Review Article

The Effect of Exercise in Surviving Patients with Breast Cancer: A Systematic Review

Andria Syka, RN, BSc, MSc in Health Management, PhD (c)
Frederick University, Nicosia, Cyprus
Nurse Melathron of EOKA Veterans, Recovery Section, Limassol, Cyprus

Corespondence: Andria Syka, Melathron of EOKA Veterans, Recovery Section, Mosxatou 1, Agios gewrgios xabouzas, lemesos, Cyprus e-mail: ssweeet@live.com

Abstract

Introduction: Physical activity has been recognized as an important intervention for improving the quality of life of women with breast cancer.
Objective: We sought to summarize the available evidence on the effects of exercise in surviving patients with breast cancer.
Material - Method: We searched articles on the topic in the databases Cochrane, MEDLINE, EMBASE, CINAHL, PsychINFO, CANCERLIT, Pedro and SportDiscus, as well as in conference proceedings, in clinical practice guidelines and other unpublished sources. In the study are included only randomized controlled trials evaluating a) exercise interventions for surviving patients with breast cancer and b) how exercise affects the quality of life, cardiorespiratory fitness or physical functioning.
Results: Out of the 136 studies identified, only 14 met all the inclusion criteria. Despite significant heterogeneity and relatively small samples of studies, the point estimates on the benefits of exercise for all outcomes were positive even when statistical significance was not reached. Exercise resulted in statistically significant improvement in the quality of life of survivors of breast cancer, was evaluated after the general - functional assessment cancer therapy (weighted mean difference [WMD] 4,58, 95% confidence interval [CI] 0,35 - 8.80) and the functional Assessment of treatment of breast cancer (WMD 6.62, 95% CI 01.21 - 12.03) as the exercise led to significant improvements in physical function and maximal oxygen consumption and reduce symptoms of fatigue.
Conclusions: Exercise is an effective intervention for improving quality of life; it helps cardiorespiratory endurance in physical function and fatigue survivors in patients with breast cancer. Among women living in Western countries, breast cancer is an important disease in terms of incidence and mortality.

Key words: exercise, quality of life, cardiorespiratory fitness, physical functioning

Introduction:

The improvement in technology and medicine over the last 20 years has led to a significant increase of the number of survivors of breast cancer, many of whom is expected to have a normal life expectancy. Increasingly, the cancer care directed toward to the development of interventions for improving the overall quality of life and longevity of cancer patients (Brown et al., 2003).

Exercise has repeatedly been recognized as a central element of recovery for many chronic diseases 5-8 and was successful in improving the quality of life (Farrell et al., 2002). Recent data from research studies show that moderate physical activity can reduce even the risk of death from breast cancer, and therefore exercise may prove to be a valuable intervention for improving not only the quality of life and overall survival (Holmes et al., 2005).

The effectiveness of exercise as an intervention in cancer patients and survivors has been evaluated in two quality systematic reviews and meta-analyzes including all types of cancer and all types of trial designs (non-randomized, uncontrolled studies) (Galvao et al., 2005).

It is known, however, that the groups cancer survivors is clinically heterogeneous regarding the demographic profile (e.g., age, gender distribution), behavioral profile (e.g., smoking, alcohol consumption, obesity),

pathophysiology of the disease, treatment protocols, symptoms and side effects. Accordingly, the summary of the effects of exercise interventions in all these disparate groups is questionable. It is clear from the foregoing comments that the vast majority of the research exercise interventions included patients with breast cancer who have survived. In addition, there are now newer studies, that there is sufficient research in this group surviving cancer. It is also well known that the inclusion of non-randomized or uncontrolled studies overstate the impact of an intervention. Recommended meta-analysis is limited to randomized controlled trials (RCTs), whenever possible (Altman et al., 2001).

The purpose of this systematic review is to summarize the available evidence on the effects of exercise in surviving patients with breast cancer.

Material - method

We searched the following electronic databases up to March 2011: Cochrane, MEDLINE, EMBASE, CANCERLIT, CINAHL, PsychINFO, Pedro and SportDiscus. We used the search terms related to breast cancer (eg, breast tumors, mastectomy, axillary dissection), exercise (eg, exercise, physical activity, sport) and the type of issue (eg ax., randomized clinical trial).

A modified search strategy was used for each database separately. Only articles in English were included. Identified and clinical practice guidelines for breast cancer, and investigated and websites were clinical trials and dissertations. The criteria for the inclusion of the studies (randomized controlled trials) comparing exercise with a placebo, or controlled or comparison with standard care.

For the purposes of the review exercise was defined as a form were as leisure physical activity performed on a repetitive basis over an extended period with the intention of improving physical fitness, or the performance or health (Bouchard et al., 1994). Studies with combined intervention (eg, exercise and diet modification) were included only if the effects of exercise could isolate. Studies involving other cancers other than breast cancer were excluded. Were included such studies only if it was available for the subset of breast cancer distinct elements.

Exercise regimens addressing only specific lesions associated with shoulder, arm, or both were not included. In trials included only if enrolled women with early - late stage breast cancer (Stage O - III) or who had undergone surgery for breast cancer with or without adjuvant treatment of cancer. The studies should be included as a primary outcome was quality of life of exercise, the benefits of exercise on cardiovascular function and physical function. Secondary landmarks for the study included the symptoms of fatigue and some features for the composition of the body e.g. body weight or body mass index. While it took and for events arising from intervention through exercise.

The methodological quality of each RCT was assessed using the following criteria:

1 method of randomisation well described and it was appropriate?

2 describes the evaluation of the outcome?

3 evaluate the results described properly?

There were 4 withdrawals less than 10%;

5. compliance intervention through exercise if it was greater than 70% (for participation or completion of the exercise session)?

All items were scored as positive (+) or negative (-) or unclear. The studies were defined as "high quality" if they met four or more of the quality criteria. The results of the study were collected during the event. All results were calculated with 95% confidence intervals (Brown et al., 2003).

Results

Identified 140 articles, of which 25 were considered potentially relevant. A review of these 25 articles led to the inclusion of 14 studies involving 717 participants. The study methodology Articles differed significantly, particularly as regards the timing of the exercise intervention. The chosen exercise regimen and the results are reported in Table 1. The mean score for the methodological quality of all included studies was 3, with a range of 0-8 (Courneya et al., 2003).

Three studies involving 194 patients were compared with the performance and with the usual care. (Campbell et al., 2005; Courneya et al., 2003; Segal et al., 2001). The exercise was superior to usual care on both the scale of the Functional Assessment of Cancer Therapy-General (FACT-G) and the scale of the Functional Assessment of Cancer Breast (FACT-B) quality of life. Pooled data from three studies showed that exercise led to significant improvements in quality

of life, using both the FACT-G (WMD 4,58, 95% CI 0,35 - 8.8) and the FACT-B (WMD 6.62, 95% CI 1.21 - 12.3) scale.

The Cardiorespiratory effect of the exercise was reported to result in 9 studies from 14 studies and included 473 patients (Campbell et al., 2005; Courneya et al., 2003 Drouin 2002; MacVicar et al., 1989; Mustian 2003; Nieman et al., 1995; Pinto et al., 2005; Segal et al., 2001).

Because significant heterogeneity among the nine studies, the data are not combined and referred only to a specific outcome measure (Table 2). Three of the studies reported in the 18-20 peak oxygen consumption in mL / kg per minute of symptomatic patients through graded exercise test successfully (Courneya et al., 2003; Crowley 2003; Drouin 2002). The pooled results of the three studies showed significant improvement in peak oxygen consumption with exercise (WMD 3.39, 95% CI 1,67 - 5,10).

Four studies attended body weight, and other four studies 18,20,34,35 reported in BMI as a result. Pooled results from four observational studies showed a weight not statistically significant weight reduction (WMD -0.03 kg, 95% CI -0,44 - 0,38). The individual results of the study, and the consolidated results for the BMI also showed statistically significant reductions in favor of exercise (WMD -0.02, 95% CI -0,09 - 0,05) (Table 2) (Courneya et al., 2003; Drouin 2002; Schmitz et al., 2005; Segal et al., 2001).

Four studies included 208 patients who reported physical function or physical well-being components of quality of life (Campbell et al., 2001; Courneya et al., 2003; McKenzie et al., 2003; Segal et al., 2001). Two studies used the physical well-being of the subscale FACT for quality of life (Campbell et al., 2001; Courneya et al., 2003 , and in the other two trials used (Galantino et al., 2003; Segal et al., 2001). The range of the physical operation of Short Form Survey (Ware et al., 1993). The pooled results of four studies showed statistically significant increase in physical functioning and well-being of the exercise (SMD 0,84, 95% CI 0,36 - 1,32) (Table 2).

Six studies included 319 patients who evaluated the effect of exercise on symptoms of fatigue (Battagliani 2004; Campbell et al., 2005; Courneya et al., 2003; Drouin 2002; Mock et al., 2005; Pinto et al., 2005). In a study of was measured by using the fatigue subscale of the functional assessment cancer therapy - fatigue (FACT-F) (Courneya et al., 2003), while four studies (Battagliani 2004; Campbell et al., 2005; Drouin 2002; Mock et al., 2005) used the revised Piper Fatigue Scale While one study used a visual analog scale for fatigue (Pinto et al., 2005).

Although all studies showed improvement in symptoms of fatigue with exercise, only two studies (Courneya et al., 2003; Pinto et al., 2005) reported statistically significant improvements. These two studies were the only studies conducted after cancer treatment. Pooled results from all studies showed that exercise significantly improved symptoms of fatigue (SMD 0.46, 95% CI 0,23 - 0,70) (Courneya et al., 2003; Pinto et al., 2005).

Pooled results from studies operating performance during adjuvant cancer treatment showed a statistically significant effect on fatigue (SMD 0.28, 95% CI -0,02 - 0,57) (Battagliani 2004; Campbell et al., 2005; Drouin 2002; Mock et al., 2005).

The adverse effects of exercise programs reported in four studies. (Courneya et al., 2003; Crowley 2003; Drouin 2002; Schwartz et al., 2006). There were reports of injury (n = 4) and tendonitis in the shoulder (n = 1) associated with participation in resistance exercise intervention during the first six months (Schwartz et al., 2006). While back injuries (n = 4), wrist (n = 1), the lower leg and ankle (n = 5) and the rotator cuff (n = 1) in relation to the exercise were also reported in 7-12 months with the implementation of exercise. In another study, shoulder tendinitis (n = 1) and worsening of fatigue (n = 2) were reported as adverse outcomes associated with the study of the implementation of the exercise. The lymphedema occur in participants practiced the exercise in two studies (Courneya et al., 2003; Crowley 2003).

Table 1: Characteristics of randomized controlled trials examining the effectiveness of exercise for breast cancer

Study	Features	Participants	Intervention	Key Endpoints	Comments
Battagliani 2004. (US)	Supervised exercise during adjuvant radiotherapy or chemotherapy	20 women, mean age 57 (SD 20)	Mixed aerobic and resistance exercise. 2 x / week for 15 weeks in 40% -60% of the predicted exercise capacity. percentage of 1RM not mentioned. 60 minutes per session	• lean body mass • VO2peak • UE and LE strength: 1RM • Fatigue	Insufficient data for lean body mass, the VO2 peak and measures resistance.
Campbell et al, 2005 (UK)	Supervised exercise during adjuvant radiotherapy or chemotherapy	19 women, mean age 47.5 (SD 8)	Mixed aerobic and resistance exercise. 2 x / week for 12 weeks 60% -75% maximum HR. 10-20 minutes per session	• quality of life • Test 12-minute walk	Adhesion exercise involving 70%
Courneya et al, 2003 (Canada)	Supervised exercise after treatment for 1 year	52 postmenopausal women, mean age 59 (SD 6)	Aerobic exercise (upright or lying on a cycle ergometer). 3 x / week for 15 weeks in 70% -75% VO2 max progressive increase 15-35 minutes per session	• quality of life • maximum VO2 • Weight • Body composition (BMI, SSF)	Participation in the exercise of 98%:
Crowley, 2003 (US)	Exercise at Home-based exercise during a given adjuvant chemotherapy with adriamycin and cyclophosphamide therapy	22 women, aged 35-60 years	Mixed aerobic exercise (walking) and resistance (tubing). 3-5 x / week for 13 weeks at 60% of maximal HR,	• quality of life • VO2peak • UE and LE • Strength: 1 RM	Can not use certain relevant parameters because the data is presented in graphical form.

			exercise duration per session unclear		
Drouin,20 2002 (US)	Exercise at Home-based exercise during adjuvant therapy with radiation	23 women, mean age 50 (SD 8,2)	Aerobic (self-monitored walking program with monitorigk pulse). 3-5 x / week for 7 weeks at 50% -70% of the maximal HR for 20-45 minutes per session	• quality of life • maximum VO2 • Weight • Body composition (BMI, SSF)	Not complied with if the performance of the whole population
MacVicar et al, 1989 (US)	Supervised exercise during adjuvant chemotherapy or hormonal therapy, or both	45 women, mean age 45 (SD 9,9)	Aerobic exercise (interval training on a stationary cycle ergometer). 3 x / week for 10 weeks in 60% -85% of the workforce, the duration increased progressively.	• VO2 peak	Not complied with if the performance of the whole population
McKenzie et al, 2003 (Canada)	Supervised exercise after treatment	14 women with unilateral arm lymphedema, mean age 56 (SD 9)	Aerobic exercise and resistance exercise .3 x / week for 8 weeks with a progressive increase in intensity 8-25 watts (aerobic) and 2-3 sets 10 reps (resistance). 5-20 min (aerobic)	• quality of life • UE (volume and circumference) • All individuals included in the analysis	Not complied with if the performance of the whole population
Mock et al,	Headquartered	119 women	Aerobic	quality of life	12-minute

2005 (US)	exercise at home. The exercise was performed during the adjuvant or radiotherapy or chemotherapy	with sedentary, middle-age 52 (SD 9) yr	exercise (walking) 5-6 x / week for 6 weeks (radiation treatment group) or 3-6 mo (chemotherapy group). 50% - 70% maximum HR and RPE. gradual increase from 15 to 30 minutes	• Test 12-minute walk	walk. and testing for physical function not reported . Snap: exercise Completed 72%
Mustian, 2003 (US)	Supervised exercise after treatment within 3 years from diagnosis	27 women, mean age 52 (SD 9) yr	Tai Chi Chuan. 60 minutes 3 x / wk for 12 weeks	• 6-minute walk on foot • Muscular fitness (dynamometer and handle) • Body composition (bioelectrical resistance)	Adhesion to the exercise involved 72%
Nieman et al, 1995 (US)	Supervised exercise therapy after diagnosis	16 women, range 35-72 years	Mixed aerobic (walking) and resistance (weights) training (2 sets of 12 repetitions for 7 exercises). 3 x / week for 8 weeks at 75% intensity. Not for resistance. Duration of activity: 60 minutes (30 minutes of aerobic, resistance 30 minutes)	• 6-minute walk on foot • LE strength	Adhesion participated in exercise 87%
Pinto et al, 2005 (US)	Home-based exercise after treatment in 5 year of diagnosis	86 women with sedentary age 53,1 (SD 10)	The aerobic exercise. 2 x / wk for progressive exercise. 5 x / week	• Test 1 mile walk • BMI • Percentage of body fat (SSF) • Fatigue	Compliance unclear

			over 12 weeks in 55% -65% With maximum HR. 30 minutes per session		
Schmitz et al,35 2005 (US)	Supervised exercise (13 weeks) after treatment	85 women, mean age 53.0 (SD 8,2)	Exercise Resistance 2 x / week for 26 weeks LE on 8 RM and UE starting from the lightest weight proceed systematically one set for 3 sets of 8-10 reps	UE and LE strength • Weight • BMI • DEXA: Lean body mass and fat	Missing data for measures of resistance. Exercise participation 92%:
Schwartz et al, 2006 (US)	Home-based exercise during adjuvant chemotherapy Three groups: aerobic, strength and control exercise	66 women, mean age 48,2 (SD 10,5)	1) Aerobic (walking or jogging): 4 days / week for 6 months limited symptoms; moderate intensity for 15-30 minutes 2) Resistance exercise: 4 days / week for 6 mo progressive resistance using bands and tubing. 2 sets of 8-10 reps of 4 UE and 4 LE exercises	• Test 12-minute walk • UE and LE strength • Bone density (spine)	Compliance unclear
Segal et al, 2001 (Canada)	The supervision and self-directed exercise groups in subsidiary treatment (chemotherapy, radiotherapy or hormone therapy) Three groups:	123 women, mean age 50.9 (SD 8,7)	1) Supervised aerobic exercise: 3 x / wk and 2 x / week self-directed in 50% -60% with the expected	• quality of life • Estimated VO2peak (submaximal test) • Weight	Compliance with the exercise reached 72%

	supervised, self-directed and control		progressive increase in% of VO2peak. duration not stated 2) of self-directed aerobic exercise: 5 x / wk at 50% -60% with the expected progressive increase in% of VO2peak. during exercise is not stated.		

Note: SD = standard deviation, HR = heart rate, QoL = quality of life, VO2peak = peak oxygen consumption, measured using an incremental exercise test (aerobic fitness),
BMI = body mass index, SSF = sum of skin folds, UE = upper extremity, LE = lower extremity, RM = repetition maximum for muscular strength, DEXA = dual–energy x–ray
absorptiometry, RPE = rating of perceived exertion.

Table 2: Effects of exercise on cardiorespiratory fitness, body composition and physical functioning

Outcome	No. of studies	N	Weighted mean difference (95% CI)	p value	Standardized mean difference (effect size) (95% CI)	p value
Cardiorespiratory fitness						
VO2peak absolute, L/min	2	95	0.30 (0.2 to 0.41)	0.00001	Not estimated	----------
VO2peak relative, mL/kg per min	3	95	3.39 (1.67 to 5.1)	0.0001	1.14 (0.47 to 1.81)	0.0009
Predicted VO2, mL/kg per min	2	150	0.99 (–0.21 to 2.18)	0,07	Not estimated	----------
6-min walk test, m	2	39	35 (12.6 to 58.1)	0.002	Not estimated	----------
12-min walk test, m	1	19	101 (62.5 to 140.4)	0.00001	Not estimated	----------
1-mile walk test, min	1	89	–1.31 (–0.42 to –0.20)	0.004	Not estimated	----------
Body composition						
Weight, kg	4	277	–0.03 (–	0.88	–0.07 (–0.36	0.61

			0.44 to 0.38)		to 0.21)	
Body mass index, kg/m2	4	240	–0.02 (–0.09 to 0.05)	0.58	–0.12 (–0.38 to 0.13)	0.35
Percent body fat	1	81	–1.38 (–1.57 to –1.19)	0.03	Not estimated	----------
Lean body mass, kg	1	81	0.86 (0.76 to 0.96)	0.008	Not estimated	----------
Bone density, %	1	66	3.79 (2.55 to 4.17)	0,02	Not estimated	----------
Physical functioning	4	208	Not estimated	--------	0.84 (0.36 to 1.32)	0.0006

Conclusions

This review summarizes the best available evidence on the effects of exercise on quality of life and physical effects for surviving patients with breast cancer. Only three studies provided sufficient data to evaluate the quality of life. The pooled estimate showed a statistically significant increase of more than 4.0 points in the FACT scale represents a clinically significant improvement in quality of life by exercising (Cella et al., 2002).

Furthermore, analyzes of physical functioning and physical well-being through subscale of quality of life showed large improvements (effect size = 0.84) of exercise. Given that cardiovascular endurance is an important predictor of mortality for these women, is likely that improved cardiorespiratory endurance will have similar impact on women. However, the duration of these studies was insufficient to produce stable evidence (Farrell et al., 2002).

Pooled results from six studies examining the effect of exercise on symptoms of fatigue showed a moderate to large effect (effect size = 0.72). However, statistically significant improvements in symptoms of fatigue were reported in only two studies (Courneya et al., 2003; Pinto et al., 2005). Both studies looked at the performance after initial cancer treatment (Courneya et al., 2003; Pinto et al., 2005). During the adjuvant treatment of cancer, found that no effect of fatigue on exercise. The data show that exercise has a statistically significant and possibly a small effect on the symptoms of fatigue in women undergoing adjuvant treatment of cancer. Despite the statistical differences in the four studies, all point estimates were in favor of the exercise, suggesting the need for more research before you reject this result. As an example, Schmitz and colleagues examined the body composition by means of dual absorptiometry x-ray and reported positive changes in lean body mass, as well as significant reductions in body fat percentage in favor of the exercise intervention (Table 2) (Schmitz et al., 2005). As well, the Schwartz and colleagues evaluated the bone mineral density of the lumbar spine using dual absorptiometry x-ray and said that people who participate in aerobic exercise had significantly lower BMD loss than the control group (Table 2) (Schwartz et al., 2006). This means that there may be positive changes in body composition rather than changes in body weight and body mass index. A remarkable feature of the tests included in this review was great variability in the interventions of the study. Many different exercise regimens were recorded. Furthermore, there is no evidence to support the use of exercise in preventing cancer recurrence. A further limitation is the non-specificity with respect to the timing of action (exercise). Clinical heterogeneity was evident, particularly in trials conducted during adjuvant treatment of cancer. This resulted from trials in which participants were subjected to a treatment of a variety of immune - supportive therapies (eg, chemotherapy, radiotherapy and hormone therapy). Finally, small samples of the population does not provide sufficient power to detect significant differences in rates of rare adverse events. For example, lymphedema is a possible side effect of cancer therapy and is a barrier to exercise for some patients, yet none of the studies included official controls this side effect.

Evidence suggests that exercise is an effective intervention for improving the quality of life in cardiorespiratory fitness, physical function in surviving

patients with breast cancer. Although these preliminary findings are promising, the results are based on a relatively small number of tests at substantially methodological weaknesses.

Furthermore, there is currently no evidence to support the use of exercise regimens to reduce body weight or body mass index. Based on our findings, we make the following research recommendations:

1. Methodologically rigorous studies designed to examine different exercise regimens (eg, moderate vs. low intensity) required to better understand the role of physical activity among patients with breast cancer.

2. Type of exercise should be reported (frequency, intensity, time and type of exercise) to allow for the determination of dose-response exercise. For this purpose, the respect of the exercise should be reported both to complete the exercises (participation) and the type of exercise (intensity and duration).

References

American Cancer Society. Cancer facts and figures (2004). Available:www.cancer.org/docroot/STT/stt_0_2004.asp?sitearea=STT&level=1 (accessed 2013 May 8).

Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gøtzsche PC, Lang T. (2001)The Revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 134:663-94.

Atlantis E, Chow CM, Kirby A, Singh MF. (2004). An effective exercise-based intervention for improving mental health and quality of life measures: a randomized controlled trial. *Prev Med* 39:424-34.

Battagliani CLL. (1994) A randomized study on the effects of a prescribed exercise intervention on lean mass and fatigue changes in breast cancer patients during treatment.Greeley, *CO: University of Northern Colorado* p. 214.

Bouchard C, Shephard RJ. (1994) Physical activity, fitness, and health: The model and key concepts. *In*: Bouchard CS, Shephard RJ, Stephens T, editors. Physical activity, fitness, and health: international proceedings and consensus statement. Champaign, IL: Human Kinetics;. p. 77-88.

Brown JK, Byers T, Doyle C, Brown JK, Byers T, Doyle C, Coumeya KS, Demark-Wahnefried W, Kushi LH, McTieman A, Rock CL, Aziz N, Bloch AS, Eldridge B, Hamilton K, Katzin C, Koonce A, Main J, Mobley C, Morra ME, Pierce MS, Sawyer KA. American Cancer Society. (2003) Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. *CA Cancer J Clin* 53:268-91.

Campbell A, Mutrie N, White F, McGuire F, Kearney N. (2005) A pilot study of a supervised group exercise program as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. *Eur J Oncol Nurs* 9:56-63.

Canadian Cancer Society. Canadian Cancer Statistics 2004. Available: www.cancer.ca/ccs/internet/mediareleaselist/0,,3172_210504871_194634551_langId-en,00.html (accessed 2013 May 8).

Cella D, Eton DT, Lai JS. (2002) Combining anchor and distribution based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales. *J Pain Symptom Manage* 24:547-61.

Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. (2003) Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. *J Clin Oncol* 21:1660-8.

Crowley SA. (2003) The effect of a structured exercise program on fatigue, strength, endurance, physical self-efficacy, and functional wellness in women with early stage breast cancer. Ann Arbor, MI: University of Michigan p. 127.

Drouin J. (2002) Aerobic exercise training effects on physical function, fatigue and mood, immune status, and oxidative stress in subjects undergoing radiation treatment for breast cancer. *Detroit: Wayne State University*. p. 1-142.

Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. (2003) Effects of exercise training on fasting insulin, insulin resistance, insulin-like growth factors, and insulin-like growth factor binding proteins in postmenopausal breast cancer survivors: a randomized controlled trial. *Cancer Epidemiol Biomarkers Prev* 12:721-7.

Farrell SW, Braun L, Barlow CE, Cheng YJ, Blair SN. (2002) The relation of body mass index, cardiorespiratory fitness, and all-cause mortality in women. *Obes Res* 10:417-23.

Holmes MD, Chen WY, Feskanich D, et al. (2005) Physical activity and survival after breast cancer diagnosis. *JAMA* 293:2479-86.

Galantino ML, Capito L, Kane RJ, et al. (2003) Effects of Tai Chi and walking on fatigue and body mass index in women living with breast cancer: a pilot study. *Rehabil Oncol* 21:17-22.

Galvao DA, Newton RU. (2005) Review of exercise intervention studies in cancer patients.*J Clin Oncol* 23:899-909.

Jassem J, Buchanan M, Janicke F, Baum M, Cataliotti L, Kyriakides S, Piccart M, Rutgers EJ, Costa A. (2004) The Hamburg statement: the partnership driving the European agenda on breast cancer. *Eur J Cancer* 40:1810-1.

Kalda AL. (1999) The effect of upper body exercise on secondary lymphedema following breast cancer

treatment. Vancouver: Faculty of Education, School of Human Kinetics, University of British Columbia p. 50.

Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G. (2005) Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled trials. *J Clin Oncol* 23:3830-41.

MacVicar MG, Winningham ML. (1986) Promoting the functional capacity of cancer patients. *Cancer Bull* 38:235-9.

MacVicar MG, Winningham ML, Nickel JL. (1989) Effects of aerobic interval training on cancer patients' functional capacity. *Nurs Res* 38:348-51.

McKenzie DC, Kalda AL. (2003) Effect of upper extremity exercise on secondary lymphedema in breast cancer patients: a pilot study. *J Clin Oncol* 21:463-6.

Mock V, Burke MB, Sheehan P, Creaton EM, Winningham ML, McKenney-Tedder S, Schwager LP, Liebman M. (1994) A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncol Nurs Forum* 21:899-907.

Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, Quitasol W, Mitchell S, Chakravarthy A, Gage I. (1997) Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncol Nurs Forum* 24:991-1000.

Mock V, Pickett M, Ropka ME, Muscari Lin E, Stewart KJ, Rhodes VA, McDaniel R, Grimm PM, Krumm S, McCorkle R. (2001) Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Pract* 9:119-27.

Mock V, Frangakis C, Davidson NE, Ropka ME, Pickett M, Poniatowski B, Stewart KJ, Cameron L, Zawacki K, Podewils LJ, Cohen G, McCorkle R. (2005) Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. *Psychooncology* 14(6):464-77.

Mustian K. (2003) Breast cancer, Tai Chi Chuan, and self-esteem. Greensboro, NC: University of North Carolina; p. 217.

Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. (2002) Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 346:793-801.

Nieman DC, Cook VD, Henson DA, Suttles J, Rejeski WJ, Ribisl PM, Fagoaga OR, Nehlsen-Cannarella SL. (1995) Moderate exercise training and natural killer cell cytotoxic activity in breast cancer patients. *Int J Sports Med* 16:334-7.

Nixon S, O'Brien K, Glazier RH, Tynan AM. (2002) Aerobic exercise interventions for adults living with HIV/AIDS. *In*: The Cochrane Library; Issue 2 Oxford: Update Software.

Pickett M, Mock V, Ropka ME, Cameron L, Coleman M, Podewils L. (2002) Adherence to moderate-intensity exercise during breast cancer therapy. *Cancer Pract* 10:284-92.

Pinto BM, Frierson GM, Rabin C, Trunzo JJ, Marcus BH. (2005) Home-based physical activity intervention for breast cancer patients. *J Clin Oncol* 23:3577-87.

Schulz KH, Gold SM, Witte J, Bartsch K, Lang UE, Hellweg R, Reer R, Braumann KM, Heesen C.(2004) Impact of aerobic training on immune-endocrine parameters, neurotrophic factors, quality of life and coordinative function in multiple sclerosis. *J Neurol Sci* 225:11-8.

Schmitz KH, Ahmed RL, Hannan PJ, Yee D. (2005) Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin and insulin-like growth factor axis proteins. *Cancer Epidemiol Biomarkers Prev* 14:1672-80.

Schwartz AL, Winters K, Gallucci B. (2006) A randomized trial to examine effects of exercise on bone mineral density in premenopausal and postmenopausal women receiving chemotherapy for breast cancer. Unpublished manuscript.

Segal R, Evans W, Johnson D, Smith J, Colletta S, Gayton J, Woodard S, Wells G, Reid R. (2001) Structured exercise improves physical functioning in women with stages I and II breast cancer: results of a randomized controlled trial. *J Clin Oncol* 19:657-65.

Segar ML, Katch VL, Roth RS, Garcia AW, Portner TI, Glickman SG, Haslanger S, Wilkins EG. (1998) The effect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. *Oncol Nurs Forum* 25:107-13.

Stevinson C, Lawlor DA, Fox KR. (2004) Exercise interventions for cancer patients: systematic review of controlled trials. *Cancer Causes Control* 15:1035-56.

Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. (2004) Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 116:682-92.

Ware JE, Snow KK, Kosinski MK, Grandek, B (1993) SF-36 Health Survey manual and interpretation guide. *Boston: Nimrod Press*.

Winningham ML, MacVicar MG. (1988) The effect of aerobic exercise on patient reports of nausea. *Oncol Nurs Forum* 15:447-50.

Winningham ML, MacVicar MG, Bondoc M, Anderson JI, Minton JP. (1989) Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. *Oncol Nurs Forum* 16:683-9.