

Metabolic Risk Factors, Exercise Capacity And Inflammation In Postmenopausal Women

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Background

- Metabolic syndrome (MS) and increased inflammation are more prevalent in postmenopausal women .
- The MS prevalence in postmenopausal women was approached 50% in US, 35% in aged 50-59 years of Chinese and 31.2% in the Korean.(Cho et al., 2009; Ruan et al., 2010)
- The abnormalities of MS components (central obesity, hypertension, dyslipidemia and insulin resistance) and pro-inflammatory are related to accumulate adipose tissue in elderly females especially in postmenopausal women.

- The high incidence of MS in menopausal is proved by numerous factors including sedentary lifestyles, decreased exercise capacity, weight gain and central obesity facilitated by low levels of estrogens, dyslipidemia, decreased glucose tolerance, and increased pro-inflammatory states (Mercuro et al., 2006).
- Increasing evidence suggests that increased physical activity may improve exercise capacity, inflammation and decrease the MS risks (Beckie, Beckstead, & Groer, 2010).

- Previous exercise studies of postmenopausal women were mostly focused the obese, overweight, moderately elevated blood pressure, and type 2 diabetes (Arsenault et al., 2009; Imayama et al., 2011; Lee, Kim & Kim, 2012; Silverman, Nicklas, & Ryan, 2009).
- The exercise protocol were vary including of resistance exercise (Wooten et al., 2011), a partly supervised aerobic exercise (Friedenreich et al. 2011), or combined diet and aerobic exercise (Imayama et al., 2011; Silverman et al., 2009).

- Results from these exercise studies cannot be generalized into a comprehensive exercise recommendation for healthy postmenopausal women.
- The relationships among changes in components of MS risks, exercise capacity and inflammation markers following exercise training have not been well examined.

Purpose of the Study

- To investigate components of the MS, inflammation state (mainly in interleukin-6[IL-6]), and exercise capacity in postmenopausal women
- To evaluate the effect of a supervised aerobic exercise training program on these study variables
- To test the hypothesis that beneficial effects on serum IL-6 and exercise capacity in response to exercise training would be related to the improvements in MS components

Study Design

- This study was a prospective, randomized control trail. A two-group, pre- and post- test experimental research design was used in this study.



Participants

- Postmenopausal women were referred by their physicians from metabolic and/or cardiovascular clinics of a medical center in Taiwan between April 2011 and February 2012.
- Postmenopausal was defined as an absence of menstruation for at least 12 months under nature menopause without medicine or surgery (Bhagat et al., 2010).



- Inclusion Criteria of the participants:
 - postmenopausal women aged 45-70 years,
 - were sedentary life style (not exercising > 30min on > 3days/week) for the past 6 months
 - were not taking any medications including lipid-lowering agents, non-steroid anti-inflammatory drugs, anti-hypertension drugs, or hormone replacement therapy.

- Exclusion Criteria :

- positive history or clinical signs of ischemic heart disease
- diabetes mellitus (fasting glucose > 126 mg/dL)
- systolic blood pressure (SBP) > 160mmHg or diastolic blood pressure (DBP)>100mmHg
- had orthopedic limitation.

Procedure

- The study protocol was approved by the ethics committee of the study medical center.
- Data on the MS components (blood pressure, Triglyceride (TG), HDL-C levels, fasting blood sugar, and waist circumference), serum IL-6 levels, and exercise capacity were analyzed at baseline and the end of the 12 weeks study.

Measurement

The components of MS risk factors

- The NCEP/ATP III criteria of MS were modified for Asian population.
- MS was defined by the presence of three or more of the five metabolic risk components:
 - (1) SBP >130mmHg or DBP >85mmHg
 - (2) HDL-C <50 mg/dL
 - (3) fasting glucose between 100 and 125 mg/dL
 - (4) triglycerides (TG)>150 mg/dL
 - (5) waist circumference >80 cm

(Cheung et al., 2008)

The MS score

- For the purpose of measuring overall effects of exercise training, individual component of MS risks as well as the MS score were examined in our study.
- The MS score was calculated as the sum of the components of MS risks present in each subject (Vidal et al., 2008).

Anthropometric Assessment

- Waist circumferences of all participants were determined on the study day following the guidelines recommended by the ACSM (2010).
- Waist circumferences were measured to the nearest 0.1 cm at the end of exhalation using a Gulick measuring tape (Creative Health Products, Plymouth, MI).
- The average of the two readings was obtained for data analysis.

Blood Pressure (BP)

- BP measurements were taken using one calibrated automated oscillometric BP monitor (Datascope, Mahwah, NJ).
- The subject was seated in a chair. After a rest period of 10 minutes, three BP assessments were taken at 2-minute intervals (ACSM, 2010).
- The mean of the three BP readings was calculated as the baseline resting BP.

Blood Sampling

- Blood samples were collected between 8 and 10 a.m. after an overnight fast.
- Blood analyses in TG concentrations, HDL-C levels and fasting glucose were performed in a laboratory of the study medical center using standard equipment and assays.

- The concentration of serum IL-6 of each study participant was determined using DuoSet enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, USA).
- The intra-assay and inter-assay coefficients of variation was 6% and 8% respectively in our study.

Exercise Testing

- Each participant performed a graded exercise test on a treadmill (T-2100, GE Healthcare, WI) using the modified Bruce's protocol (ACSM, 2010).
- The exercise capacity (VO_2max) was calculated by a formula described by the ACSM (2010):

$$\text{VO}_2\text{max (ml/kg/min)} = 3.5 + (0.1 \times \text{speed}) + (1.8 \times \text{speed} \times \% \text{ grade})$$

achieved at peak exercise

- The exercise test was terminated when at least two of following criteria were present :
 - maximal HR $>90\%$ of age-predicted maximal HR ($220 \text{ bpm} - \text{age}$)
 - Score on the Borg's Scale reaches >19
 - SBP $> 220 \text{ mmHg}$ or DBP $> 110 \text{ mmHg}$
 - the presence of chest pain, cold sweating or abnormal ECG waveforms (e.g. ST segment elevation or depression $> 2 \text{ mm}$, or T wave inverted)

(ACSM, 2010)

Exercise training protocol

- Women in the exercise group performed 30 minutes moderate-intensity (60% to 80% of their HRR) treadmill exercise three times each week for 12 weeks.
- HRR of each exercise participant was calculated by the Karvonen Formula (1957):

$$\text{Desired exercise intensity (\%)} \times (HR_{max} - HR_{rest}) + HR_{rest}$$

- Exercise training began with 5 min of warm-up and ended with 5 min of cool down.

- During treadmill exercise, each participant's BP values and rate of perceived exertion on the Borg's Scale were collected every 5 min.
- HR was continuously monitored to secure the exercise intensity and to calculate mean exercise HR.

Data Analysis

- All variables were tested for normality by the Kolmogorov-Smirnoff test.
- Differences between the two groups were identified by t tests, Mann-Whitney-U tests, or Wilcoxon Matched-Pairs test.
- The Generalized Estimating Equation (GEE) (Zeger & Liang, 1986) was used to explore the main effects of the exercise training on study variables.

- Pearson or Spearman correlations were used to examine the relationships among changes in components of the MS, serum IL-6, and exercise capacity.
- All analyses were two-tailed and a p-value $<.05$ was considered statistically significant.
- Sample power of our study was calculated by the G*Power 3 analysis (Faul, Erdfelder, Lang, & Buchner, 2007).

Results

- A total of 53 postmenopausal women were recruited.
- Forty-six women completed the 12 weeks study (23 women in each group).
- A sample power of 83% was obtained in this study.
- There were no statistical differences of characteristic and baseline data between the subjects dropped out and those who completed the study.
- Thirty-one women (67.4%) met the criterion of MS

Table 1. Baseline subjects characteristics and study

variable	<u>All</u> (n=46) Mean±SD	<u>Exercise group</u> (n=23) Mean±SD	<u>Control group</u> (n=23) Mean±SD	p value
Age (years)	56.02±7.02	56.91±6.15	55.13±7.84	0.49
Menopausal year (years)	5.80±5.40	5.86±5.62	5.74±5.30	0.89
The components of MS				
Waist circumference (cm)	91.87±9.11	93.35±9.13	90.39±9.05	0.30
SBP (mmHg)	125.79±9.64	124.58±9.23	127.00±10.08	0.48
DBP (mmHg)	77.88±8.75	76.78±8.13	78.97±9.38	0.53
Fasting glucose (mg/dL)	105.24±14.64	106.78±16.87	103.70±12.18	0.39
Triglyceride (mg/dL)	149.65±54.60	164.43±60.67	134.87±44.26	0.11
HDL-C (mg/dL)	46.35±9.25	46.22±11.33	46.48±6.84	0.83
MS score	3.13±1.09	3.35±1.02	2.91±1.12	0.15
IL-6 (pg/ml)	3.29±1.28	3.59±1.27	2.99±1.24	0.07
VO ₂ max (ml/kg/min)	24.30±5.25	24.09±5.99	24.52±4.52	0.73

- The average exercise intensity of the exercise participants was 73% of their HRR.
- The mean compliance rate of exercise was 98% among women in the exercise group.



- The intervention effect on the MS score in the exercise group were significantly better than the control group at the end of the study ($p = .01$).

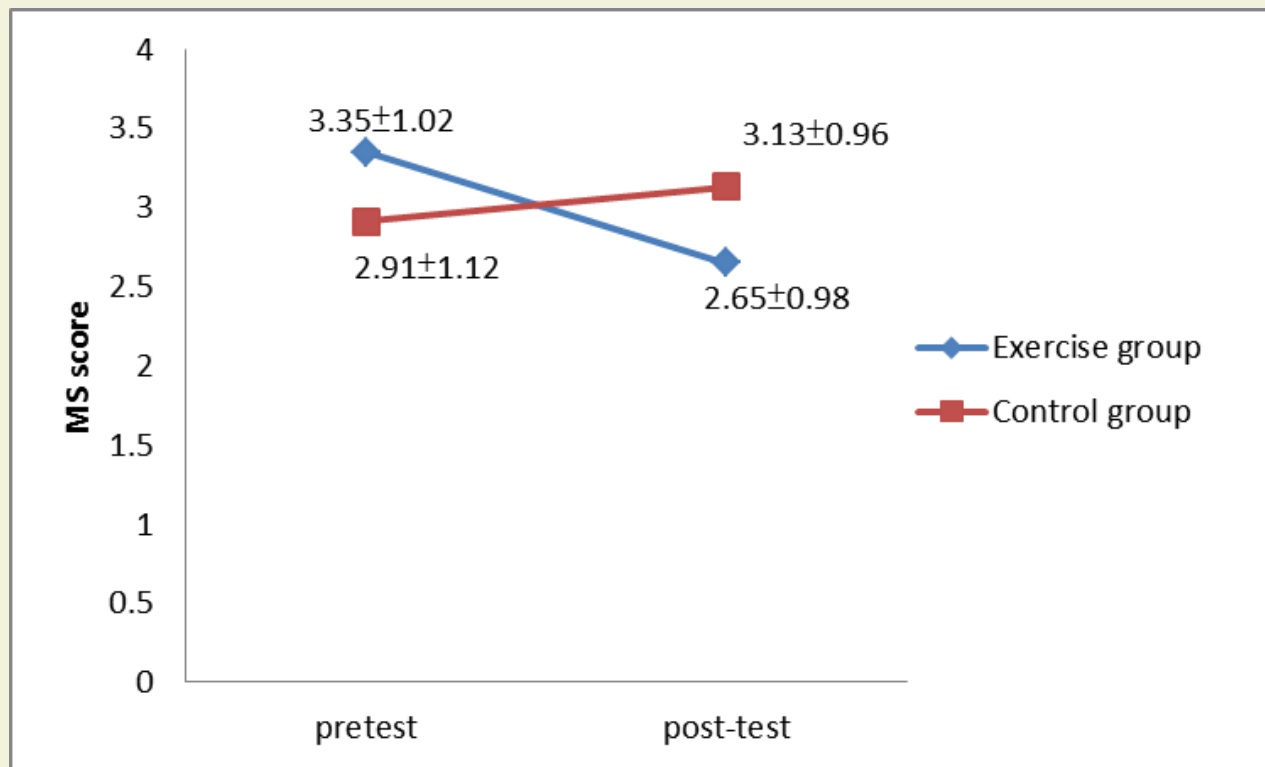


Figure 1. *Effects of exercise on the MS score*

- Mean waist circumference were more significantly improved in the exercise group compared with those in the control ($p = .001$).

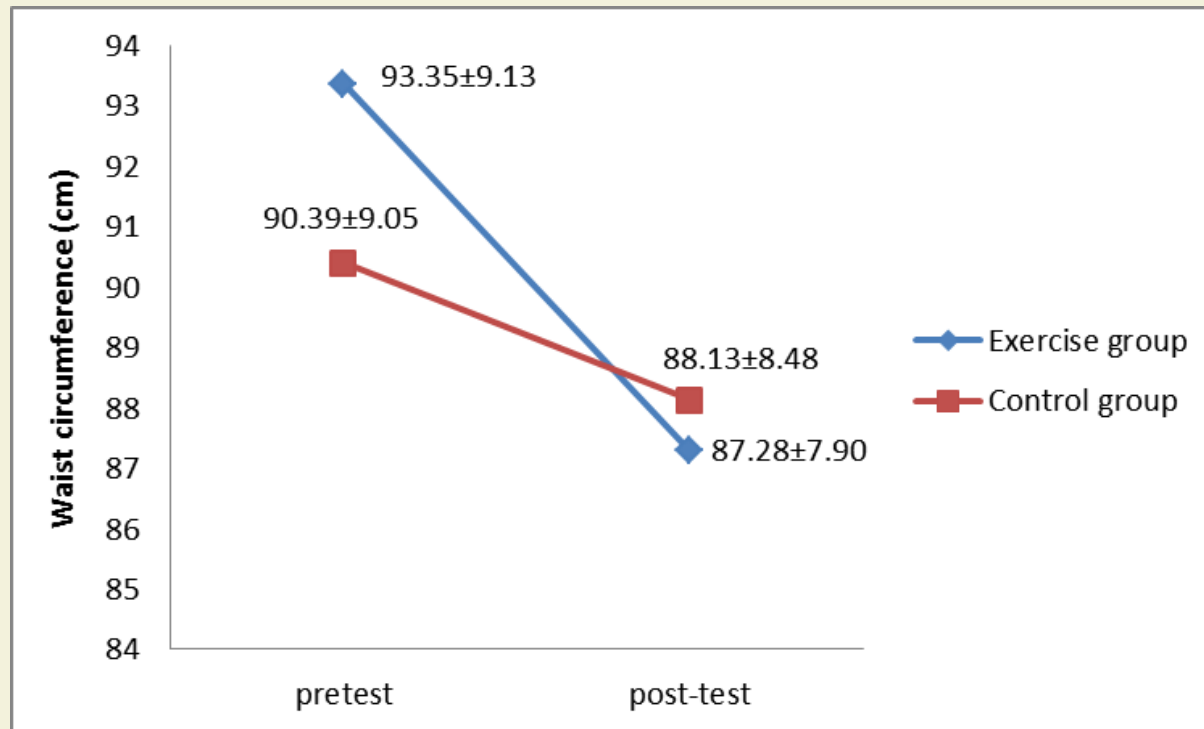


Figure 2. *Effects of exercise on waist circumference*

- Mean HDL-C levels were significantly improved in the exercise group compared with their counterparts ($p < .001$).

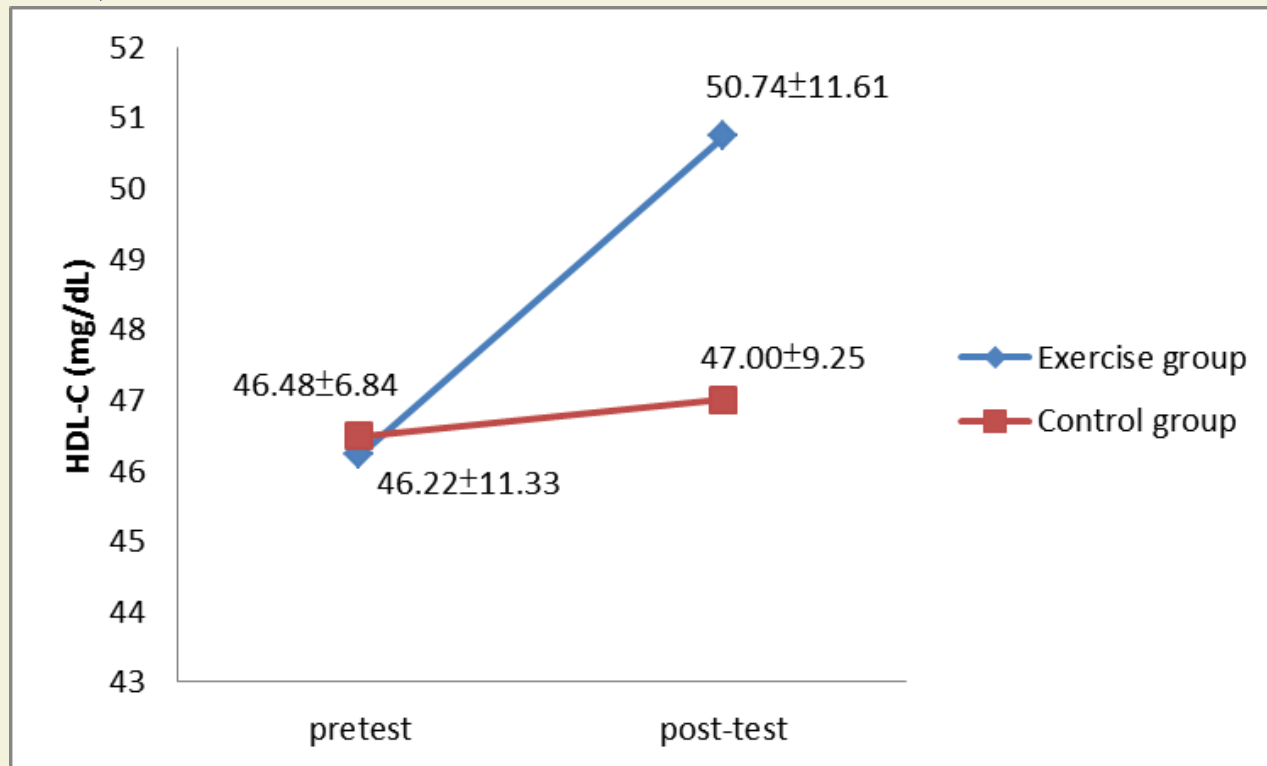


Figure 3. *Effects of exercise on HDL-C*

- Significant improvements in serum IL-6 levels ($p = .03$) were observed among exercise participants.

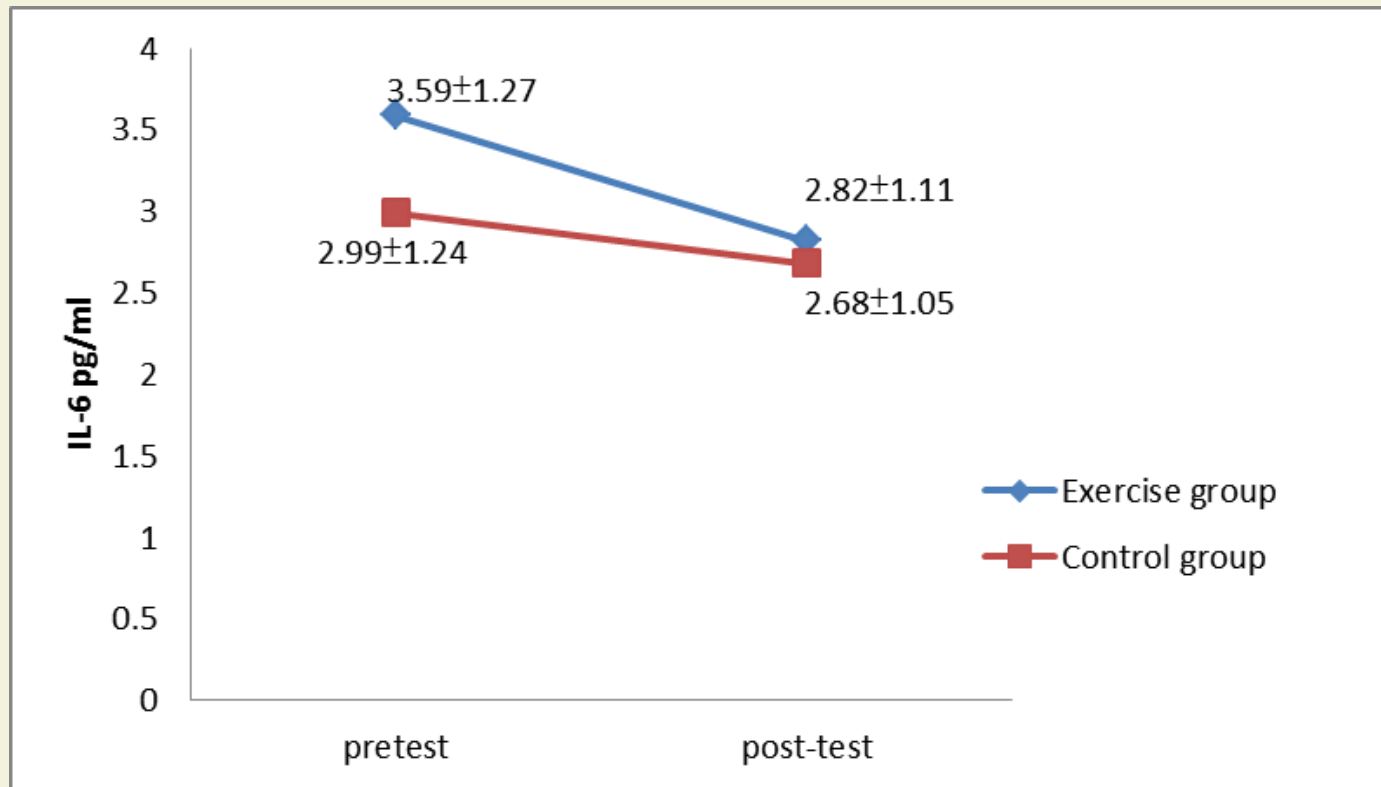


Figure 3. *Effects of exercise on IL-6*

- The intervention effect on exercise capacity in exercise group was significantly better than those in the control ($p < .001$).

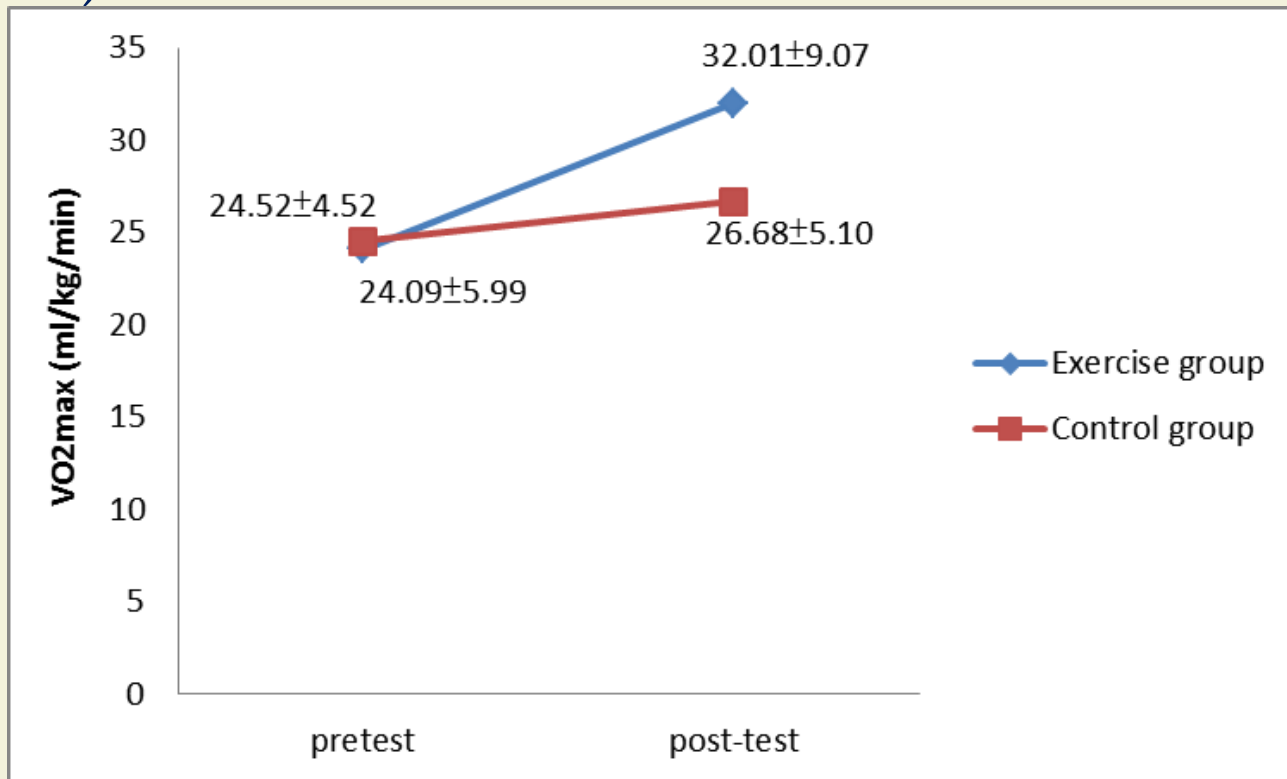
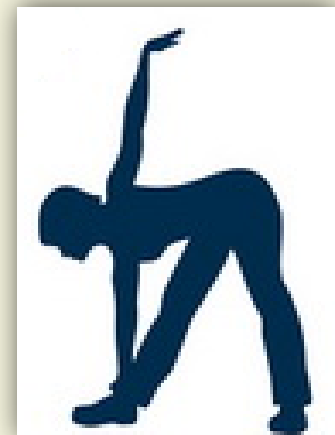


Figure 4. *Effects of exercise on exercise capacity (VO₂max)*

- No statistically significant differences of changes in serum TG levels, fasting glucose, and blood pressure were obtained between the two groups.



The relationship among study variables at baseline

- The MS score was significantly positively correlated with the waist circumference, SBP, fasting glucose, TG and inversely correlated with HDL-C levels (all $p < 0.05$).
- The serum IL-6 level was significantly correlated with waist circumference ($r = 0.34$, $p = 0.02$) and HDL-C level ($r = -0.44$, $p < 0.01$).
- Exercise capacity was not associated with any components of MS and IL-6 levels at the beginning of our study (Table 2).

Table 2. The relationship among study variables at baseline

	WC	SBP	DBP	AC	TG	HDL-C	MS score	IL-6
WC	1.00							
SBP	0.16	1.00						
DBP	-0.18	0.64**	1.00					
AC	0.35*	0.07	-0.10	1.00				
TG	0.36*	-0.16	-0.26	-0.01	1.00			
HDL-C	-0.09	0.30*	0.34*	0.06	-0.27	1.00		
MS score	0.48**	0.30*	0.04	0.36*	0.50**	-0.37*	1.00	
IL-6	0.34*	-0.06	0.05	0.06	0.25	-0.44**	0.28	1.00
EC	-0.14	-0.14	0.04	-0.10	0.28	-0.23	-0.05	0.17

WC, Waist Circumference; AC, Fasting glucose; TG, Triglyceride; HDL-C, High Density Lipoprotein Cholesterol; IL-6, Interleukin-6; EC, Exercise Capacity

*Spearman's correlation test p value <0.05

** Spearman's correlation test p value <0.01

The relationship among changes on the study variables

- On completion of the study, the declined mean MS score in exercise participants were positively correlated with the magnitude of improvements in TG, SBP, DBP, fasting glucose, IL-6 and HDL-C levels (all $p < 0.05$).
- The decline in IL-6 levels were paralleled with the improvements in the MS score ($r = 0.30$, $p = 0.04$) and HDL-C levels ($r = -0.42$, $p = 0.026$) in exercise group.
- The magnitude of increased exercise capacity was positively correlated with the improvements in HDL-C levels, and waist circumference ($r = 0.31$, $p = 0.04$; $r = -0.35$, $p = 0.02$, respectively) (Table 3).

Table 3. The relationship among changes on the study variables (n=46)

	Δ WC	Δ SBP	Δ DBP	Δ AC	Δ TG	Δ HDL-C	Δ MS score	Δ IL-6
Δ WC	1.00							
Δ SBP	0.13	1.00						
Δ DBP	0.07	0.70**	1.00					
Δ AC	0.11	0.05	0.13	1.00				
Δ TG	0.32*	-0.03	0.13	0.33*	1.00			
Δ HDL-C	-0.26	0.08	0.04	-0.29	-0.57**	1.00		
Δ MS score	0.23	0.31*	0.51**	0.49**	0.49**	-0.42**	1.00	
Δ IL-6	0.20	0.21	0.03	-0.11	0.22	-0.33*	0.30*	1.00
Δ EC	-0.35*	-0.06	0.07	-0.07	-0.16	0.31*	-0.21	-0.02

WC, Waist Circumference; AC, Fasting blood glucose; TG, Triglyceride; HDL-C, High Density Lipoprotein Cholesterol; IL-6, Interleukin-6; EC, Exercise Capacity

* Spearman's correlation test p value <0.05

** Spearman's correlation test p value <0.01

Conclusion & Implication

- In our study, the postmenopausal women mostly are central obesity, have higher mean fasting glucose values and lower mean HDL-C levels.
- There are beneficial effects on the MS score, waist circumference, HDL-C levels, serum IL-6, and exercise capacity in postmenopausal women following a 12 weeks, moderate-intensity (60 to 80% HRR) endurance exercise program.

- Decline in serum IL-6 levels are significantly associated with the improvement in HDL-C levels and MS score in exercise participants.
- Intervention effects on exercise capacity from our exercise training program also help postmenopausal women improving their HDL-C levels and waist circumference.

- Moderate-intensity exercise shall be incorporated into regular daily activities of postmenopausal women to improve their exercise capacity and decrease abnormalities of the MS components.





Thank you for your attention
