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Null Results in Brief

Cancer Epidemiology, Biomarkers & Prevention

No Effect of Exercise on Insulin-Like Growth Factor-I, Insulin, and Glucose in Young Women Participating in a 16-Week Randomized Controlled Trial

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Abstract

Introduction: Insulin-like growth factor I (IGF-I) and IGF binding protein 3 (IGFBP-3) have been associated with increased risk of breast cancer.

Methods: We report our findings on the effects of 16 weeks of aerobic exercise on IGF axis proteins, insulin, glucose, and insulin resistance of 319 young sedentary women. Demographics, health surveys, body composition, dietary intake, and blood samples were collected at baseline and 16 weeks. IGF-I and IGFBP-1, IGFBP-2, and IGFBP-3 were measured by ELISA.

Results: Exercise adherence was 88%. The dropout rates for the exercise and control groups were 21.7% and 14.5%, respectively. There was a small significant change from baseline in IGFBP-3 concentrations. IGFBP-3 levels decreased in controls and increased in exercisers. The between-group difference was significant. No other changes were noted.

Conclusion: Sixteen weeks of exercise had minimum or no effect on IGF proteins of young women.

Impact: Our study supports findings from previous studies conducted in older populations and raises the question of what type of intervention is needed to change circulating levels of IGF proteins in humans.
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Introduction

Insulin-like growth factor 1 (IGF-I) and IGF binding protein 3 (IGFBP-3) have been associated with increased risk of premenopausal breast cancer (1). Recently, results from a pooled data analysis of 17 prospective studies revealed that IGF-I levels were positively associated with estrogen receptor–positive breast cancer regardless of menopausal status (2). It is unclear whether exercise training affects circulating levels of IGF-I and binding proteins. Previous exercise trials in postmenopausal women have reported mixed results (3-5). In young women, although strength training has been found to decrease IGF-I and insulin levels (6), there is a lack of large longitudinal studies examining the effects of aerobic exercise on IGF proteins. We conducted a randomized clinical trial to examine the effects of exercise training on insulin, glucose, and IGF axis proteins in sedentary young women. We hypothesized that exercise training would lower IGF-I, insulin, glucose, and the molar ratio of IGF-I/IGFBP-3, and increase binding protein levels in the direction associated with decreased breast cancer risk.

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Materials and Methods

The Women in Steady Exerciser Research (WISER) study was a randomized clinical trial comparing the effects of a 16-week aerobic exercise intervention versus no exercise on markers associated with breast cancer risk (7). The study was approved by the University of Minnesota Human Subjects Review Committee. Participants were healthy women ages 18 to 30 years, with a body mass index between 18.5 and 40 kg/m^2, sedentary, not taking hormonal contraceptives, and not dieting. Women were randomly assigned to the exercise intervention (n = 166) or the control group (n = 153).

The exercise intervention consisted of 30 minutes of weight-bearing aerobic exercise, five times per week, at a specified intensity based on age-predicted heart rate maximum (HRmax). Exercise intensity increased every 4 weeks to reach 80% to 85% of HRmax. The control group was asked to maintain their usual levels of physical activity.

At baseline and 16 weeks, the following were collected: demographic information, anthropometrics, body composition through DXA (Lunar Radiation Corp.), dietary intake through 3-day food records, health habits, fitness level through submaximal tests, and blood samples, which were collected in the morning during the follicular phase of participants' cycles.

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Fasting glucose and insulin levels were measured at the Fairview University Diagnostic Laboratories. IGF proteins were measured by enzyme-linked immunosorbent assays (DSL). Intra-assay and inter-assay coefficients of variation for IGF-I, IGFBP-1, IGFPB-2, and IGFBP-3 were 1.8%, 1.9%, 2.2%, and 1.3% and 7.2%, 9.3%, 10.6%, and 4.9%, respectively. All samples from the same participant were analyzed in the same batch.

Unadjusted comparisons of demographic characteristics were done by *t* tests and χ^2 tests for continuous and categorical variables, respectively. Comparisons between groups were adjusted for age and body mass index strata with a general linear model. This was an intent-to-treat analysis. Insulin and IGFBP-1 were analyzed on the log scale; changes in outcome variables were analyzed on the original scale. We had 80% power to detect a difference in change from baseline to 16 weeks between exercisers and controls of 20.7 ng/L for IGF-I; 1.29 mU/L for insulin; 0.146 mmol/L for glucose; and 4.97, 51.4, and 161 ng/mL for IGFBP-1, IGFBP-2, and IGFBP-3, respectively. All analyses were done with SAS software (version 9.2, SAS Institute).

Results

We randomized 391 participants into the study, and 319 successfully completed the study. The dropout rates for the exercise and control groups were 21.7% and 14.5%, respectively. Three participants (two controls and one exerciser) were excluded from analysis because of unusually high follow-up insulin levels (i.e., more than a 5-fold increase from baseline).

There were no baseline differences in demographic characteristics and other variables between groups (Table 1). Fitness increased by 0.91 metabolic equivalents of task (METs) in the exercisers compared with 0.14 METs in controls ($P < 0.0001$). Exercisers completed an average 92% of assigned minutes of exercise, and 140 women (86%) exercised for at least 14 weeks.

IGFBP-3 levels decreased in controls and increased in exercisers with the difference in change between groups

Table 1. Baseline characteristics of controls and exercisers

	Controls (*n* = 151)	Exercisers (*n* = 165)	*P*
Age (y)	25.3 ± 3.5	25.4 ± 3.4	0.8
Body fat (%)	36.2 ± 8.3	36.3 ± 8.7	0.86
Weight (kg)	67.7 ± 14.7	67.4 ± 14.6	0.86
Fitness (METS)	7.0 ± 1.5	6.9 ± 1.5	0.59
Ethnicity			
Hispanic	6 (4.0)	8 (4.8)	0.7
Non-Hispanic	145 (96.0)	157 (95.2)	
Race			
American Indian	0	1 (0.6)	0.59
Asian/Pacific Islander	26 (17.2)	20 (12.1)	
Black	11 (7.3)	13 (7.9)	
White	106 (70.2)	124 (75.1)	
Other/multirace	8 (5.3)	7 (4.2)	
Education			
Less than college	49 (32.5)	53 (32.0)	0.27
College degree	63 (41.7)	56 (34.0)	
Graduate/professional degree	39 (25.8)	56 (34.0)	
Marital status			
Never married	122 (80.8)	137 (83.0)	0.62
Married/partnered	26 (17.2)	25 (15.2)	
Divorced/separated	3 (2.0)	3 (1.8)	
BMI (kg/m^2)			
≤25	99 (65.5)	101 (61.2)	0.2
25-30	30 (19.9)	46 (27.9)	
≥30	22 (14.6)	18 (10.9)	

NOTE: Values are presented as mean ± SD for continuous variables or *n* (%) for categorical variables.
Abbreviations: BMI, body mass index; METS, metabolic equivalents of task.

Table 2. Changes in glucose, insulin, insulin resistance, and IGF proteins for controls versus exercisers

	Baseline	4 mo	Change at 4 mo	% Change at 4 mo
Glucose (mmol/L)				
Control (*n* = 151)	4.44 ± 0.03	4.40 ± 0.03	−0.76 ± 0.7	−0.50 ± 0.9
Exercise (*n* = 165)	4.52 ± 0.03	4.50 ± 0.03	−0.39 ± 0.7	0.08 ± 0.8
P	0.12	0.04	0.7	0.63
Insulin (mU/L)				
Control (*n* = 151)	6.22 (5.7-6.8)	6.31 (5.8-6.9)	0.10 ± 0.3	19.0 ± 5.6*
Exercise (*n* = 165)	6.14 (5.6-6.7)	5.82 (5.3-6.3)	−0.51 ± 0.3	8.2 ± 5.4
P	0.84	0.19	0.19	0.16
HOMA index				
Control (*n* = 151)	1.49 ± 0.08	1.49 ± 0.07	0.00 ± 0.07	20.6 ± 6.2
Exercise (*n* = 165)	1.48 ± 0.07	1.37 ± 0.06	−0.12 ± 0.07	9.5 ± 5.9
P	0.95	0.23	0.24	0.19
QUICKI				
Control (*n* = 151)	0.393 ± 0.0	0.375 ± 0.0	−0.02 ± 0.0*	−4.50 ± 0.8*
Exercise (*n* = 165)	0.391 ± 0.0	0.378 ± 0.0	−0.01 ± 0.0*	−3.30 ± 0.7*
P	0.16	0.46	0.25	0.25
IGF-I (ng/mL)				
Control (*n* = 151)	394.7 ± 7.8	382.1 ± 7.8	−11.1 ± 5.5	−1.63 ± 1.5
Exercise (*n* = 165)	386.0 ± 7.4	377.3 ± 7.3	−9.8 ± 5.2	−0.84 ± 1.4
P	0.42	0.65	0.87	0.7
IGFBP-1 (ng/mL)				
Control (*n* = 151)	21.1 (18.9-23.6)	20.5 (18.1-23.1)	−0.25 ± 1.3	15.4 ± 7.1*
Exercise (*n* = 165)	24.5 (22.0-27.2)	22.9 (20.4-25.6)	−0.90 ± 1.3	12.2 ± 6.8
P	0.06	0.18	0.71	0.74
IGFBP-2 (ng/mL)				
Control (*n* = 151)	347.6 ± 20.6	408.0 ± 21.5	52.2 ± 14.8	37.4 ± 24.5*
Exercise (*n* = 165)	370.6 ± 19.4	414.3 ± 20.3	37.4 ± 14.4	51.8 ± 23.8*
P	0.41	0.83	0.41	0.64
IGFBP-3 (ng/mL)				
Control (*n* = 151)	4,942.1 ± 69.4	4,837.1 ± 68.7	−103.1 ± 42.6	−1.49 ± 0.9
Exercise (*n* = 165)	4,863.6 ± 65.5	4,883.9 ± 64.8	18.7 ± 40.7	0.99 ± 0.9
P	0.41	0.62	0.04	0.05
IGF-I/IGFBP-3†				
Control (*n* = 151)	0.29 ± 0.00	0.28 ± 0.00	−0.317 ± 0.3	−0.45 ± 1.1
Exercise (*n* = 165)	0.29 ± 0.00	0.28 ± 0.00	−0.817 ± 0.3	−1.85 ± 1.0
P	0.96	0.54	0.22	0.33

NOTE: Values are expressed either as mean ± SEM or geometric mean (lower CI-upper CI) for baseline data and as mean ± SEM for changes.
Abbreviations: HOMA, homeostasis model assessment; QUICKI, quantitative insulin sensitivity check index.
*Significant change from baseline within treatment group at $P < 0.05$.
†Values for change at 4 months were multiplied by 100 to facilitate presentation.

being significant (Table 2). There were no differences between groups in the other outcomes.

Discussion

This randomized trial suggests that 16 weeks of aerobic exercise, 30 minutes per day, 5 days per week, has minimal or no effect on levels of insulin, glucose, IGF-I, and IGFBPs among young, healthy eumenorrheic women. The strengths of the WISER study include the type of exercise intervention chosen, which was based on current public health guidelines and excellent retention and adherence rates. Furthermore, previous studies examining the effects of exercise on IGF axis proteins have focused on postmenopausal women and found mixed results (3, 4). The WISER study is the first large trial to assess the effects of aerobic exercise on IGF axis proteins in young women. Although we found minimal effects, it may be that longer exercise interventions or alternative approaches to the current physical activity interventions are needed to change the levels of these markers in young women.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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