iii) included muscle strength, physical function, self-reported functional ability, range of motion and/or performance-based test as an outcome measure.

Data extraction

Participants age, gender, diagnosis, surgical procedure and sample size were extracted from the included studies along with a description of the exercise intervention including; muscle group or groups exercised, contraction effort, number of repetitions and frequency, length of

programme, length of follow up, group or individual exercise programme, home or supervised exercise programme, timing of programme (pre- and /or post-surgery).

Data synthesis and analysis

The aim of this review was to evaluate the effect of resistance muscle strengthening on physical function in people undergoing abdominal surgery for cancer. For each study, means and standard deviations of outcomes focussed on physical function were extracted. Outcomes relating directly to surgery, length of stay, infection and other post-surgical complications were not considered in this review.

Assessment was made of the outcome measures for physical function that were used in different studies, before progression to pooling of data for analysis of the most common outcome measure. Treatment effect of individual studies is reported as mean difference and 95% confidence intervals, and the data summarised.

Risk of bias was assessed with the Physiotherapy Evidence Database (PEDrO) scale[20]. Items assessed included: exclusion criteria, procedures for group allocation and missing data, participant, therapist and assessor blinding, and reporting of results. Studies were then graded using the Cochrane Reviews GRADE criteria[21].

RESULTS

Search strategy and selection of articles

The initial search strategy resulted in 588 publications. Following screening of titles and abstracts, 24 studies met the inclusion criteria and were accessed for review of the full-text, of which, 2 eligible studies[22-23] where included in the review (see Table 1 and Figure 1). Full text studies were excluded for a number of reasons: (i) the study lacked a well-defined muscle-strengthening intervention (n=18); (ii) did not include patients undergoing abdominal

surgery for cancer (n=4); and (iii) did not use a physical function outcome measure (muscle strength, self-report questionnaires, or physical performance measures).

Description of included studies

Characteristics of the participants and intervention of the two included studies are presented in Table 1. Both were small (n = 42 and 31) single-centre studies investigating participants undergoing abdominal surgery for excision of cancer of the colon. Dronkers et al.[22] investigated the effect of a pre-operative exercise programme on pre-operative outcomes and Ahn et al.[23] investigated the effect of a post-operative exercise programme on short-term outcomes at discharge from hospital. The participants in the pre-operative study were aged 10-15 years older than those in the post-operative study. In terms of gender, a higher proportion of men participated in both studies.

The pre-operative intervention of Dronkers et al.[22] included a twice-weekly supervised exercise programme and a home-based programme of walking or cycling for a minimum of 30 minutes per day for 2-4 weeks before admission for surgery. In addition to a single set of resistance strengthening exercises of the leg (8-15 repetitions at 60-80% of the one repetition maximum), the programme included inspiratory muscle training, aerobic training at 55-75% max HR or perceived exertion of 11-13 Borg Scale for 20-30 minutes, and functional activities. A full description of the resistance exercise was not published. Three of the intervention group (13.6%) did not complete the study with their data analysed as intention to treat.

The post-operative intervention of Ahn et al.[23] comprised a twice-daily fifteen-minute supervised exercise programme performed by the participant until discharge from hospital (mean 8.87±2.28 days). In addition to resistance strengthening exercises of the chest, shoulder, arm, thigh, and calf leg, the programme included stretching exercises for the (neck, shoulder, wrist, ankle, and pelvis, core trunk exercises and ambulation. In terms of the strengthening exercises, resistance was applied manually by the therapist initially and then

utilising 1-lb free weights. During phase 2, one set of 10 repetitions was performed and in Phase 3, three sets of 12 repetitions were performed. Because these studies used different outcome measures, it was not possible to pool the data in order to analyse mean changes in physical function outcomes.

Risk of bias of included studies

The methodological quality of the two included studies was rated as moderate according to the GRADE criteria; i.e. randomised studies with unclear bias OR well-designed observational studies with large, consistent and precise estimates of the magnitude of an intervention effect. Difficulty in blinding trial participants and therapists to the intervention meant studies were not rated as high. Both studies scored eight out of eleven on the PEDro scale. Block randomisation using prepared envelopes; stratified for age (60-70 and > 70) by someone independent of the study was utilised in the pre-operative study. Randomisation, at a one-to-one ratio, into study groups via minimization to balance prognostic factors between groups (age and gender) was utilised in the post-operative study. In the pre-operative study the gender distribution was similar in the control and intervention groups; however, in the post-operative study, twice as many males were randomised to the exercise group than the control group despite the minimisation procedures to balance gender between groups. In relation to the description of the intervention, some information was lacking in terms of equipment and methodology with regards to the aerobic and functional activity components of the pre-operative intervention.

Effect of strengthening exercise

<u>Pre-operative muscle strengthening</u>

The mean difference and upper and lower 95% CI between the control and intervention group in the study by Dronkers et al.[22] are shown in Table 2. The 5-session pre-operative exercise programme had no significant effect on pre-operative Timed Up and Go (TUG), chair rise time test, self-reported physical activity, quality of life and fatigue. Statistical power

for six out of the seven measures was unacceptably low. Effect on post-surgery outcomes was not evaluated.

Post-operative muscle strengthening

The mean difference and upper and lower 95% CI between the control and intervention group in the study by Ahn et al.[23] is also shown in Table 2. The in-patient post-operative exercise programme had no significant effect at time of discharge from hospital on ability to balance on one leg, number of sit-to stands in 30 seconds or aerobic capacity (estimated from performance of the Tecumseh step test). Statistical power was not sufficient to allow any conclusion for or against the preferential use of any of the outcome measures that were used in this trial. Effect on functional recovery post-discharge from hospital was not evaluated.

DISCUSSION

Our aim was to systematically review the evidence on the effectiveness of pre- and post-operative strengthening exercise on short- and long-term recovery of physical function in patients undergoing abdominal surgery for cancer. Two studies were included, which represented 73 patients (48 males and 25 females) undergoing abdominal surgery for cancer. One exercise programme was undertaken pre-operatively and the other post-operatively until discharge from hospital. This represents insufficient evidence to determine whether this type of pre- or post-operative resistance muscle-strengthening exercise programme improves or negatively affects functional outcomes in patients undergoing abdominal surgery for cancer.

The study by Dronkers et al.[22] which investigated a pre-operative exercise programme was statistically underpowered with the exception of the functional measure derived from the quality of life scale. The programme included resistance strengthening of the lower limb muscle extensors and was performed for a mean of 5 sessions. This may not be sufficient to

provide an adequate training stimulus to significantly increase muscle strength. Indeed, guidelines published by the American College of Sports Medicine recommend resistance exercise 2-3 times per week with 2-4 sets of 10-15 repetitions to improve strength in middle-age and older persons[24].

In contrast, the study by Ahn et al.[23] investigated a post-operative exercise programme, but this was also statistically underpowered and provides inconclusive evidence in support of the intervention and the use of particular outcome measures. The intervention was different to that of Dronkers et al.[22] in that it used a progressive resistance programme involving the upper and lower limbs, together with stretching, functional balance strengthening and walking. Also, isometric strengthening exercises were commenced early post-operatively whilst the patient was still in bed and then progressed to 'resistance-through-range' strengthening as well as balance strengthening exercises, until discharge from hospital. Mean hospital length of stay, for the study of Dronkers et al.[22], was seven days for the control group and in the exercise group it was eight days. Similarly, for the study by Ahn et al.[23], it was eight days of exercise and it is likely that this will not provide an adequate training stimulus to significantly increase muscle strength and function.

There are some limitations to our review. We limited our inclusion by study design, only including randomised or quasi-randomised studies where there was a clear resistance muscle strengthening component as part of an exercise programme. It is possible that other studies have included muscle strengthening exercises or functional exercises that will have an effect on muscle strength that have not been included in this review due to our inclusion criteria. The two studies included in the review recruited almost twice as many males as females and the results may not reflect the general population. Future studies should focus on detailed descriptions of the exercise intervention, consistent outcome measures and longer intervention and follow-up times.

Our systematic review suggest that the use of resistance exercise interventions for recovery of physical function in patients undergoing abdominal surgery for cancer must be considered with caution. The small number of included underpowered studies and the inability to pool the results due to the heterogeneity of outcome measures means that there is a lack of evidence for or against the use of this type of resistance muscle-strengthening exercise programmes to improve functional outcomes in these patients. While the studies give encouraging preliminary evidence that muscle strengthening programmes may be feasible for abdominal cancer surgery patients, further large-scale well designed clinical trials are required to determine whether this type of exercise intervention is beneficial for this group of patients.

Acknowledgements

The study was funded by a NIHR Research for Patient Benefit grant; PB-PG-0613-31107.

DS, FH, KC performed the systematic review. DS, FH, KC, AB, MG, NH, MH, IH, DL, TPH, CS, IS, LT, WH and HA contributed to study design, data analysis and interpretation and preparation of the manuscript.

What is already known?

- Abdominal and thoracic cancers cause debilitating illness, and surgery is associated with significant decline in physical functional
- Exercise initiated after completion of active cancer treatment has a beneficial effect on health-related quality of life

What are the new findings?

- There is insufficient evidence that pre- or post-operative resistance muscle strengthening exercise improves or negatively effects functional outcomes for patients undergoing abdominal surgery for cancer
- Large scale well designed clinical trials are required to determine whether resistance muscle strengthening exercise is beneficial for patients undergoing abdominal surgery for cancer

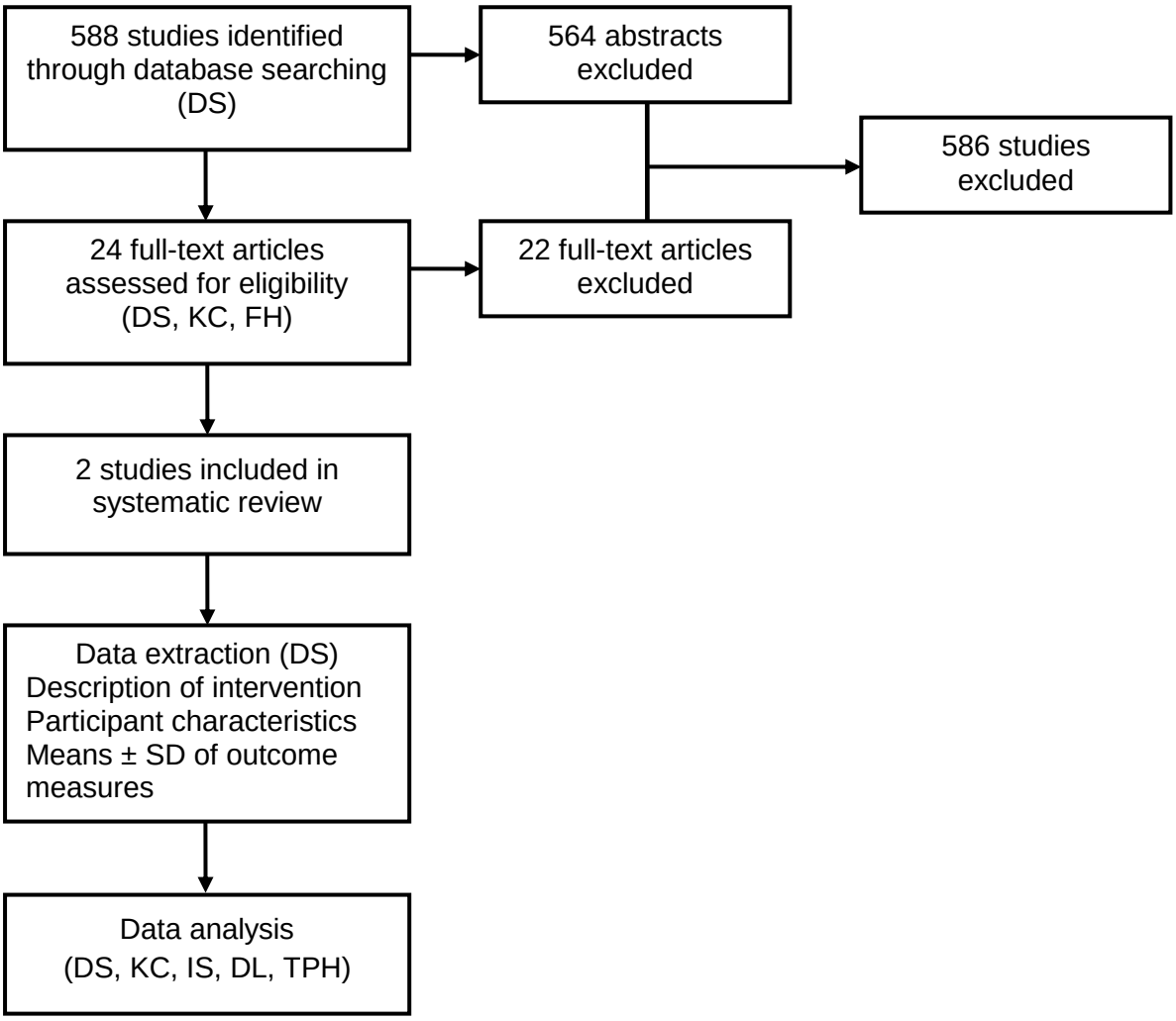

Figure 1. Flowchart for systematic review of studies

Table 1. Characteristics of included studies

	Methods	Participants	Intervention	Relevant outcomes	Risk of Bias
Dronkers et al., 2010	Randomised study investigating the pre-operative effect of an exercise programme in participants with colon cancer	Exercise group n=22 Age: 71.1 ± 6.3 Gender: 15M, 7F Control group n=20 Age: 68.8 ± 6.4 Gender: 16M, 4F	Supervised programme 2xweek for 2-4 weeks (mean 5.1±1.9) and home-based programme of walking or cycling for minimum of 30 minutes per day (perceived exertion of 11-13 Borg Scale) Programme - warm up - resistance training of the lower limb extensors – equipment and method not stated (maximum of 1 set of 8-15 repetitions at 60-80% of the one repetition maximum) - Inspiratory muscle training (10-60% max inspiratory pressure for 240 breathing cycles - Aerobic training – method and equipment not stated (55-75% max HR or perceived exertion of 11-13 Borg Scale for 20-30 min) - Functional activities according to patients capabilities and interests (Vreede et al., regime – no other information provided) -	Timed up and Go Chair Raise Time Physical Activity Questionnaire Abbreviated Fatigue Questionnaire EORTC QLQ-C30 Global Health/ Functional Scale/ Symptom Scale	PEDro Score 8/11 Grade Criteria - Moderate
Ahn et al., 2013	Randomised study investigating the effect of a postsurgical, inpatient exercise program in patients with stage I-III colon cancer.	Exercise group n=17 Age: 55.61 ± 7.11 Gender: 12M, 5F Control group n=14 Age: 57.43 ± 6.12 Gender: 5M, 9F	Supervised exercise programme 2xday, 15 min/session Subdivided into three phases: (1) implemented while subjects were still unable to get out of bed; Stretching (neck, shoulder, wrist, ankle, and pelvis), pelvic tilt – isometric; resistance exercise (ankle dorsi- and plantar flexion against the hand	Timed one-leg stand Sit to stand in 30 seconds Tecumseh step test	PEDro- Score 8/11 Grade Criteria - Moderate

			of the therapist), unsupervised sitting or walking in the ward (2) performed once subjects were able to get out of the bed, but had limited ambulation; Stretching (whole body, leg, and shoulder), pelvic tilt and thrust, one leg raise, crunch, resistance exercise (1 set, 10 repetitions) with 1-lb weight (chest, shoulder, arm, thigh, and calf), unsupervised walking (3) performed when subjects were able to ambulate without any discomfort; in addition to phase 2 exercises, resistance strengthening increased to 12 repetition×3 sets, supervised balance exercises – one leg standing, one leg calf raise, hip adduction, hip abduction, hip flexion with knee bent, hip extension, unsupervised walking		

Table 2.Summary of effect of exercise intervention

	Mean Between-group Difference	Lower 95% CI	Upper 95% CI	Statistical Power^
Dronkers et al., 2010 Pre-operative intervention				
TUG (sec)	-1.20	-2.78	0.38	31.2
Chair rise (sec)	-5.40	-9.24	-1.56	77.3
Physical activity (min/day)	44.00	-141.82	229.82	7.3
Abbreviated Fatigue Questionnaire	-3.90	-7.41	-0.39	57.6
EORTC QLQ-C30 (Global Health)	-4.00	-15.57	7.57	10.2
EORTC QLQ-C30 (Functional Scale)	12.00	-28.26	52.86	87.4
EORTC QLQ-C30 (Symptom Scale)	36.00	-31.09	103.09	17.7
Ahn et al., 2013 Post-operative intervention				
Timed one-leg stand (sec)	-7.28	-16.25	1.69	40.0
Sit to Stand (repetitions)	-2.00	-5.78	1.78	17.7
Tecumseh step test (Heart rate – beats/min)	10.29	1.63	18.95	64.8

^ Probability of rejecting a false null hypothesis (where $\alpha = 0.05$), for a between group comparison of means at study endpoint.

REFERENCES:

1. Stevinson C, Lawlor DA, Fox KR. (2004) Exercise interventions for cancer patients: systematic review of controlled trials. Cancer Causes and Control; 15 (10): 1035-1056.

2. Mishra SI, Scherer RW, Geigle PM, Berlanstein DR, Topaloglu O, Gotay CC, Snyder C. Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD007566. DOI: 10.1002/14651858.CD007566. pub2.

3. Pinto B. Exercise in the rehabilitation of breast cancer survivors. Psychology, 8: 191-206, 1999.

4. Courneya K. Exercise in cancer survivors: An overview of research. Medicine and science in sport and exercise, 35: 1846-1852, 2003.

5. Dimeo F. Effects of exercise on cancer related fatigue. Cancer, 15: 1689-1693, 2001.

6. Fairey A, Courneya K, Field CJ, et al. Physical exercise and immune system function in cancer survivors: A comprehensive review and future directions. Cancer 94: 539-551, 2002.

7. Komi PV, Viitasalo JT, Rauramaa R, Vihko V. Effect of isometric strength training on mechanical, electrical, and metabolic aspects of muscle function. European Journal of Applied Physiology and Occupational Physiology, 40: 45-55, 1978.

8. Cheema B, Gaul C A, Lane K, Singh M A F. Progressive resistance training in breast cancer: a systematic review of clinical trials. Breast Cancer Res Treatment, 109: 9–26, 2008.

9. Lenk K, Schuler G, Adams V. Skeletal muscle wasting in cachexia and sarcopenia: molecular pathophysiology and impact of exercise training. Journal of Cachexia, Sarcopenia and Muscle. 1: 9-21, 2010.

10. Schwartz A: Daily fatigue patterns and effect of exercise in women with breast cancer: Cancer Pract 8:16-24, 2000.

11. Schwartz A: Fatigue mediates the effects of exercise on quality of life. Qual Life Res 8:529-538, 1999.

12. Schwartz A, Mori M, Gao R, et al: Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. Med Sci Sports Exerc 33:718-723,

2001.

13. Courneya K, Keats M, Turner A: Physical exercise and quality of life in cancer patients following high dose chemotherapy and autologous bone marrow transplantation. Psychooncology 9:127-136, 2000

14. Dimeo F, Rumberger B, Keul J: Aerobic exercise as therapy for cancer fatigue. Med Sci Sports Exerc 30:475-478, 1998

15. Courneya K, Friedenreich C: Physical exercise and quality of life following cancer diagnosis: A literature review. Ann Behav Med 21:171-179,1999.

16. Courneya K: Exercise interventions during cancer treatment: Biopsychosocial outcomes. Exerc Sports Sci Rev 29:60-64, 2001

17. Friedenreich C, Courneya K: Exercise as rehabilitation for cancer patients. Clin J Sport Med 6:237-244, 1996.

18. Galvão D A, Newton R U. Review of Exercise Intervention Studies in Cancer Patients. Journal of Clinical Oncology 23, no. 4, 899-909, 2005.

19. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al., The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. British Medical Journal, 2009; 339:b2700.

20. Herbert R, Moseley A, Sherrington C. PEDro: a database of randomised controlled trials in physiotherapy. Health Information Management 1998;28(4):186-188.

21. Cochrane Handbook Chapter 11 (Presenting results and 'Summary of findings' tables): http://handbook.cochrane.org/chapter_11/11_presenting_results_and_summary_of_findings_tables.htm

22. Dronkers J J, Lamberts H, Reutelingsperger I M M D, Naber R H, Dronkers-Landman C M, Veldman A, van Meeteren N L U. Preoperative exercise program for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. Clinical Rehabilitation 24(7): 614-22, 2010.

23. Ahn K-Y, Hur H, Kim D-H, Min J, Jeong D H, Chu S H, Lee J W, Ligibel J A, Meyerhardt J A, Jones L W, Jeon J Y, Kim K. The effects of inpatient exercise therapy on the length of hospital stay in stages I–III colon cancer patients:

randomized controlled trial. International Journal of Colorectal Disease, 28: 643–651. 2013.

24. Garber CE, Blissmer B, Deschenes MR, et al. Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise. Medicine & Science in Sports & Exercise 2011; 43(7): 1334-1359.