**Name of journal:** *World Journal of Clinical Oncology*

**ESPS Manuscript NO:** 8340

**Columns:** TOPIC HIGHLIGHT

WJCO 5th Anniversary Special Issues (2): Breast cancer

**Exercise in patients coping with breast cancer: An overview**

Eyigor S *et al*. Exercise in patients with breast cancer

Sibel Eyigor, Selcen Kanyılmaz

**Sibel Eyigor,**Department of Physical Medicine and Rehabilitation, Ege University, Medical Faculty, Izmir 35100, Turkey

**Selcen Kanyılmaz,** Physical Medicine and Rehabilitation Clinic, Okmeydani Training and Research Hospital, Istanbul 34382, Turkey

**Author contributions:** Eyigor S designed the concept of the review; Kanyilmaz S performed literature search; Eyigor S and Kanyilmaz S drafted and revised the article accordingly.

**Correspondence to: Sibel Eyigor, MD, Associate Professor,** Department of Physical Medicine and Rehabilitation, Ege University, Medical Faculty, Bornova, Izmir 35100, Turkey. eyigor@hotmail.com

**Telephone:** +90-232-3903687 **Fax:** +90-232-3881953

**Received:** December 24, 2013 **Revised:** March 12, 2014

**Accepted:** May 28, 2014

**Published online:**

**Abstract**

Breast cancer is the most common type of cancer in women and fortunately has high survival rates. Many studies have been performed to investigate the effects of exercise in patients diagnosed with breast cancer. There is evidence that exercise after the diagnosis of breast cancer improves mortality, morbidity, health related quality of life, fatigue, physical functioning, muscle strength, and emotional wellbeing. Based on scientific data, breast cancer patients should be recommended to participate in rehabilitation programs including aerobic and strength training. The aim of this article is to review the recently published data on the effect of exercise in patients with breast cancer in order to hereby present the current perspective.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

**Keywords:** Breast cancer; Exercise; Rehabilitation; Physical activity; Cancer

**Core tip:** Exercise is not merely safe and feasible for breast cancer patients, but moreover a complementary treatment for one to achieve physiological and psychological improvements. Drawing clinicians’ attention to this issue is important for improving patients’ quality of life. We advise a multidisciplinary approach to encourage breast cancer patients into engaging in rehabilitation programs combining both strengthening and aerobic exercises for maximum profit.

Eyigor S, Kanyılmaz S. Exercise in patients coping with breast cancer: An overview. *World J Clin Oncol* 2014; In press

**INTRODUCTION**

Breast cancer is the most frequent cancer in females and it is estimated that there are more than 2.8 million breast cancer survivors in the United States[1,2]. For many years, breast cancer has been like a nightmare for women and health care providers with its high mortality and morbidity rates[3]. However due to recent advances in diagnosis and treatment of breast cancer, survival rates have increased[3]. Overall, 5-year survival rate for breast cancer in all stages has been reported as 89% by the American Cancer Society[2]. This successful rate of survival brings many problems either from the disease itself or relating to the treatment in patients living with the disease.

Due to the high prevalence of breast cancer especially in developed countries, the increased rates of survival as well as the high expectations in the quality of life for women with breast cancer ultimately led patients and health care providers to seek for alternative or additional approaches in the management of cancer[4]. All of these factors create a bigger interest in physical activity among cancer patients as time passes. Thus, there has been many researches on the effect of exercise on breast cancer patients and survivors within the medical community in last decades[5].

This might be evaluated in some items according to the disease stage, which may all be considered as different major topics of interest. Among those, preventive effects of exercise for breast cancer and effectiveness of exercise in breast cancer patients are the most covered areas in the research topics. Preventive effect of exercise for breast cancer, has been shown in epidemiological studies[6,7]. Risk reduction with physical activity for breast cancer in females is estimated to be up to 25%-30%[1,6]. To achieve such an effect, women are recommended to follow a 150-min per week of moderate to vigorous intensity of sports or physical activity[4].

Fortunately in many cases, cancer patients are no more considered as isolated people in many aspects of life. Traditional approach of clinicians advising rest and avoid physical activity to breast cancer patients and survivors have changed in time and both patients and the medical community are seeking for ideal level, type and intensity of physical activity[8]. This brings us to the other aspect researched: the effect of exercise in breast cancer patients.

Although, the additional effect of exercise in breast cancer has been investigated in numerous studies throughout the last decades, due to wide variety of patients’ status in terms of disease stage, associating co-morbid conditions and physical function etc, there have been no clear consensus or a standard approach yet[5,8]. Also recently systematic reviews and meta-analysis were published on the effect of exercise interventions[5,9,10]. Considering all these accumulated huge amount of literature on the subject, we sought the need to overview the effects of exercise specifically for breast cancer and discuss the need for research for future trials. Therefore, the aim of this article is to review the recently published data on the effect of exercise in patients with breast cancer in order to hereby present the current perspective.

**POSSIBLE MECHANISMS OF EXERCISE**

A variety of robust studies clearly showed beneficial effects of exercise in a healthy population with a wide spectrum varying from positive changes of physiological to psychological effects[11]. Hence, it is a matter of question how these positive effects of exercise impact breast cancer patients.

The effect of treatment of cancer on immune functions and the positive effects of good immune function on survival and morbidity in cancer patients have been linked[12]. Scientific data has suggested cancer and its treatment are related with the disruption of immune functions[12,13]. Pro-inflammatory cytokines are found in higher levels in the advanced stage, metastatic and recurrent disease compared with the non-metastatic, non-recurrent and the early stage disease[14]. Although researchers have investigated the relation between inflammatory markers and exercise in cancer patients, there is no significant data showing effects of exercise on the immune system markers in cancer patients[13,15]. Recently, a few studies have showed some positive results in cytokine and insulin levels with Tai Chi exercises in breast cancer patients[16,17].

Angiogenesis and apoptosis are related with the progression and metastasis of the tumor with vascular endothelial growth factor being the most studied angiogenic molecule[18]. Ergun *et al*[19] have showed the positive effects on levels of angiogenic molecules with supervised and home exercises in breast cancer patients compared to the education-only-group. Most of these studies investigating the relationship between immune functions and exercise in breast cancer patients have limitations such as their small sample size and this should be investigated in future randomized clinical trials (RCT) with large populations.

Being overweight and obese are clearly associated with an increased risk of developing many cancer types, including breast cancer in postmenopausal women[4,20]. The mechanism underlying obesity and breast cancer is considered to be immune function and inflammation, levels of estrogen and IGF-1[21,22]. And yet there are studies exploring the effects of reducing breast cancer risk with intentional weight loss[23,24]. The American Cancer Association recommends a healthy diet and advices against gaining weight due to its negative effects on the treatment success and recurrence[25]. The established ways for losing weight is either to reduce dietary intake or to increase physical activity. Besides obtaining a healthy diet, regular exercise in breast cancer patients will be helpful to maintain their ideal weight.

Hahm *et al*[26] showed that the disruption of the circadian rhythm such as night shift work might have an association with the progression of breast cancer. Exercise also acts as a regulator on the circadian rhythm and sleep; so hypothetically regular exercise might indirectly have an effect on preventing the progression of breast cancer. However, this theory needs be proven with clinical studies in breast cancer patients.

One descriptive study showed that the prevalence of fibromyalgia might be high in hospitalized breast cancer patients[27]. Fibromyalgia symptoms additional to the typical cancer symptoms, for instance fatigue, might influence the patients’ quality of life inversely. Thus it should be taken into account to consider fibromyalgia in prescribing exercises to the patients diagnosed with breast cancer.

**EFFECTS OF EXERCISE IN BREAST CANCER**

There is a growing interest among patients to search for alternative options to achieve a better life quality among cancer patients. If the effect of practicing exercise in breast cancer patients on mortality as well as morbidity were well understood, that would create an important clinical impact in the future.

Prospective-observational studies have demonstrated that physical activity after cancer diagnosis is associated with a reduced risk of cancer recurrence and improved overall mortality among multiple cancer survivor groups, including breast, colorectal, prostate and ovarian cancer[25,28-30]. Several studies in breast cancer survivors have demonstrated that being physically active compared to sedentary living after the diagnosis of breast cancer leads to a 24%–67% reduction in the risk of total deaths and 50%–53% reduction in the risk of breast cancer deaths[31-33]. Also some studies show that physical activity is inversely related with co-morbidities in patients diagnosed with breast cancer[34].

Fatigue is an important symptom, occurring frequently in breast cancer patients with a negative impact on the quality of life[35]. Studies have reported prevalence of fatigue in cancer patients up to 96%[36]. A Cochrane review published in 2006 has concluded that aerobic and resistive exercises in breast cancer patients on adjuvant therapy have significant positive effects on cardiorespiratory fitness and non-significant effects on fatigue and weight gain[37]. A meta analysis published by McNeely *et al*[5] has also showed the significant positive effect of exercise on symptoms of fatigue in breast cancer patients AZ. An updated report from Cochrane review in 2012 has shown a benefit on fatigue for breast cancer patients during or adjuvant chemotherapy from aerobic exercise[35].

Literature suggests that exercise in breast cancer survivors or in patients receiving therapy improves cardiorespiratory fitness, physical function and muscular strength[5,37-39]. However, there is a need for long-term studies for a better interpretation of these results.

Studies show that exercise and physical activity improve depression, anxiety in breast cancer patients receiving adjuvant therapy[38-40]. Carayol *et al*[40] suggested that, relatively low doses consisting 90–120 min of weekly moderate physical exercise seems efficacious in patients receiving adjuvant therapy for such improvements according to their meta-analysis.

A meta-analysis performed for trials on the effect of exercise in breast cancer patients showed a significant pooled effect of exercise on patients’ quality of life[5]. Confirming this data, recent Cochrane reviews evaluating the effects of exercise on health related quality of life in cancer patients and cancer survivors in randomized and controlled trials have suggested that cancer patients may benefit from exercise in some domains including physical functioning, role function, social functioning, and fatigue[38,39].

**INDICATIONS AND CONTRAINDICATIONS**

Indications for the exercise treatment in this patient population include to regain or improve physical functions, aerobic capacity, strength, flexibility, body image, body composition, quality of life, the ability to withstand physically and psychologically to any current and future cancer treatments and to withstand the anxiety with the current or recurrent disease[41]. Indications also include the reduction of long-term and late effects of cancer treatment, and the potential delay in any recurrence or progress of the disease[41].

Contraindications for exercise prescription in breast cancer patients include but are not limited to: acute post-operative period (up to 8 wk), acute arm and shoulder problems for upper body exercises, patients with extreme fatigue, anemia or ataxia and general cardiovascular and respiratory contraindications for an exercise regimen[41].

Traditionally, upper extremity exercises were avoided in breast cancer patients with lymph node dissection and radiotherapy. However, some recent studies have shown that upper body exercises do not have a negative impact on lymphedema[42].

**EXERCISE TYPE AND CONTENT**

There is no standard approach to recipe an exercise regimen for a breast cancer patient. This is mainly due to the wide spectrum of patients in terms of age, stage of the disease, co-morbid situations and physical function etc. Considering this variety, it doesn’t seem possible to ever have a standard approach for each single patient. Besides, prior functional status and exercise habits of each patient should always be taken into account when an exercise program is being prescribed.

There are various studies among the effects of different types of exercises on breast cancer patients. Types of exercises studied in breast cancer patients range from regular aerobic exercise to exercises such as Tai Chi[16,17,42]. The most frequent ones that are studied in these patient populations are aerobic exercises (group, home, walking, cycling, *i.e.*,), resistive exercises and special types of exercises like Pilates, Tai Chi and Yoga[17,42-44]. Exercise regimens can be prescribed as either group exercises instructed by a trainer or self practiced home exercises.

Resistance exercises in breast cancer patients are gaining more attention by their ability to decrease muscle waste and fatigue[45]. Combined Aerobic and Resistance Exercises (CARE) Trial, have investigated standard dose aerobic (25-30 min per session of 3 d per week), high dose aerobic (50-60 min per session of 3 d per week) or combined aerobic and resistive exercise (standard aerobic in addition to standard resistance training; 3 d per week, 2 set of 10-12 repetitions) schemes in breast cancer patients. Results have shown that higher intensity and resistance exercises are safe in this population and high and combined resistive-aerobic exercise regimen are superior to standard aerobic regimen in terms of certain domains such as muscle strength, endocrine symptoms and quality of life aspects like bodily pain[45].

Pilates[43] exercises improve physical strength, flexibility and postural control and it is well accepted by women as a fitness activity in developed countries. In a randomized trial it has been showed in a RCT that Pilates exercises have significant effects in females with breast cancer on functional capacity, fatigue, flexibility and quality of life compared to the control group.

Tai Chi exercises are respected as exercises of mindfulness, and are known to improve physical and psychological wellbeing. Some studies demonstrated that Tai-Chi exercises for 10-12 wk improved fatigue, body composition, QoL, muscular functions, memory and cognitive functions in breast cancer survivors[16,17].

Yoga is also another type of meditative physical activity including breathing, posture, flexibility and core strength exercises that can be used in these patients. Sudarshan *et al*[46] published in 2013 a study in breast cancer patients that weekly Yoga therapy improved physical function.

According to the data pooled from cancer studies, the American Cancer Society recommends cancer survivors to engage in regular physical activity avoiding inactivity and for them to exercise for at least 150 min per week including strength-training for at least 2 d per week and to obtain a healthy weight[25].

Kirkham *et al*[47] have compared different methods used for intensity arrangement for a precise prescription of an aerobic exercise regimen. The American College of Sports Medicine’s metabolic equation for treadmill walking and heart rate reserve are found to be the most accurate methods for exercise intensity prescription in breast cancer patients and survivors[47].

Joyful exercises like Pilates, Tai Chi, Yoga, Nordic walking and dance may be chosen according to the expectation and motivation of the patient by carefully adjusting intensity to the individual.

**ADVERSE EVENTS**

In most of the clinical trials that evaluate different types of exercises, adverse events are not even reported[38,39].In the clinical studies that have reported safety associated with exercise, most of them reported no adverse events at all or very rare and usually non-serious adverse events. Exercise related adverse events were mainly dizziness, dyspnea, musculoskeletal injuries or lymphedema, which were similar to the control group in numbers[38-39].In general, no differences what so ever were observed regarding recurrence, progression of the disease or the increased mortality in exercise versus control groups. Although limited, studies show that appropriate exercise regimens in breast cancer patients are quite safe to implement. However, the adverse events of exercise regimens in this patient group should be studied and reported more seriously in future trials.

**LIMITATIONS AND RECOMMENDATIONS**

Although many studies have investigated the effects of exercise in breast cancer patients, there is still a need for randomized controlled trials for the clarification of the type as well as the duration and intensity for standardization of the program.

Most of the trials are conducted in small groups and for short-term periods. Therefore, the results of these trials are difficult to implement in long-term periods and for big populations. On the other hand, it is an advantage that most cancer trials on the impact of exercise are researched in breast cancer survivors, even though very few of these are powered randomized controlled trials with enough sample sizes[9,10].

Also, considering the heterogeneity of breast cancer patients, individualized programs according to the stage of the disease, treatment status, and co-morbid situations should be tailored and addressed in future research questions. Along with RCTs, long-term real life data from registries and databases on the outcome of exercises in female breast cancer patients might help in directing these questions.

Additionally, compounding factors that would have an effect on exercise and its outcome such as the patients’ previous exercise habits, co-morbid situations (*i.e.*, lymphedema) as well as the patients’ functional status need to be evaluated.

Lack of knowledge on the effects of exercise and physical activity among the medical community and fear to recipe an exercise regimen with regards to the seriousness of the disease is a social burden that results in an unnecessary avoidance from physical activity in patients diagnosed with breast cancer. So, in order for this substantial issue to be settled, the mindset of physicians should be changed, which will happen in time as the evidence based data accumulates.

Raising awareness and information in this area for the patient, caregiver and healthcare providers would have a great impact in approaching these patients’ exercise need. This emphasizes the importance of the multidisciplinary approach to overcome the barriers in this area and help the patients to get the best outcome from the treatment. Little to no data is available on the cost-effectiveness of exercise treatment for breast cancer patients, which in long term needs to be evaluated.

Despite the crucial need for physical activity and exercise in this patient population, patients’ demand for physical treatment varied from 2%-81%[3,48]. Patient awareness about physical activity after diagnosis can be a vital factor in determining this variation.

**CONCLUSION**

As a result, exercise is not merely safe and feasible for breast cancer patients, but moreover a complementary treatment for one to achieve physiological and psychological improvements. There is increasing evidence that regular exercise after the diagnosis of breast cancer might have a substantial impact in mortality, morbidity, prognosis and quality of life. We advise a multidisciplinary approach to encourage breast cancer survivors into engaging in rehabilitation programs combining both strengthening and aerobic exercises for maximum profit.

**REFERENCES**

1 http://www.who.int/cancer/detection/breastcancer/en/index1.html

2 http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-key-statistics

3 **Jemal A**, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* ; **60**: 277-300 [PMID: 20610543 DOI: 10.3322/caac.20073]

4 **Kushi LH**, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, Gapstur S, Patel AV, Andrews K, Gansler T. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 2012; **62**: 30-67 [PMID: 22237782 DOI: 10.3322/caac.20140]

5 **McNeely ML**, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *CMAJ* 2006; **175**: 34-41 [PMID: 16818906 DOI: [10.1503/cmaj.051073](http://dx.doi.org/10.1503/cmaj.051073)]

6 **Friedenreich CM**, Cust AE. Physical activity and breast cancer risk: impact of timing, type and dose of activity and population subgroup effects. *Br J Sports Med* 2008; **42**: 636-647 [PMID: 18487249 DOI: 10.1136/bjsm.2006.029132]

7 **Eliassen AH**, Hankinson SE, Rosner B, Holmes MD, Willett WC. Physical activity and risk of breast cancer among postmenopausal women. *Arch Intern Med* 2010; **170**: 1758-1764 [PMID: 20975025 DOI: 10.1001/archinternmed.2010.363]

8 **Volaklis KA**, Halle M, Tokmakidis SP. Exercise in the prevention and rehabilitation of breast cancer. *Wien Klin Wochenschr* 2013; **125**: 297-301 [PMID: 23653151 DOI: 10.1007/s00508-013-0365-8]

9 **Speck RM**, Courneya KS, Mâsse LC, Duval S, Schmitz KH. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *J Cancer Surviv* 2010; **4**: 87-100 [PMID: 20052559 DOI: 10.1007/s11764-009-0110-5]

10 **Jones LW**, Pituskin E, Battaglini CL. Exercise Training in Oncology: Systematic Review and Clinical Practice Recommendations. *ACSMS HEALTH FIT J* 2012; **5**(1), 47-63

11 Physical Activity Guidelines for Americans. D. U. D. o. Washington and H. a. H. Services. 2008

12 **Kay NE**, Leong TL, Bone N, Vesole DH, Greipp PR, Van Ness B, Oken MM, Kyle RA. Blood levels of immune cells predict survival in myeloma patients: results of an Eastern Cooperative Oncology Group phase 3 trial for newly diagnosed multiple myeloma patients. *Blood* 2001; **98**: 23-28 [PMID: 11418458 DOI: [10.1182/blood.V98.1.23](http://dx.doi.org/10.1182/blood.V98.1.23)]

13 **Fairey AS**, Courneya KS, Field CJ, Bell GJ, Jones LW, Mackey JR. Randomized controlled trial of exercise and blood immune function in postmenopausal breast cancer survivors. *J Appl Physiol (1985)* 2005; **98**: 1534-1540 [PMID: 15772062 DOI: [10.1152/japplphysiol.00566.2004](http://dx.doi.org/10.1152/japplphysiol.00566.2004)]

14 **Benoy I**, Salgado R, Colpaert C, Weytjens R, Vermeulen PB, Dirix LY. Serum interleukin 6, plasma VEGF, serum VEGF, and VEGF platelet load in breast cancer patients. *Clin Breast Cancer* 2002; **2**: 311-315 [PMID: 11899364 DOI: [10.3816/CBC.2002.n.008](http://dx.doi.org/10.3816/CBC.2002.n.008)]

15 **Gómez AM**, Martínez C, Fiuza-Luces C, Herrero F, Pérez M, Madero L, Ruiz JR, Lucia A, Ramírez M. Exercise training and cytokines in breast cancer survivors. *Int J Sports Med* 2011; **32**: 461-467 [PMID: 21380980 DOI: [10.1055/s-0031-1271697](http://dx.doi.org/10.1055/s-0031-1271697)]

16 **Sprod LK**, Janelsins MC, Palesh OG, Carroll JK, Heckler CE, Peppone LJ, Mohile SG, Morrow GR, Mustian KM. Health-related quality of life and biomarkers in breast cancer survivors participating in tai chi chuan. *J Cancer Surviv* 2012; **6**: 146-154 [PMID: 22160628 DOI: 10.1007/s11764-011-0205-7]

17 **Janelsins MC**, Davis PG, Wideman L, Katula JA, Sprod LK, Peppone LJ, Palesh OG, Heckler CE, Williams JP, Morrow GR, Mustian KM. Effects of Tai Chi Chuan on insulin and cytokine levels in a randomized controlled pilot study on breast cancer survivors. *Clin Breast Cancer* 2011; **11**: 161-170 [PMID: 21665136 DOI: 10.1016/j.clbc.2011.03.013]

18 **Jain L**, Vargo CA, Danesi R, Sissung TM, Price DK, Venzon D, Venitz J, Figg WD. The role of vascular endothelial growth factor SNPs as predictive and prognostic markers for major solid tumors. *Mol Cancer Ther* 2009; **8**: 2496-2508 [PMID: 19755511 DOI: 10.1158/1535-7163.MCT-09-0302]

19 **Ergun M**, Eyigor S, Karaca B, Kisim A, Uslu R. Effects of exercise on angiogenesis and apoptosis-related molecules, quality of life, fatigue and depression in breast cancer patients. *Eur J Cancer Care (Engl)* 2013; **22**: 626-637 [PMID: 23731173 DOI: 10.1111/ecc.12068]

20 **Norat T**, Chan D, Lau R, Vieira R. The Associations Between Food, Nutrition and Physical Activity and the Risk of Breast Cancer. WCRF/AICR Systematic Literature Review Continuous Update Project Report. London: World Cancer Research Fund/American Institute for Cancer Research; 2008

21 **Coffer PJ**. When less is more: the PI3K pathway as a determinant of tumor response to dietary restriction. *Cell Res* 2009; **19**: 797-799 [PMID: 19581877 DOI: 10.1038/cr.2009.81]

22 **Slattery ML**, Fitzpatrick FA. Convergence of hormones, inflammation, and energy-related factors: a novel pathway of cancer etiology. *Cancer Prev Res (Phila)* 2009; **2**: 922-930 [PMID: 19892662 DOI: 10.1158/1940-6207.CAPR-08-0191]

23 **Eng SM**, Gammon MD, Terry MB, Kushi LH, Teitelbaum SL, Britton JA, Neugut AI. Body size changes in relation to postmenopausal breast cancer among women on Long Island, New York. *Am J Epidemiol* 2005; **162**: 229-237 [PMID: 15987723 DOI: [10.1093/aje/kwi195](http://dx.doi.org/10.1093/aje/kwi195)]

24 **Harvie M**, Howell A, Vierkant RA, Kumar N, Cerhan JR, Kelemen LE, Folsom AR, Sellers TA. Association of gain and loss of weight before and after menopause with risk of postmenopausal breast cancer in the Iowa women's health study. *Cancer Epidemiol Biomarkers Prev* 2005; **14**: 656-661 [PMID: 15767346 DOI: [10.1158/1055-9965.EPI-04-0001](http://dx.doi.org/10.1158/1055-9965.EPI-04-0001)]

25 **Rock CL**, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, Bandera EV, Hamilton KK, Grant B, McCullough M, Byers T, Gansler T. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin* 2012; **62**: 243-274 [PMID: 22539238 DOI: 10.3322/caac.21142]

26 **Hahm BJ**, Jo B, Dhabhar FS, Palesh O, Aldridge-Gerry A, Bajestan SN, Neri E, Nouriani B, Spiegel D, Zeitzer JM. Bedtime misalignment and progression of breast cancer. *Chronobiol Int* 2014; **31**: 214-221 [PMID: 24156520]

27 **Eyigor S**, Karapolat H, Korkmaz OK, Eyigor C, Durmaz B, Uslu R, Uyar M. The frequency of fibromyalgia syndrome and quality of life in hospitalized cancer patients. *Eur J Cancer Care (Engl)* 2009; **18**: 195-201 [PMID: 19267737 DOI: 10.1111/j.1365-2354.2008.00997.x]

28 **Kenfield SA**, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. *J Clin Oncol* 2011; **29**: 726-732 [PMID: 21205749 DOI: 10.1200/JCO.2010.31.5226]

29 **Moorman PG**, Jones LW, Akushevich L, Schildkraut JM. Recreational physical activity and ovarian cancer risk and survival. *Ann Epidemiol* 2011; **21**: 178-187 [PMID: 21296269 DOI: 10.1016/j.annepidem.2010.10.014]

30 **Meyerhardt JA**, Ma J, Courneya KS. Energetics in colorectal and prostate cancer. *J Clin Oncol* 2010; **28**: 4066-4073 [PMID: 20644082 DOI: 10.1200/JCO.2009.26.8797]

31 **Irwin ML**, Smith AW, McTiernan A, Ballard-Barbash R, Cronin K, Gilliland FD, Baumgartner RN, Baumgartner KB, Bernstein L. Influence of pre- and postdiagnosis physical activity on mortality in breast cancer survivors: the health, eating, activity, and lifestyle study. *J Clin Oncol* 2008; **26**: 3958-3964 [PMID: 18711185 DOI: [10.1200/JCO.2007.15.9822](http://dx.doi.org/10.1200/JCO.2007.15.9822)]

32 **Holmes MD**, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. *JAMA* 2005; **293**: 2479-2486 [PMID: 15914748 DOI: [10.1001/jama.293.20.2479](http://dx.doi.org/10.1001/jama.293.20.2479)]

33 **Peel JB**, Sui X, Adams SA, Hébert JR, Hardin JW, Blair SN. A prospective study of cardiorespiratory fitness and breast cancer mortality. *Med Sci Sports Exerc* 2009; **41**: 742-748 [PMID: 19276861 DOI: 10.1249/MSS.0b013e31818edac7]

34 **Elme A**, Utriainen M, Kellokumpu-Lehtinen P, Palva T, Luoto R, Nikander R, Huovinen R, Kautiainen H, Järvenpää S, Penttinen HM, Vehmanen L, Jääskeläinen AS, Ruohola J, Blomqvist C, Saarto T. Obesity and physical inactivity are related to impaired physical health of breast cancer survivors. *Anticancer Res* 2013; **33**: 1595-1602 [PMID: 23564803]

35 **Cramp F**, Byron-Daniel J. Exercise for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev* 2012; **11**: CD006145 [PMID: 23152233 DOI: 10.1002/14651858.CD006145.pub3]

36 **Stasi R**, Abriani L, Beccaglia P, Terzoli E, Amadori S. Cancer-related fatigue: evolving concepts in evaluation and treatment. *Cancer* 2003; **98**: 1786-1801 [PMID: 14584059 DOI: [10.1002/cncr.11742](http://dx.doi.org/10.1002/cncr.11742)]

37 **Markes M**, Brockow T, Resch KL. Exercise for women receiving adjuvant therapy for breast cancer. *Cochrane Database Syst Rev* 2006; : CD005001 [PMID: 17054230 DOI: 10.1002/14651858]

38 **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 Syst Rev* 2012; **8**: CD007566 [PMID: 22895961 DOI: 10.1002/14651858.CD007566.pub2]

39 **Mishra SI**, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev* 2012; **8**: CD008465 [PMID: 22895974 DOI: 10.1002/14651858.CD008465.pub2]

40 **Carayol M**, Bernard P, Boiché J, Riou F, Mercier B, Cousson-Gélie F, Romain AJ, Delpierre C, Ninot G. Psychological effect of exercise in women with breast cancer receiving adjuvant therapy: what is the optimal dose needed? *Ann Oncol* 2013; **24**: 291-300 [PMID: 23041586 DOI: 10.1093/annonc/mds342]

41 **Schmitz KH**, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 2010; **42**: 1409-1426 [PMID: 20559064 DOI: 10.1249/MSS.0b013e3181e0c112]

42 **Schmitz KH**, Ahmed RL, Troxel AB, Cheville A, Lewis-Grant L, Smith R, Bryan CJ, Williams-Smith CT, Chittams J. Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial. *JAMA* 2010; **304**: 2699-2705 [PMID: 21148134 DOI: 10.1001/jama.2010.1837]

43 **Eyigor S**, Karapolat H, Yesil H, Uslu R, Durmaz B. Effects of pilates exercises on functional capacity, flexibility, fatigue, depression and quality of life in female breast cancer patients: a randomized controlled study. *Eur J Phys Rehabil Med* 2010; **46**: 481-487 [PMID: 21224783]

44 **De Backer IC**, Schep G, Backx FJ, Vreugdenhil G, Kuipers H. Resistance training in cancer survivors: a systematic review. *Int J Sports Med* 2009; **30**: 703-712 [PMID: 19585401 DOI: 10.1055/s-0029-1225330]

45 **Courneya KS**, McKenzie DC, Mackey JR, Gelmon K, Friedenreich CM, Yasui Y, Reid RD, Cook D, Jespersen D, Proulx C, Dolan LB, Forbes CC, Wooding E, Trinh L, Segal RJ. Effects of exercise dose and type during breast cancer chemotherapy: multicenter randomized trial. *J Natl Cancer Inst* 2013; **105**: 1821-1832 [PMID: 24151326 DOI: 10.1093/jnci/djt297]

46 **Sudarshan M**, Petrucci A, Dumitra S, Duplisea J, Wexler S, Meterissian S. Yoga therapy for breast cancer patients: a prospective cohort study. *Complement Ther Clin Pract* 2013; **19**: 227-229 [PMID: 24199978 DOI: 10.1016/j.ctcp.2013.06.004]

47 **Kirkham AA**, Campbell KL, McKenzie DC. Comparison of aerobic exercise intensity prescription methods in breast cancer. *Med Sci Sports Exerc* 2013; **45**: 1443-1450 [PMID: 23439424 DOI: 10.1249/MSS.0b013e3182895195]

48 **Kärki A**, Simonen R, Mälkiä E, Selfe J. Postoperative education concerning the use of the upper limb, and exercise and treatment of the upper limb: cross-sectional survey of 105 breast cancer patients. *Support Care Cancer* 2004; **12**: 347-354 [PMID: 15064932 DOI: [10.1007/s00520-004-0612-7](http://dx.doi.org/10.1007/s00520-004-0612-7)]

**P-Reviewers:** ArsenijevicN, Hojan K, Harrington SN,Lacomba MT, **S-Editor:** Ji FF **L-Editor: E-Editor:**