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The Effect of Six Months of Aerobic training on Renal Function Markers in Untrained Middle-Aged Women

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Abstract

Purpose: The aim of this study was to investigate the effects of six months of aerobic training on some renal function markers in untrained middle-aged women.
Methods: Nineteen healthy female middle-aged were selected by convenience sampling method and were randomly divided into two experimental (n=11) and control (n=8) groups. The exercise protocol included aerobic exercise training lasted for 6 months and 3 sessions per week and every session lasted for 60 minutes and with intensity of 55-65 percent of maximum heart rate reserve (MHR). Blood samples were taken to measure uric acid, creatinine and BUN before and after aerobic training program .Also, eGFR and BUN-to-creatinine ratio was measured with formula. A general linear-repeated measure was used to comparing of within, interactive and between means groups. The level of significance was set at P< 0.05.
Results: Our results showed the changes of weight, BMI, body fat percent, WHR was not significantly. However, findings showed that Uric Acid in the experimental group increased significantly (P<0/05), but the levels of Creatinine, BUN, and eGFR did not change significant.
Conclusion: Results showed that six months of aerobic training does not induce significant change in estimated Glomerular Filtration Rate and blood Urea Nitrogen, however, if the aerobic exercise training performs in adequate time and intensity and cause the loss of weight and fat percentage, probably can improve the renal function.

Keywords: BUN, Creatinine, eGFR, Exercise, Uric Acid, Women

Introduction

Exercise induces profound changes in the renal hemodynamics and protein excretion. Strenuous exercise provokes a major fall of the renal plasma flow and a reduction of the glomerular filtration rate (Poortmans, 1995). Physical activities by making changes in the liquid mass of the body, body temperature, increasing the nutrition demands, producing fecal materials affect various systems of the body like kidneys (Foran et al., 2003; Gailiūnienė et al., 2007). These alterations after the long period of training can cause changes in Glomerular Filtration Rate and re-absorption mechanisms in a way that affects the renal function markers
Kidneys have an important role in controlling the Osmotic pressure and Electrolytic content. Kidneys are also the main way for excreting the waste products of metabolism including urea, creatinine, and uric acid (Shalmani et al., 2003). Analysis of the levels of nitrogen compositions (creatinine, urea, and uric acid) and estimated Glomerular Filtration Rate in blood reflects the pathological and physiological changes of kidneys and the changes in these indexes after long-term exercising can be a sign of renal function (Poortmans et al., 2001).
The serum creatinine concentration is widely interpreted as a measure of the glomerular filtration rate (GFR) and is used as an index of renal function in clinical practice (Soleimani et al., 2009). Creatinine is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant

rate by the body (depending on muscle mass). During the reaction Creatine to phosphocreatine, catalyzed by Creatine Kinase, spontaneous conversion to creatinine may occur. Creatinine is chiefly filtered out of the blood by the kidneys (glomerular filtration and proximal tubular secretion). There is little or no tubular reabsorption of creatinine (Patricia, 2012). If the filtering of the kidney is deficient, serum creatinine levels rise. The typical human reference ranges for serum creatinine are 0.5 to 1.0 mg/dl (about 45-90 μmol/l) for women and 0.7 to 1.2 mg/dl (60-110 μmol/L) for men. While a baseline serum creatinine of 2.0 mg/dl (150 μmol/l) may indicate normal kidney function in a male body builder, a serum creatinine of 1.2 mg/dl (110 μmol/l) can indicate significant renal disease in an elderly female (Delanghe et al., 1989).

It is known that changes in serum Creatinine during the physical activities depend on the type, intensity and time of exercise. Straznicky et al., (2011) have examined the effects of 12 weeks of aerobic exercise on renal function of men and women and showed that regular exercise have led to decrease in the level of Creatinine; Also, he showed the increase of Glomerular Filtration Rate as well as the aerobic capacity; They stated that moderate weight loss in obese patients is associated with an improvement in GFR which is augmented by exercise co-intervention. However, Banfi and Del Fabbro (2006) administered an investigation on eight groups of elite athletes and observed that the levels of serum Creatinine have increased as a result of their sport training.

Kidney function is assessed best by means of level of glomerular filtration rate (GFR)(Stevens and Stoycheff, 2008). Estimated GFR (eGFR) has become widely adopted in research studies and clinical practice. GFR is difficult to measure directly and therefore usually is estimated from serum levels of endogenous markers. Serum creatinine is the most common measure used to estimate level of kidney function (Lippi, 2008). Based on the findings, effective renal plasma flow is reduced during exercise. The reduction is related to the intensity of exercise and renal blood flow may fall to 25% of the resting value when strenuous work is performed. The combination of sympathetic nervous activity and the release of catecholamine substances is involved in this process (Fauci et al., 2008; Poortmans, 1984). The reduction of renal blood flow during exercise produces a concomitant effect on the glomerular filtration rate (Guyton, Edward, 2006). However, after the physical activities, increasing in the stroke volume and cardiac output increases the renal blood flow and this action leads to excretion of toxic and waste materials and therefore amplification of the eGFR (Wilmore et al., 2007). In terms of the effects of regular physical activities on eGFR, we are faced with contradictions in the studies; Finkelstein et al (2006) stated renal function will improve in athletic as a result of improvement in eGFR (Finkelstein et al., 2006). However Chad et al., (2004) showed with the gradual increase in the speed and intensity of 12-week program exercise of elite cyclists, GFR will be reduce.

A blood urea nitrogen (BUN) test measures the amount of nitrogen in your blood that comes from the waste product urea. The liver produces urea in the urea cycle as a waste product of the digestion of protein. The urea cycle (also known as the ornithine cycle) is a cycle of biochemical reactions occurring in many animals that produces urea ($(NH_2)_2CO$) from ammonia (NH_3). The urea cycle consists of five reactions: two mitochondrial and three cytosolic. The cycle converts two amino groups, one from NH_4^+ and one from Asp, and a carbon atom from HCO_3^-, to the relatively nontoxic excretion product urea at the cost of four "high-energy" phosphate bonds (3 ATP hydrolyzed to 2 ADP and one AMP) (Baum et al., 1975; Macedo, 2011). BUN is an indication of renal health. Normal human adult blood should contain between 7 to 21 mg of urea nitrogen per 100 ml (7–21 mg/dL) of blood. The severe increase of BUN (more than 60mg/dL) indicates minor to acute renal disorders (Clarkson et al., 2008). BUN should be interpreted with respect to creatinine test. Increased of BUN, while the serum creatinine is normal, probably is physiologic response to the decrease of blood flow of the kidney (as a result of dehydration) and not a sign of renal failure. In medicine, the BUN-to-creatinine ratio is the ratio of two serum laboratory values, the blood urea nitrogen (BUN) (mg/dL) and serum creatinine (mg/dL) (Cr). The ratio may be used to determine the cause of acute kidney injury or dehydration. The normal range of this ratio is 10-20 (Finco and Duncan, 1976; Morgan et al., 1977).

Uric Acid is an independent new factor in renal failures (Ficociello et al., 2010; Domrongkitchaiporn et al., 2005); Furthermore, elevations in uric acid and abnormalities in this variable that constitute the metabolic syndrome have been identified as risk factors for cardiovascular disease (Church et al., 2002; Feig, 2008). Also, in humans over half the antioxidant capacity of blood plasma comes from uric acid (Maxwell et al. 1997; Shemshaki et al., 2007). With respect to physical activity and uric acid, previous studies have produced conflicting results. Some groups have reported uric acid concentrations to be inversely related to physical activity, while others have reported no association. Shemshaki et al., (2007) investigated the effects of six weeks of intense alpine skiing exercise on athletes and showed that uric acid increased significantly. However, Tangvarasittichai et al., (2009) showed an eight-week period of progressive exercise training program was associated with a significant decrease in uric acid. Zielijski et al., (2009) also investigated the uric acid concentration

during the training season of endurance runners and indicated that uric acid changes was not significant.
There have been only limited reports examining the association between renal function and fitness or physical activity. Moreover, to our knowledge, most results of the studies are reported based on urine tests and serum indexes concentrations are considerably few. Therefore, the aim of this study is to investigate the effect of six months of aerobic training on renal function in untrained middle-aged women.

Materials and Method

Subjects

This study was semi-experimental. Furthermore, it plan was confirmed by Research Assembly of Physical Education and Sport Sciences Faculty of Ferdowsi University of Mashhad. During first stage, the subjects of this study were nineteen healthy and inactive female who randomly assigned into the experimental (n=11) and control (n=8) groups. Before starting the program, written informed consents were taken from all subjects. The levels of health and physical activity of the subjects were determined using general practice physical activity questionnaire, physical activity readiness questionnaire and medical survey (including electrocardiogram and blood pressure tests) by a specialist physician. The subjects were nonsmokers, received no drugs and had no metabolic disease and physical impairment affecting their performance. During the second stage, their height was measured in centimeters using a height determiner and their weight was calculated using a digital scale produced by a German company called Beurer (PS07-PS06). The percent of body fat (PBF) was calculated using a body compound determiner (model In-body-720 made in Korea) and based on a method called bioelectrical impedance. All of these measurements were carried out while the volunteers had stopped eating or drinking 4 hours prior to their test, and their bladder, stomach, and bowels were empty.

Exercise protocol

The exercise protocol included aerobic exercise training lasted for 6 months and 3 sessions per week and every session lasted for 60 minutes and with intensity of 55-65 percent of maximum heart rate reserve (MHRR). According to the MHRR for every single athlete was respectively calculated based on Karvonen equation (1) and was also controlled during exercise by a heart rate monitor (made in Finland–Polar).
Equation [1]: Target heart rate= [%60 or %70+[(age-220) - (resting pulse]] + Resting heart rate

Blood sampling

Blood sampling was done in the lab, two times for pretest and posttest, respectively 48 hours before and 48 hours after the six months of aerobic exercise training program. Both sampling were taken in fasting condition. Blood samples in all related studies were collected by venepunction from forearm vein after at least 15 minutes of sitting at rest or in the supine position. Blood sample were poured into a tube containing K2EDTA and mixed for 15 min before analysis. After centrifusing samples in plastic capillary tubes using Haemato Spin Centrifuge device. Serum Creatinine concentrations was determined through Japha method and by RA1000 device. Plasma Uric Acid concentration was determined by using Pars-Azmun kits (sensitivity of 0/3 mg in dl) with enzymatic colorimetric method; Measurement of the serum BUN concentration was done with the enzymatic colorimetric method.
Calculation of the GFR by using MDRD formula was done (McManus et al., 2007):
GFR (ml/min per 1.73 m^2) = 186 × [serum CR (mg/dl)] – 1.154 × [age] – 0.203 × [0.742 if female]

Statistical analysis

All statistical analyses were performed with SPSS version 15. The average and standard deviation of data were calculated after checking the data distribution normalcy using Kolmogorov-Smirnov test and Homogeneity of variance method. The comparison of between means groups and Homogeneity of groups examined using Independent *t* test. Repeated measure for comparison of variance within the group, interaction (groups × phases) and between group was used. The level of significance was set at $P < 0.05$.

Results

According to the (Table 1), our results showed the changes of weight, BMI, body far percent, WHR was not significantly. Results showed a variance between group WHR is significant ($P<0.05$).

Table 1: Comparison of within group variance and between group of body composition in Untrained Middle-Aged Women

Variables	Groups	Pre-test M±SD	Post-test M±SD	Within groups F	Within groups P-value	Between groups F	Between groups P-value
Weight (kg)	Exercise	64.85±5.83	64.70±5.76	1.25	0.27	1.70	0.20
	Control	61.37±7.84	61.36±7.84				
BMI (kg/m^2)	Exercise	26.94±2.84	26.43±2.58	0.59	0.44	0.99	0.32
	Control	25.44±2.84	25.67±2.51				
PBF(%)	Exercise	36.27±5.62	36.02±5.54	0.05	0.82	0.09	0.76
	Control	35.31±6.14	35.52±6.20				
WHR	Exercise	0.84±6.50	0.83±7.86	1.70	0.20	6.96	0.01*
	Control	0.76±6.64	0.76±6.36				

*A significant level *P*<0.05 *Data presented as mean ± standard deviation

In Table 2, the variables of uric acid, creatinine, BUN, eGFR and BUN-to-creatinine ratio are shown in control group and experimental group in pretest and posttest phases. As it is shown only the uric acid concentration in the experimental group increased significantly (P<0/05), and our results showed the changes of creatinine, BUN, and GFR was not significantly.

Table 2: Comparison of within group variance and between group of variables (uric acid, creatinine, BUN, eGFR and BUN-to-creatinine ratio) in Untrained Middle-Aged Women

Variables	Group(s)	Pre-test M±SD	Post-test M±SD	Within groups F	Within groups P-value	Between groups F	Between groups P-value
Uric Acid (mg/dl)	Exercise	4.49±0.56	4.82±0.49	5.747	0.037	0.001	0.979
	Control	4.51±0.60	4.74±0.32				
Creatinine (mg/dl)	Exercise	0.72±0.08	0.74±0.06	2.219	0.167	0.622	0.440
	Control	0.72±0.09	0.73±0.04				
BUN (mg/dl)	Exercise	14.71±1.62	14.60±1.00	0.111	0.745	4.857	0.039
	Control	14.40±1.35	14.36±0.93				
eGFR	Exercise	86.98±16.03	91.55±12.09	2.219	0.167	0.418	0.248
	Control	83.85±14.51	85.71±6.73				
BUN to Creatinine ratio	Exercise	20.44±2.16	19.56±1.31	3.048	0.111	2.616	0.121
	Control	20.11±1.41	19.69±0.98				

*A significant level *P*<0.05 *Data presented as mean ± standard deviation

Discussion and Conclusion

In the present study, no statistically significant difference was observed in exercise group subjects' body weight, body mass index and body fat percent.
Also, in present study, uric acid significantly change after the exercise program The results from the present study are consistent with findings of Shemshaki et al., (2007) and Brites et al(1999), however, it is not consistent with findings of Lamina et al., (2010) and Wang et al., (2007). One of the main causes of increasing uric acid can be its anti-oxidation properties. Shemshaki et al., (2007) showed intensive alpine ski training after six weeks can increase total antioxidant capacity of plasma probably by increasing through uric acid concentration and concluded that physical exercise is a

double-edged sword: when practiced strenuously it causes oxidative stress and cell damage; But when practiced in moderation, it increases the expression of antioxidant enzymes and thus should be considered an antioxidant. On the other hand, Lamina et al., (2010) determine the effect of continuous low intensity training program on serum uric acid level in male subjects with hypertension and findings of this study revealed significant effect of interval training program on decreasing serum Uric Acid concentration; He explained that it was due to the reduction of Carbonyl protein. Carbonyl protein is regarded as an oxidation index of proteins that is reduced after regular aerobic exercises. Lack of consistency of Lamina`s findings and the present research might be because of difference between the training program and condition of the participants.

In this study, Blood Urine Nitrogen (BUN) concentration and BUN to creatinine ratio decreased but did not significantly change after the exercise program. Results of the present study is consistent with findings of Chad et al., (2004), Rafati Fard et al., (2011), however, is not consistent with findings of Lin et al., (2011) and Li et al., (2012). The reason for not observing significant difference in the results of this study can be associated with the training program and activity type as well as environmental conditions and human race. Lin et al., (2011) showed that regular physical activity leads to the reduction of BUN levels and serum Creatinine and consequently improves the renal disorders. Li et al., (2012) investigated biochemical changes responses to low-volume pre-competition swimming training for elite swimmers and showed that the level of was significantly increased for both male and female swimmers; He stated that high level of blood urea reveals that protein catabolism becomes the dominant biochemical process in the body of the swimmer, which may have a negative impact on the body energy storage and disorder the process of glomerular filtration rate.

The present study also showed that six months of aerobic training did not significant change in the serum creatinine concentration and eGFR of the participants. Findings of Zophel Klaus et al., (2005), Leehey et al., (2009) and Hosseini Kakhk et al., (2011) are consistent with the findings of the present study. However, it is not consistent with the findings of Banfi et al., (2006), Levent et al (2004), and Kargotich et al., (1997). Kargotich et al., (1997) reported that increasing in the levels of serum creatinine is due to the reduction of renal blood flow. Hosseini Kakhak et al., (2011) showed that eight weeks of aerobic training had no significant effect on renal function markers (creatinine and eGFR) in obese girls. It seems that, probably, in obese people, weight loss is a requisite for improvement of kidney function. Studies show both in kidney patients and in healthy obese people, improvement of renal function markers requires the reduction of BMI. It has been proved that increased BMI is strongly associated with decreased eGFR (Kawamoto et al., 2008; Iseki, 2006).

Findings of the most studies show that the increase of eGFR and decrease of BUN improves the renal function. It is while the findings of the present study showed that six months of aerobic exercise could not significantly change the eGFR and BUN. It seems that in order to improve the effect of training, it is necessary to perform training programs with adequate duration and intensity (lead to weight loss). Furthermore, having a proper diet with the training program may have better effects on renal function.

Ethical considerations:

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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