Effects of Exercise Training on Physical Fitness and Biomarker Levels in Breast Cancer Survivors

Tae Ho Kim†, Jae Seung Chang†, In Deok Kong*
Department of Physiology, Yonsei University Wonju College of Medicine, Yonsei Institute of Sports Science & Exercise Medicine, Wonju, Korea

Background: Exercise has been identified as a beneficial intervention to enhance quality of life in breast cancer survivors. In addition, there has been a noteworthy increase in studies emphasizing the benefits of exercise in cancer. We sought to summarize the empirical literature concerning the effects of exercise on physical fitness and biomarker levels in breast cancer survivors according to the type of exercise.

Methods: We searched PubMed and PubMed Central for studies on the association of exercise with the levels of various biomarkers and physical fitness in breast cancer survivors. We investigated the effects of different types of exercise (aerobic, resistance, or combined) on breast cancer survivors, with changes in physical fitness and biomarker levels as the primary outcomes.

Results: In total, 118 research papers published from 2012 to July 2016 were retrieved from PubMed and PubMed Central. Of these, 24 papers met our inclusion criteria. All types of exercise were found to improve physical fitness in breast cancer survivors. However, the results with regard to biomarkers were controversial.

Conclusion: The findings of this review suggest that combined exercise is associated with better outcomes than aerobic or resistance exercise alone in breast cancer survivors.

Key Words: Breast cancer survivors, Types of exercise, Physical fitness, Biomarkers

INTRODUCTION

Worldwide, breast cancer is the most common type of cancer in women and the second leading cause of cancer death among women. In 2015, about 246,000 cases of breast cancer were diagnosed in the United States of America [1]. In Korea, approximately 141,300 women were diagnosed with invasive or non-invasive breast cancer in 2013. However, due to the improvement and development of new treatments and drugs, 90% of cancer patients now survive at least five years after diagnosis [2]. Breast cancer treatments include chemotherapy, surgery, radiation therapy, hormone therapy, and anticancer drugs [3]. It is highly probable that various therapies have positively influenced breast cancer patients and survivors. However, the most remarkable aspect is that the rates of breast cancer incidence and mortality have decreased. For this reason, the physical fitness of breast cancer survivors is an important concern [4].

Exercise and physical activity are vital to reduce risk factors and improve physical fitness, psychological controls, and quality of life in breast cancer survivors [5,6]. Several
studies have reported the benefits of exercise for breast cancer survivors. Also, exercise promotes social interaction during and after treatment and can significantly enhance the ability of cancer patients and survivors to cope with fatigue, lymphedema, and bone metastasis [7]. However, the most important point is that, after diagnosis, most breast cancer patients and survivors reduce their rate of participation in physical activity by 11% [8].

Many studies have described the effects of exercise training on the levels of biomarkers, including various adipokines. Some studies have suggested that tai chi exercise induces changes in inflammatory cytokine levels [9]. However, there have been controversial results regarding the effects of exercise on leptin and adiponectin levels. Some studies have demonstrated that serum and plasma leptin levels decreased while adiponectin levels increased after weight loss accompanied by exercise. On the other hand, other studies have indicated that plasma adiponectin level did not change in a 6-month combined exercise intervention program [10,11]. However, research on the effects of different types of exercise on physical fitness and various biomarkers in breast cancer is still in an early stage.

The purpose of the present review was to outline current research trends on the benefits of combined exercise (CE), aerobic exercise (AE), and resistance exercise (RE) on physical fitness and biomarker levels in breast cancer survivors. In this review, we focused on the demonstrated health benefits of physical fitness and various biomarkers and the informed benefits of risk management for breast cancer survivors according to the type of exercise.

MATERIALS AND METHODS

We searched the electronic databases of PubMed and PubMed Central from 2012 to July 2016. Our search was limited to human studies in the English language. We only retained experimental research studies in which participants had been diagnosed with stage I-IIIC breast cancer and were free of metastatic disease and other cancers after surgery and anticancer treatments. We reviewed 118 papers, of which 114 were considered potentially relevant. Ultimately, we found 24 research papers that met our inclusion criteria.

RESULTS

In total, we evaluated 24 studies involving 1,351 subjects and divided them according to their focus on aerobic, resistance, or combined exercise. In the case of aerobic exercise, the intensity ranged from 50% to 85% maximal heart rate and from 2 to 3 days per week. Resistance exercise included body-weight and Thera-Band resistance and ranged from 1 to 3 sets of 8 to 20 reps. Combined exercise included both resistance and aerobic exercise.

1. Aerobic exercise and improved physical fitness

Four trials examined the effects of aerobic exercise on physical fitness in breast cancer survivors. The trials ranged from 6 to 24 weeks in duration, and the number of subjects in the trials ranged from 33 to 69. Adherence to the interventions ranged from 50% to 80% maximum intensity. The percentage of body fat, maximal oxygen consumption (VO$_{2_{\text{max}}}$), hand grip strength and 6-min walking test performance were determined in four studies, and 1-mile running test performance was determined in four studies. In the four studies for aerobic exercise reported that significant physical fitness outcomes in breast cancer survivors. Aerobic exercise improved the percentage of body fat, VO$_{2_{\text{max}}}$, hand grip strength, 6-min walking test performance and 1-mile running test performance.

2. Resistance exercise and improved physical fitness

Four trials examined the effects of resistance exercise on physical fitness in breast cancer survivors. The trials ranged from 8 weeks to 12 months in duration, and the number of subjects in the trials ranged from 20 to 249. The chest, hip, arm, and leg strengths were determined in four studies. In the four studies for resistance exercise reported that significant physical fitness outcomes in breast cancer survivors. Resistance exercise improved chest, hip, arm, and leg strength.

3. Combined exercise and improved physical fitness

Four trials examined the effects of combined exercise on physical fitness in breast cancer survivors. The trials ranged from 12 weeks to 3 months in duration, and the number of subjects in the trials ranged from 28 to 58. Adherence
to the interventions ranged from 60% to 85% maximal heart rate and from 8 to 15 reps using body-weight, Thera-Band and machine resistance. The chest, hip, arm, and leg strength; functional walking performance; and predicted VO$_{2\text{max}}$ were determined. In the four studies for combined exercise that significant physical fitness outcomes in breast cancer survivors. Combined exercise improved the chest, hip, arm, and leg strength; functional walking performance; and predicted VO$_{2\text{max}}$ (Table 1).

### 4. Aerobic exercise and improved biomarkers

Four trials examined the effects of aerobic exercise on...
biomarker levels in breast cancer survivors. The trials ranged from 6 to 15 weeks in duration, and the number of subjects in the trials ranged from 23 to 94. Adherence to the interventions ranged from 55% to 80% maximal heart rate. The levels of inflammatory cytokines, metabolic biomarkers, and cancer biomarkers were determined in four studies. Only one study reported that aerobic exercise improved the levels of cancer markers. Giallauria and colleagues conducted a randomized controlled trial involving a supervised aerobic exercise intervention among 94 breast cancer survivors. The serum level of High-mobility group box 1 (HMGB-1) was obtained at baseline and at the 12-week follow-up. The authors reported that aerobic exercise reduced the serum level of HMGB-1, which consequently enhanced the health status of cancer patients.

### 5. Resistance exercise and improved biomarkers

Four trials examined the effects of resistance exercise on biomarker levels in breast cancer survivors. The trials ranged from 24 hours to 3 months in duration, and the number of subjects in the trials ranged from 12 to 103. The levels of inflammatory cytokines, metabolic biomarkers, and cancer biomarkers were determined in four studies. Two trials reported that resistance exercise improved serum interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels.

### 6. Combined exercise and improved biomarkers

Four trials examined the effects of combined exercise on biomarker levels in breast cancer survivors. The trials ranged from 8 weeks to 6 months in duration, and the number of subjects in the trials ranged from 16 to 79. The levels of inflammatory cytokines, metabolic biomarkers, and can-

---

### Table 2. Effects of exercise on mediators of inflammation

| Reference                | Cancer stage | Participants | Mode | Intervention | Outcome |
|--------------------------|--------------|--------------|------|--------------|---------|
| Martina et al. [24] (2016) | Stage I-IIa | Completing treatment. | RE 2 x / wk for 12 wks. | ↓ ∆IL-6 |
|                          |              | 49 control | 54 exercise | 8-12 reps, three sets. |
| Amanda et al. [25] (2016) | Stage I-IIa | 17 wks after treatment. | RE 3 x / wk for 16 wks. | ≅ ∆TNF-α |
|                          |              | 19 control | 20 exercise | 8-10 reps, three sets. |
| Nigel et al. [26] (2015)  | Stage I-IIIc | 12 mo. after treatment. | RE 15-20 reps, three sets. | ≅ ∆IL-6 |
|                          |              | 22 control | 20 exercise | 24 hours. |
| Swisher et al. [27] (2015) | Stage I-II | 3 mo. after treatment. | AE 2 x / wk for 12 wks at 60-75% maximum intensity. | ≅ ∆IL-6 |
|                          |              | 10 control | 13 exercise | ≅ ∆TNF-α |
|                          |              | 6 wks at 55-80% maximum intensity. | ≅ ∆Adiponectin |
| Lianne et al. [22] (2015) | Stage I-IIa | Completing treatment. | AE 3 x / wk for 12 wks at 70% maximum intensity. | ≅ ∆TNF-α |
|                          |              | 10 control | 23 exercise | ≅ ∆Insulin |
| Giallauria et al. [28] (2014) | Stage I | N/A | AE 3 x / wk for 12 wks at 70% maximum intensity. | ≅ ∆Glucose |
|                          |              | 33 control | 62 exercise | ≅ ∆HOMA-IR |
| Laura et al. [19] (2014)  | Stage I-II | 4 wks after treatment. | Comb 2 x / wk for 3 mo. | ≅ ∆IL-6 |
|                          |              | 22 control | 20 exercise | ≅ ∆IL-8 |
|                          |              | AE: 48-52 heart reserve. | RE: Whole-body band exercise, 15 reps, two sets. | ≅ ∆IL-10 |
|                          |              | 62 exercise | 20 exercise | ≅ ∆TNF-α |
| Reference             | Cancer stage | Participants | Mode | Intervention | Outcome |
|-----------------------|--------------|--------------|------|--------------|---------|
| Scott et al. [29]     | Stage III    | 18 mo. after | Comb | 3 x / wk for 3 mo. | ↓△Leptin |
| (2013)                |              | treatment.   |      | AE: 65-85% maximum intensity. | ↓△Total cholesterol |
|                       | 38 control   | 42 exercise  |      | RE: Whole-body band exercise 10-15 min. | ≃△Osteocalcin |
|                       | 78 control   | 76 exercise  |      | AE: 65-70% maximal heart rate. | ≃△Vitamin D |
|                       | N/A          | 3 yrs after | Comb | 3 x / wk for 12 mo. | ↓△CTACK |
|                       |              | treatment.   |      | AE: 70-80% maximal heart rate. | ≃△IL-1 |
|                       | 8 control    | 8 exercise   |      | RE: Whole-body progressive, 8 reps, one set. | ≃△IL-4 |
|                       | Stage III    | 18 mo. after | Comb | 3 x / wk for 8 wks | ≃△IL-6 |
| Tish et al. [30]      |              | treatment.   |      | AE: 70-80% maximal heart rate. | ≃△IL-10 |
| (2016)                | 78 control   | 76 exercise  |      | RE: Whole-body progressive, 12-15 reps, three sets. | ≃△TNF-α |
|                       | N/A          | 3 yrs after | Comb | 3 x / wk for 8 wks | ↓△IL-6 |
|                       |              | treatment.   |      | AE: 70-80% maximal heart rate. | ≃△hs-CRP |
|                       | 8 control    | 8 exercise   |      | RE: Whole-body yoga exercise, 30 min. | ≃△TNF-α |
|                       | Stage III    | 18 mo. after | Comb | 2 x / wk | ↑△C-peptide |
| Gomez et al. [31]     |              | treatment.   |      | AE: walking 3-3.5 mph 30 min. | |
| (2011)                | 28 control   | 25 exercise  |      | RE: Whole-body progressive, 8-12 reps, two sets. | |
|                       | Stage III    | Completing.  | AE   | 2 x / wk for 15 wks at 70-75% maximum intensity. | ➥△Insulin |
| Adrian et al. [32]    |              | treatment.   |      | ≃△HbA1c | |
| (2005)                | 28 control   | 25 exercise  |      | ≃△Insulin | |
|                       | Stage IIlb   | Completing.  | AE   | 2 x / wk for 15 wks at 70-75% maximum intensity. | ➥△Insulin |
|                       |              | treatment.   |      | ≃△HbA1c | |
| Sara et al. [33]      | Stage I      | 12 mo. after | Comb | 3 x / wk for 6 mo. | ↓△HDL-c |
| (2012)                | 37 intervention | 38 control |      | AE: 60-80% maximum intensity. | ➥△hs-CRP |
|                       | Stage I      | 12 mo. after | Comb | 3 x / wk for 6 mo. | ≃△hs-CRP |
| Emily et al. [38]     |              | treatment.   |      | AE: 60-80% maximum intensity. | ≃△hs-CRP |
| (2014)                | 38 control   | 38 control   |      | RE: Whole-body yoga exercise, 30 min. | ≃△hs-CRP |
| Belfort et al. [39]   | Stage I      | 36 mo. after | Comb | 2 x / wk | ↑△Lipocalcin |
| (2012)                | 36 pre- and  | post-intervention |      | AE: walking 3-3.5 mph 30 min. | |
|                       | post-interven| tion |      | RE: Whole-body progressive, 8-12 reps, two sets. | |
| Kerri et al. [18]     | Stage I      | 1 yr after   | RE   | 12 mo. | ↑△Osteocalcin |
| (2011)                | 54 control   | 54 control   |      | 8-12 reps, three sets. | |
|                       | 52 exercise  | 52 exercise  |      | 8-12 reps, two sets. | |
|                       | Stage II     | 1 yr after   | RE   | 12 mo. | ↑△Osteocalcin |
| Waltman et al. [17]   |              | 6 mo. after | Comb | 2 x / wk for 24 mo. | ↓△Alkphase B |
| (2010)                |              | treatment.   |      | 8-12 reps, two sets. | ↓△NTx |
|                       | 113 control  | 110 exercise |      | 8-12 reps, two sets. | |
| Irwin et al. [15]     | Stage II     | 6 mo. after | Comb | 3 x / wk for 24 wks at 50-80% maximum | ↓△Insulin |
| (2009)                |              | treatment.   |      | intensity. | ↓△IGF-1 |
|                       | 33 control   | 36 exercise  |      | RE: whole-body exercise, 50 min per week. | ↓△IGFBP-3 |
|                       | 36 exercise  | 36 exercise  |      | AE: 90 min per week. | |
| Ligibel et al. [40]   | Stage III    | After 3 mo.  | Comb | 16 wks. | ↓△Insulin |
| (2007)                |              | treatment.   |      | RE: whole-body exercise, 50 min per week. | |
|                       | 42 intervention | 40 control |      | AE: 90 min per week. | |

Notes: ↑ Increase, ↓ Decrease, ≃ No change.
AE: aerobic exercise, Comb: combined exercise, RE: resistance exercise, reps: repetitions, VO2max: maximal oxygen consumption. IL-1: interleukin-1, IL-4: interleukin 4, IL-6: interleukin 6, IL-8: interleukin 8, IL-10: interleukin 10, TNF-α: tumor necrosis factor α, CTACK: cutaneous T-cell-attracting chemokine, hs-CRP: high sensitivity C-reactive protein, HbA1c: hemoglobin A1c, HDL-c: high-density lipoprotein cholesterol, HOMA-IR: homeostatic model assessment of β-cell function and insulin resistance, HMGB-1: high-mobility group box 1, Alkphase B: bone-specific alkaline phosphatase, NTx: N-telopeptides of type 1 collagen, IGF-1: insulin-like growth factor gene 1, IGFBP-3: insulin-like growth factor binding protein 3.
cer biomarkers were determined in four studies. Two trials reported that combined exercises improved leptin, total cholesterol, and cutaneous T-cell-attracting chemokine (CTACK) levels (Table 2).

**DISCUSSION**

In recent years, it has been suggested that it is necessary to continue to study the guidelines for exercise prescriptions for breast cancer survivors, especially the types, localization, and side effects associated with exercise [42]. Generally, the available exercise guidelines for breast cancer survivors emphasize the importance of participating in moderate aerobic exercise, recommend with flexibility, and intermittent or minimally mention of resistance exercise [43,44]. Despite the importance of exercise, up to date, there has been minimal research regarding the effects of different types of exercise on physical fitness and biomarker levels in breast cancer survivors. Therefore, the purpose of this review is to propose the most effective type of exercise by reviewing the effects of each type of exercise on breast cancer survivors.

Some previous studies have suggested that the importance of resistance exercise for breast cancer survivors [45,46]. Although resistance exercise enhances musculoskeletal strength and bone mineral density, but has smaller effects on body composition and lipid profiles [17,25]. And also, single-type aerobic exercise interventions improve body composition and some adipokine levels, but do not affect musculoskeletal strength or the levels of biomarkers associated with bone mineral density [16,39]. In general, we found that combined exercise improves not only body composition and adipokine levels, but also musculoskeletal strength and the levels of biomarkers associated with bone mineral density [14,19,21,23]. Therefore, in view of this evidence, we suggest that the type of combined exercise is more effective for breast cancer survivors than single aerobic exercise or resistance exercise.

In conclusion, our review suggests that combined exercise could be considered a beneficial and effective exercise type for breast cancer survivors. Future trials with strict randomized controlled methodology are needed to verify the effects of different types of exercise on physical fitness and the levels of various biomarkers in breast cancer survivors.

**REFERENCES**

1. Oeffinger KC, Fontham ET, Ettzioni R, Herzig A, Michaelson JS, Shih YC, Walter LC, Church TR, Flowers CR, LaMonte Sj, Wolf AM, DeSantis C, Lorter-Tu lent J, Andrews K, Smith RA, et al, Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA* 2015;314:1599-614.

2. Oh CM, Won YJ, Jung KW, Kong HJ, Cho H, Lee JK, Lee DH, Lee KH, Community of Population-Based Regional Cancer Registries. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2013. *Cancer Res Treat* 2016;48:436-50.

3. National Comprehensive Cancer Network. Breast cancer clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2003;1:148-88.

4. Jones LW, Eves ND, Haykowsky M, Freedland SJ, Mackey JR. Exercise intolerance in cancer and the role of exercise therapy to reverse dysfunction. *Lancet Oncol* 2009;10:598-605.

5. Bernstein L, Henderson BE, Hanisch R, Sullivan-Halley J, Ross RK. Physical exercise and reduced risk of breast cancer in young women. *J Natl Cancer Inst* 1994;86:1403-8.

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

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

8. Irwin ML, Crumley D, McTiernan A, Bernstein L, Baumgartner R, Gilliland FD, Kirriska A, Ballard-Barbash R. Physical activity levels before and after a diagnosis of breast carcinoma. *Cancer* 2003;97:1746-57.

9. Mustian KM, Katula JA, Gill DL, Roscoe JA, Lang D, Murphy K. Tai Chi Chuan, health-related quality of life and self-esteem: A randomized trial with breast cancer survivors. *Support Care Cancer* 2004;12:871-6.

10. Ligibel JA, Giobbie-Hurder A, Olenzuk D, Campbell N, Salinardi T, Winer EP, Mantzoros CS. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control* 2009;20:1523-8.

11. Irwin ML, McTiernan A, Bernstein L, Gilliland FD, Baumgartner R, Baumgartner K, Ballard-Barbash R.
Relationship of obesity and physical activity with C-peptide, leptin, and insulin-like growth factors in breast cancer survivors. *Cancer Epidemiol Biomarkers Prev* 2005;14:2881-8.

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

13. Ohira T, Schmitz KH, Ahmed RL, Yee D. Effects of weight training on quality of life in recent breast cancer survivors: The Weight Training for Breast Cancer Survivors (WTBS) study. *Cancer* 2006;106:2076-83.

14. Milne HM, Wallman KE, Gordon S, Courneya KS. Effects of a combined aerobic and resistance exercise program in breast cancer survivors: a randomized controlled trial. *Breast Cancer Res Treat* 2008;108:279-88.

15. Irwin ML, Alvarez-Reeves M, Cadmus L, Mierzejewski E, Mayne ST, Yu H, Chung GG, Jones B, Knobf MT, DiPietro L. Exercise improves body fat, lean mass, and bone mass in breast cancer survivors. *Obesity* 2009;17:1534-41.

16. Kaltatsou A, Mameletzi D, Douka S. Physical and psychological benefits of a 24-week traditional dance program in breast cancer survivors. *J Bodyw Mov Th* 2011;15:162-7.

17. Waltman NL, Twiss JJ, Ott CD, Gross GJ, Lindsey AM, Moore TE, Berg K, Kupzyk K. The effect of weight training on bone mineral density and bone turnover in postmenopausal breast cancer survivors with bone loss: 24-month randomized controlled trial. *Osteoporos Int* 2010;2:1361-9.

18. Winters-Stone KM, Dobek J, Bennett JA, Nail LM, Leo MC, Schwartz A. The effect of resistance training on muscle strength and physical function in older, postmenopausal breast cancer survivors: a randomized controlled trial. *J Cancer Surviv* 2012;6:189-99.

19. Rogers LQ, McAuley E, Anton PM, Courneya KS, Vicari S, Hopkins-Price P, Verhulst S, Mochanuk R, Hoelzer K. Better exercise adherence after treatment for cancer (BEAT Cancer) study: Rationale, design, and methods. *Contemp Clin Trials* 2012;33:124-37.

20. Benton MJ, Schlairet MC, Gibson DR. Change in quality of life among breast cancer survivors after resistance training: is there an effect of age? *J Aging Phys Act* 2014;22:178-85.

21. Arem H, Sorkin M, Cartmel B, Fiellin M, Capoza S, Harrigan M, Ercolano E, Zhou Y, Sanft T, Gross C, Schmitz K, Neogi T, Hershman D, Ligibel J, Irwin ML. Exercise adherence in a randomized trial of exercise on aromatase inhibitor arthralgias in breast cancer survivors: the Hormones and Physical Exercise (HOPE) study. *J Cancer Surviv* 2016;10:654-62.

22. Dolan LB, Campbell K, Gelmon K, Neil-Sztramko S, Holmes D, McKenzie DC. Interval versus continuous aerobic exercise training in breast cancer survivors—a pilot RCT. *Support Care Cancer* 2016;24:119-27.

23. Foley MP, Hasson SM. Effects of a community-based multimodal exercise program on health-related physical fitness and physical function in breast cancer survivors: A pilot study. *Integr Cancer Ther* 2016;15:446-54.

24. Schmidt ME, Meynokohn A, Habermann N, Wiskemann J, Oelmann J, Hof H, Wessels S, Klassen O, Debus J, Potthoff K, Steinford K, Ulrich CM. Resistance exercise and inflammation in breast cancer patients undergoing adjuvant radiation therapy: Mediation analysis from a randomized, controlled intervention Trial. *Int J Radiat Oncol Biol Phys* 2016;94:329-37.

25. Hagstrom AD, Marshall PW, Lonsdale C, Papalia S, Cheema BS, Toben C, Baune BT, Fiatarone Singh MA, Green S. The effect of resistance training on markers of immune function and inflammation in previously sedentary women recovering from breast cancer: a randomized controlled trial. *Breast Cancer Res Treat* 2016;155:471-82.

26. Brockton NT, Gill SJ, Laborge SL, Paterson AH, Cook LS, Vogel HJ, Shemanko CS, Hanley DA, Maglioce AM, Friedenreich CM. The breast cancer to bone (B2B) metastases research program: a multi-disciplinary investigation of bone metastases from breast cancer. *BMC Cancer* 2015;15:512-26.

27. Swisher AK, Abraham J, Bonner D, Gillesland D, Hobbs G, Kuriain S, Yanosik MA, Vona-Davis L. Exercise and dietary advice intervention for survivors of triple-negative breast cancer: effects on body fat, physical function, quality of life, and adipokine profile. *Support Care Cancer* 2015;10:2995-3003.

28. Giallauria F, Gentile M, Chiudini P, Berrino F, Mattiello A, Maresca L, Vitelli A, Mancini M, Grieco A, Lucci R, Torella G, Panico S, Vigorito C. Exercise training reduces high mobility group box-1 protein levels in women with breast cancer: findings from the DIANA-5 study. *Monaldi Arch Chest Dis* 2014;82:61-7.

29. Scott E, Daley AJ, Doll H, Woodrooze N, Coleman RE, Mutrie N, Crank H, Powers HJ, Saxton JM. Effects of an exercise and hypocaloric healthy eating program on biomarkers associated with long-term prognosis after early-stage breast cancer: a randomized controlled trial. *Cancer Causes Control* 2013;24:181-91.

30. Knobf MT, Jeon S, Smith B, Harris L, Kerstetter J, Thompson AS, Insgoana K. Effect of a randomized controlled exercise trial on bone outcomes: influence of adjuvant endocrine therapy. *Breast Cancer Res Treat* 2015;165:491-500.

31. Gómez AM, Martínez C, Fiuza-Luces C, Herrero F, Perez M, Madero L, Ruiz JR, Lucia A, Ramírez M. Exercise training and cytokines in breast cancer survivors. *Int J Sports Med* 2011;32:461-7.
32. Fairey AS, Courneya KS, Field CJ, Bell GJ, Jones LW, Martin BS, Mackey JR. Effect of exercise training on C-reactive protein in postmenopausal breast cancer survivors: a randomized controlled trial. *Brain Behav Immun* 2005;19:381-8.

33. Jones SB, Thomas GA, Hesselwelt SD, Alvarez-Reeves M, Yu H, Irwin ML. Effect of exercise on markers of inflammation in breast cancer survivors: the Yale exercise and survivorship study. *Cancer Prev Res (Phila)* 2013;6:109-18.

34. Long Parma D, Hughes DC, Ghosh S, Li R, Trevino-Whitaker RA, Ogden SM, Ramirez AG. Effects of six months of Yoga on inflammatory serum markers prognostic of recurrence risk in breast cancer survivors. *Springerplus* 2015;26:143.

35. Nock NL, Owusu C, Kullman EL, Austin K, Roth B, Cerne S, Harmon C, Moore H, Vargo M, Hergenroeder P, Malone H, Rocco M, Tracy R, Lazarus HM, Kirwan JP, et al. A community-based exercise and support group program in African-American breast cancer survivors (ABCs). *J Phys Ther Health Promot* 2013;1:15-24.

36. Guinan E, Hussey J, Broderick JM, Lithander FE, O'Donnell D, Kennedy MJ, Connolly EM. The effect of aerobic exercise on metabolic and inflammatory markers in breast cancer survivors—a pilot study. *Support Care Cancer* 2013;21:1983-92.

37. Campbell KL, Van Patten CL, Neil SE, Kirkham AA, Gotay CC, Gelmon KA, McKenzie DC. Feasibility of a lifestyle intervention on body weight and serum biomarkers in breast cancer survivors with overweight and obesity. *J Acad Nutr Diet* 2012;112:559-67.

38. Simonavice E, Liu PY, Ilich JZ, Kim JS, Arjmandi B, Panton LB. The effects of a 6-month resistance training and dried plum consumption intervention on strength, body composition, blood markers of bone turnover, and inflammation in breast cancer survivors. *Appl Physiol Nutr Metab* 2014;39:730-9.

39. Befort CA, Klemp JR, Austin HL, Perri MG, Schmitz KH, Sullivan DK, Fabian CJ. Outcomes of a weight loss intervention among rural breast cancer survivors. *Breast Cancer Res Treat* 2012;132:631-9.

40. Ligibel JA, Campbell N, Partridge A, Chen WY, Salinardi T, Chen H, Adloff K, Keshaviah A, Winer EP. Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. *J Clin Oncol* 2008;26:907-12.

41. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, Cannady Rs, Pratt-Chapman ML, Edge SB, Jacobs LA, Hurria A, Marks LB, LaMonte SJ, Warner E, Lyman GH, Ganz PA. American Cancer society/American society of clinical oncology breast Cancer survivorship care guideline. *J Clin Oncol* 2016; 66:43-73.

42. Ferrer RA, Huedo-Medina TB, Johnson, BT, Ryan S, Pescatello LS. Exercise interventions for cancer survivors: a meta-analysis of quality of life outcomes. *Ann Behav Med* 2011;41:32-47.

43. Cheema BS, Gaul, CA. Full-body exercise training improves fitness and quality of life in survivors of breast cancer. *J Strength Cond Res* 2006;20:14-21.

44. Fujimoto J, Sakaguchi H, Aoki I, Tamaya T. Clinical implications of expression of interleukin 8 related to angiogenesis in uterine cervical cancers. *Cancer research* 2000;60:2632-5.

45. Loprinzi PD, Cardinal BJ. Effects of physical activity on common side effects of breast cancer treatment. *Breast Cancer* 2012;19:4-10.

46. Knols R, Aaronson NK, Uebelhart D, Fransen J, Aufdemkampe G. Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. *J Clin Oncol* 2005;23:3830-42.