

Practical guide for exercise prescription in Breast cancer

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Mechanism and effects of physical activity on breast cancer

- Sex hormone
Physical activity decreases estrogen and increases SHBG
- Metabolic hormone
Insulin and IGF-1 also may increase the risk of breast cancer via alterations in circulating estrogen levels. Physical activity can reduce insulin levels, insulin resistance, thereby decreasing fasting glucose, total IGF-1
- Inflammation
Chronic Inflammation cause breast cancer development and progression
Inflammation cause upregulation of enzyme aromatase (breast and adipose tissue) is responsible biosynthesis of estrogen

Mechanism and effects of physical activity on breast cancer

- Adipokine

Adipose tissue secretes adiponectin, leptin, resistin and other cytokine, potential role in the regulation of angiogenesis and tumor growth. Also physical activity increase women lose body fat by exercising, less estrogen is produced

- Oxidative stress

Free radical (Reactive oxygen species) are known to cause chromosomal aberrations, DNA damage, and mutations that inactivate tumor suppressor genes or increase expression of proto-oncogenes exercise training stimulates antioxidant defenses

Reducing the Risk of Breast Cancer Recurrence: an Evaluation of the Effects and Mechanisms of Diet and Exercise

Exercise recommendations

Aerobic exercise

- 150 min per week of moderate intensity
- OR
- 75 min per week of vigorous intensity

Resistance exercise

- Include all major muscle groups at least 2 days per week
- Increase intensity progressively over time under the supervision of a trained exercise specialist
- Use of compression garments are recommended per guidance from a healthcare professional

Adults older than 65 years

- Follow above recommendations
- Exercise as allowed by their abilities when chronic conditions exist
- Avoid long periods of physical inactivity

Examples of aerobic exercise by intensity:

- Moderate—walking briskly, biking on level ground, doubles tennis, water aerobics, ballroom dancing
- Vigorous—hiking uphill, jogging, running, lap swimming, singles tennis, jumping rope

Physical activity, sedentary behavior, adiposity, and weight change and breast cancer risk

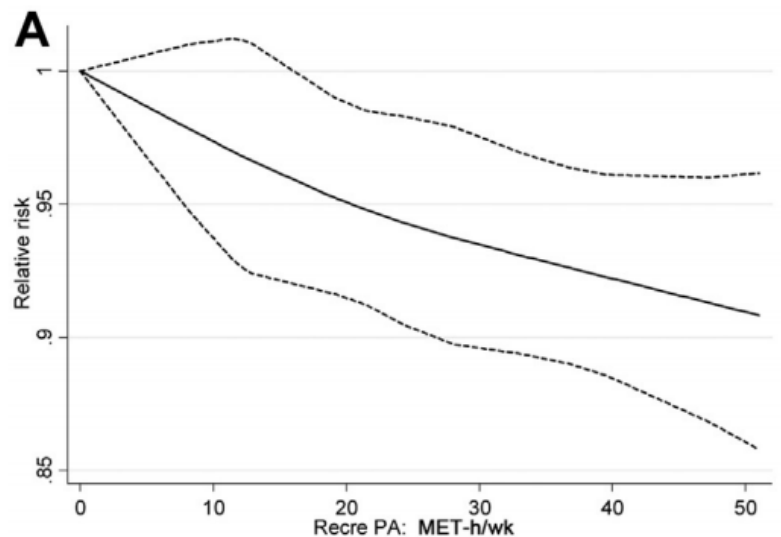
- Meta-analysis of observational cohort studies
- 22,900 premenopausal and 103,000 postmenopausal women
- Physical activity ↑ risk of pre- and post menopausal women ↓
sitting time ↑ adult weight gain and greater body adiposity ↑
risk in postmenopausal women ↑
- higher early adult BMI (ages 18–30 years) ↑ pre- and
postmenopausal breast cancer ↓

Physical Activity and Risk of Breast Cancer Meta-Analysis of 38 Cohort Studies

- Physical activity overall relative risk (ORR) for breast cancer was 0.87 (95% CI 0.84-0.90).

ORR was 0.83 (95% CI 0.79-0.87) for premenopausal

0.91 (95% CI 0.85-0.97) for postmenopausal status



ORR was reduced by 3% (ORR 0.97; 95% CI 0.95-0.99) for every 10 MET-h/wk increment, with a 9% (ORR 0.91; 95% CI 0.85-0.98) reduction for every 30 MET-h/wk increment and a 15% (ORR 0.85; 95% CI 0.76-0.96) reduction for every 50 MET-h/wk increment

Effects of Exercise Interventions on Breast Cancer Patients During Adjuvant Therapy

- SR and meta-analysis of RCT
- 29 studies and 2989 patients
- Exercise interventions: average of 150 minutes, 3 times per week, for 17 weeks and moderate to vigorous (~60% of VO_{2peak}), aerobic, resistance, or combined exercises
- Exercise Improve on VO_{2peak} , hand grip strength, QoL, fatigue, depression, anxiety

Exercise for women receiving adjuvant therapy for breast cancer

- Cochrane review of 32 studies with 2626 women
- Improves physical fitness and probably slightly reduces fatigue, cognitive function
- little or no difference in depression and cancer-specific QoL
- May lower the risk of lymphoedema
- may lead to little or no improvement in health-related QoL

Effects of physical and mind–body exercise on sleep problems

- SR, meta-analysis, 22 trials with 2107 participants
- Physical exercise interventions : walking, aerobic exercise, resistance exercise or a combination of both.
- Mind–body exercise interventions included yoga, Tai Chi and Qigong
- Improvements of total sleep scores on physical (SMD – 0.32; 95% CI – 0.54 to – 0.10) and mind–body exercise interventions (SMD – 0.27; 95% CI – 0.44 to – 0.09)
- Improvement on subjective sleep problems not on objective sleep measures

Exercise interventions for upper-limb dysfunction due to breast cancer

- Upper-limb dysfunction after breast cancer treatment : decreased shoulder ROM and strength, pain and lymphedema
- 24 studies and 2132 participants
- Intervention
 - 1) Active or active-assisted ROM exercises
 - 2) Passive ROM/manual stretching exercises
 - 3) Stretching exercises (including formal exercise interventions ,yoga and Tai Chi)
 - 4) Strengthening or resistance exercises.
- early vs delayed exercise (1~3 days following surgery) vs (day 4 or later)
early exercise more effective than delayed exercise
 - improve average shoulder flexion ROM(SMD:10.6 degrees; (CI): 4.51to16.6)
 - increase in wound drainage volume (SMD 0.31) and duration (1.15 days)

Exercise interventions for upper-limb dysfunction due to breast cancer

- upper-limb exercise interventions administered following surgery compared to usual care/comparison/control.
- post-operative period significantly improved shoulder flexion ROM in the short-term (WMD: 12.92 degrees; 95%CI: 0.69 to 25.16).
- Physical therapy treatment yielded additional benefit for shoulder function post-intervention (SMD: 0.77; 95%CI: 0.33 to 1.21) and at six-month follow-up (SMD: 0.75; 95%CI: 0.32 to 1.19).
- No evidence of increased risk of lymphedema from exercise

Pilates for women with breast cancer

- Pilates interventions 3 to 12 weeks. 3 times/wk, 40 to 60min
core muscle strengthening, spine flexibility and shoulder ROM exercise
- 4 RCT for meta-analysis
- Pilates had a positive effect on shoulder ROM, QOL, pain and self-reported upper extremity function,
- Not significantly greater than those resulting from other exercise programs

Effectiveness of Yoga Interventions in Breast Cancer-Related Lymphedema

- Yoga intervention program: breathing exercises, physical postures, meditation and relaxation skills
- weekly 90-minute yoga classes with a professional trainer, and a 45–50-minute CD- or DVD- based program at home, for 4~8weeks
- significant improvement in lymphedema status, ROM of shoulder motion and spinal mobility after an 8-week yoga
- no difference in lymphedema status, extracellular fluid and tissue resistance outcomes in the affected arm following a long-term yoga practice.
- could not be clearly demonstrated that yoga as an addition to usual care

Aquatic therapy for People with Lymphedema

- Aquatic exercises : activate muscle pump mechanism and hydrostatic pressure is thought to assist with lymphatic circulation and protect or reduce limb edema.
- The massage effect of the water on the skin to improve lymphatic clearance and water facilitates strengthening and aerobic exercise in people
- SR and meta-analysis, 4 RCTs involved 134 participants
- no significant short-term differences in lymphedema status between patients with aqua lymphatic therapy (ALT) compared to land-based standard care (standardized mean difference [SMD]: 0.14; 95% confidence interval [CI]: -0.37 to 0.64, I² = 0%, p = 0.59)
- No difference on UL function, strength, pain, ROM and QOL between both groups

Progressive resistance training of breast cancer

- Meta analysis of RCT
- Incidence/exacerbation of Breast cancer related lymphedema
5 studies of RCT (n=647), 4 studies of quasi RCT (n=479)
PRT reduced the risk of BCRL versus control conditions
[OR = 0.53 (95 % CI 0.31–0.90), I² = 0 %]
PRT did not worsen arm volume or symptom severity
- Upper and lower extremity muscle strength
11 studies (n=1252), 9 studies (n=1079)
PRT significantly improved upper [SMD = 0.57 (95 % CI 0.37–0.76) I²= 58.4%]
lower body muscular strength [SMD = 0.48 (95 % CI 0.30–0.67); I²= 46.7 %]

Resistance exercise and breast cancer–related lymphedema

- Resistance exercise strength: 40%이상, 80~90% 1RM, 2~3/week
- significant reduction of BCRL after RE was seen in bioimpedance spectroscopy (95% CI – 1.10 [– 2.19, – 0.01] L-Dex score)
- significant improvements of muscular strength in the upper and lower extremities (95% CI 8.96 [3.42, 14.51] kg and 95% CI 23.42 [11.95, 34.88] kg, respectively)

The effect of exercise on aromatase inhibitor-induced musculoskeletal symptoms in breast cancer survivors

- SR and meta analysis, 9 studies involving 743 participants
- Exercise intervention: aerobic exercise and resistance exercise duration of the interventions: 6 weeks to 12 months with at least 120 mins/week
Training intensity varied ranging from 60 to 80% of predicted maximal heart rate.
- pain (SMD = -0.46, 95% CI -0.79 to -0.13, P = 0.006)
stiffness (SMD = -0.40, 95% CI -0.71 to -0.08, P = 0.01)
grip strength (SMD = 0.43, 95% CI 0.16 to 0.71, P = 0.002)

Exercise therapies for preventing or treating aromatase inhibitor-induced musculoskeletal symptoms in early breast cancer, Cochrane review

- Seven studies with 400 participants
- Unclear whether exercise has a positive or negative effect on pain, grip strength, or the quality of life of women with AIMSS, because of the very low certainty of the evidence
- Despite of inconclusive findings, exercise should still be recommended as part of routine care for women with breast cancer, due to its wide-ranging benefits.

Interventions for the Treatment of Aromatase Inhibitor associated Arthralgia

Criteria	Subgroup	n	SMD (95% Confidence Interval)	Test for Subgroup Difference
Study type	Pharmacological approaches	4	-1.186 (-2.312 to -0.060)	$Q = 14.815, df = 4, P = .005$
	Acupuncture	3	-1.150 (-1.729 to -0.571)	
	Nutritional supplementation	3	-0.124 (-0.341 to 0.092)	
	Relaxation techniques	2	-0.667 (-1.274 to -0.060)	
	Physical exercise	3	-0.562 (-1.499 to 0.375)	

- pharmacological approaches, acupuncture, and relaxation techniques moderate to large effects on pain
- nutritional supplementation and physical exercise no significant effects

Axillary web syndrome following breast cancer surgery



- common condition occurring in up to 86% of patients following breast cancer surgery with ipsilateral lymphadenectomy of one or more nodes
- single cord or multiple thin cords in the subcutaneous tissues of the ipsilateral axilla
- symptomatic between 2 and 8 weeks postoperatively but can also develop and recur months to years after surgery
- Intervention: Physical therapy (manual therapy, exercise, education, and other rehabilitation modalities to improve range of motion and decrease pain) is recommended in the treatment of AWS

Therapeutic Physical Exercise Post-Treatment in Breast Cancer : A Systematic Review of Clinical Practice Guidelines

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Table 4. Levels of Evidence and degrees of recommendation of the therapeutic physical exercise to reduce the adverse effects of breast cancer treatment, shown in the clinical practice guidelines (CPGs).

CPG	Doyle, C [13]	Rooney, M [14]	Manchon, P [15]	Murray, N [16]	Gradishar, WJ [17]	Harris, SR [18]	Greenlee, H [19]	Komoike, Y [20]	Runowicz, CD [21]	Paluch-Shimon, S [22]	Greenlee, H [23]	Senkus, E [24]
Treatment Aim												
Mortality reduction	D **											
Recurrence risk reduction	C *				A †							
Increase quality of life	B †	A *										
Pain reduction							B **		A **			
Fatigue reduction	A **	B †				C **			A **		B **	
Lymphedema reduction	B †					D †			B **			
Musculoskeletal changes reduction									B **			
Increase in range of movement of the shoulder								A **				
Reduction of body weight alterations	A †	A †							B †			B *
Reduction of bone alterations	D †					D			A †	C †		
Reduction of gastrointestinal disorders	**		*									
Hot flashes reduction					D †							
Neuropathy reduction									C *			
Stress							B *					
Depression		B †					B *				B *	*
Anxiety							B *				B *	*

* Very recommendable, ** Moderately recommendable, † Controversy.

Table 1. Agreement for the stratification of the levels of evidence.

Level of Evidence	Type of Study	Solidity
A	Meta-analysis	Very strong
	Systematic reviews.	Strong
B	Randomized clinical trials.	Moderate
	Cohort studies. Case-control studies.	
C	Non-analytical or experimental studies	Low
D	Opinion of the committee of experts.	Very Low

Home based multidimensional survivorship program

- The survivorship program of three components
 - Educational (provision of information and advice on how to self-manage)
 - Physical (exercise or resistance training)
 - Psychological (counselling and cognitive therapies)
- RCT two of three components vs usual care (routine medical follow-up)
- Outcome
 - Quality of life (FACT-B, EORTC, SF 36)
- Meta analysis for 22 RCTs and four quasi-RCTs on 2272 participants
- Short term benefit (1~3months) on quality of life, anxiety, depression, fatigue)