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Effects of aerobic exercise on Cystatin C and metabolic syndrome in females with transplanted kidney

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ABSTRACT

Chronic kidney disease is a significant general disease, which affects a large number of people around the world. If kidney function and glomerular filtration rate decline, the blood levels of cystatin C (Cys C) rises. Also studies showed that metabolic disorders are very common among recipient of a transplanted kidney (TK). The aim of this study was to determine the effects of eight weeks of aerobic exercises on Cys C and metabolic syndrome (Mets) in females with transplanted kidney. 20 females with transplanted kidney age of 24.3 ± 2.5 years participated. Subjects were divided into two equal groups. Prior and after study both groups underwent a blood test to check Cys C and metabolic syndrome. The experimental group conducted eight weeks of submaximal activities and 3 sessions each week. To analyze the data independent and dependent t-test were used. To validate if the data distribution is normal, Kolmogorov-Smirnov test was utilized. The results show experimental group had decreased their TC (0.026), TG (0.002), FBS (0.026) and SBP (0.024) and increase of HDL (0.003), however there were no Differences between both groups for all aforementioned factors but for TG (0.031). Also there were no changes of Cys C (0.899), WC (0.896) and DBP (0.081). According to the results we can express eight weeks of aerobic training does not have a significant effect on Cys C while decreases Mets. So it can be concluded that aerobic exercise is useful for females with KT.

Keywords: Cystatin c, metabolic syndrome, aerobic exercise, transplanted kidney.

INTRODUCTION

Chronic kidney disease is a significant general disease, which affects a large number of people around the world. Patients suffering from this disease are exposed to an advanced form of kidney disease that results in dialysis and kidney transplantation (KT)¹. Kidney dysfunction increases the risk of death and cardiovascular disease, reduced muscle mass, attenuated muscle strength and power, and an apparent decreased tolerance to exercise²⁻⁴. In order to estimate the health status of kidney, it is possible to estimate the glomerular filtration rate (GFR) by serum creatinine. However it is not precise, so other substances, such as CYS C, are being explored to estimate GFR⁵. CYS C, a non-glycosylated 13 kDa protein, has the potential to improve estimates of GFR, because it is thought to be less influenced by muscle mass or diet.^{6,7}

CYS C has been reported as a simple and early marker of renal damage and a predictor of cardiovascular mortality beyond classical risk factors in patients with cardio artery disease (CAD)⁸⁻¹⁰.

Also, it seems that the relationship exists between CYS C and type 2 diabetes. Studies have shown increased levels of Cys C in patients with the Mets^{11,12}; increase the risk of diabetes and CKD¹³⁻¹⁶.

Mets is a disorder of energy utilization and storage, diagnosed by a co-occurrence of three out of five of the following medical conditions, waist circumference (central obesity), elevated blood pressure and elevated fasting plasma glucose, high serum triglycerides, and low high-density lipoprotein cholesterol (HDL-C) levels¹⁵.

Aerobic exercise has been shown to improve renal and cardiac function in individuals with chronic kidney disease (CKD)¹⁷. Serin et al (2009) studied CYS C serum level after submaximal exercises. The results showed a six weeks submaximal exercise does not have an effect on kidney performance¹⁸. Baxman et al (2008) studied body composition and activities effect on urinary creatinine and CYS C. They concluded that Serum and urinary creatinine correlated significantly with body weight, but the level of correlation with lean mass was even greater. There was no significant correlation between body weight and lean mass with CYS C. Conversely, mean serum CYS C did not differ between active and inactive groups¹⁹.

Studies show that kidney damage probability rises with the increase of metabolic disorders and Mets is very common among recipient of transplant kidney²⁰⁻²².

Evidences show that participation in regular, moderate-intensity physical activity may be a preventive intervention of the Mets and that activity of greater intensity may provide even greater benefit^{23,24}.

According to the fact that the recent evidences prove that Mets is related with high risk of exposure to CKDs, and because of the rise in recent decades of CKD incidence and its

Associated with cardiovascular risks and damage thus the growing epidemic of obesity and old societies, Mets and CKD are considered as health problem globally²⁵. Furthermore, there are few, if any, randomized control trials that have been published examining the effects of exercise on changes in CYS C and Mets in females diagnosed with kidney transplantation (KT) especially in Iran, the purpose of this study was to investigate the effect of aerobic exercise on changes in CYS C and Mets components as risk factors of kidney.

MATERIALS AND METHODS

Subjects characteristics

Twenty inactive females voluntarily with average age of 24.3 ± 2.5 years with TK from Association of Specific Patients and Organ Transplant of Shiraz Iran participated in the study. Subjects with TK complications that prohibited participation in exercise and smokers were excluded from the study. Subjects were not engaged in any systematic exercise programs at least 6 months before the study. They take anti- immunity medications of Mycophenolic acid(1500 mg per day) and Cyclosporine (100mg per day).

Written informed consent was obtained from each subject prior to participation. The subjects were informed of the protocol and the possible risks and difficulties of the study. Subjects were divided into two similar groups' experimental and control based on their BMI. The study was approved by the ethics Committee of Islamic Azad University, Fars science and research branch.

Cys C and Metabolic syndrome measurement

Blood samples were obtained in the morning after 8-12 hours fasting a day prior to the start of the study and again 8 weeks after at the end of the study under the same conditions. CYS C was evaluated by enzymatic kits (Poway Model US Diazyme laboratories mg/dl). The definition of Mets was based on the presence of three or more components out of five defined criteria for metabolic syndrome by the amended National Cholesterol Education Program's Adult Treatment Panel III (ATP-III)¹⁷. The ATP-III criteria include (1) waist circumference > 88 cm (women); (2) SBP > 130 mmHg, DBP > 85 mmHg, or use of antihypertensive medications (3) fasting plasma glucose > 110 mg/dl or use of diabetes medications; (4) fasting triglycerides > 150 mg/dl or lipid medications and (5) HDL cholesterol <50 mg/dl (women). Serum triglyceride levels was measured by enzymatic kits (Mann Chemical Company) using an auto analyzer. HDL-C was measured by an Auto analyzer using commercial kits (Pars Azema Company, Teheran, Iran). Serum fasting blood sugar levels was measured by Selectra-E auto analyzer using an enzymatic kit (Mann Chemical Company).

Anthropometric and Blood Pressure Measurements

All anthropometrical measurements were done with the subjects wearing light underwear and without shoes. Body weight was measured to the nearest 0.5 kg; using digital scale (made in Germany). Height was measured to the nearest 0.5 cm against a wall mounted tape. Body mass index was calculated by dividing the weight in Kilograms by height in meters squared and according to World Health Organization²⁶. Central obesity was measured in centimeters at the midpoint between the iliac crest and the rib cage using a non- stretchable tape without compression of the skin and defined on the basis of waist circumference (WC). Blood pressure was measured on the right arm after resting for 10 min in the supine position, using the standard mercury sphygmomanometer pre and post study²⁶.

Protocol of study

The experiment group involved in eight weeks of exercise, 3 sessions a week with 55-70 percent of maximum heart beat rate. The exercise program of each session included 10 minutes of warm-up, 30 minutes running, and at the end of each session, cool down for 10 minutes was done. 55-60% of maximum heart beat rate, for the first two weeks, 60-65% for the next 3 weeks, and 65-70% for the last three weeks. The experimental group did not involve in any other exercise aside from the program. Control group underwent the same testing battery but did not participate in any exercise training during eight weeks of study. The protocol was designed by researchers.

Statistical Analysis

Methods: In this randomized clinical trial study data were analyzed using descriptive statistics (mean and standard deviation) and statistical method of covariance analysis. Also in order to validate if the data distribution is normal Kolmogorov-Smirnov test was utilized. Statistical significance was set at ($p < 0 / 05$). Data were analyzed using SPSS version¹⁸.

RESULTS AND DISCUSSION

In total 20 subjects with KT participated in this study. There were no significant differences between groups for any of the variables at baseline. Following the exercise experimental group had significantly decreased their TG (0.002), FBS (0.026) and SBP (0.024) and increase of HDL (0.003), however there were no Differences between both groups for all aforementioned factors but for TG (0.031). Also there were no changes of Cys C (0.899), WC (0.896) and DBP (0.081) following exercise (table 1).

Table 1: Pre and post study of Anthropometric and Blood Biochemistry Factors of Subjects

GROUP VARIABLES	Control		Experimental	
	Pre Exercise	Post Exercise	Pre Exercise	Post Exercise
Age(year)	23.9±2.6	-	24.4±2.5	-
High(cm)	162±2.4	-	161±4.2	-
Wight(kg)	59.5±4.02	58.9±4.6	57.9±1.8	56.5±3.6
BMI(kg/m ²)	23.8±1.2	23.7±3.6	23.6±2.1	22.1±1.8
WC	89±0.07	90±0.07	89±0.05	89±0.03
Cys C (ng/mL)	973.2±10.08	959±9.26	0.62±0.29	0.61±0.25
TG(mg/dl)	144±5.4	151.2±5.9	145.2±7.2	138.8±6.9
SBP(mmHg)	134±6.9	132±7.8	131±6.7	122.5±5.2
DBP (mmHg)	81±3.1	82±4.8	79±3.03	77±4.07
HDL-C(mg/dl)	39±2.1	41±2.6	39±2	44±4.27
FBS(mg/dl)	105±9.4	107±8.8	106±7.03	100±6.07

Chronic kidney disease is developing and it is associated with various diseases including cardiovascular disease, metabolic syndrome and mortality, especially in patients with kidney transplantation²⁷.

SO the aim of this study was to investigate the effect of aerobic exercise on Cys C and Mets in patients with KT as risk factors of CKD.

The study showed a significant effect of aerobic training on SBP, TC, TG, HDL-C and FBS. Although there were no significant effect on Cys C, DBP, and WC.

Serin et al (2009) studied Cys C serum level after submaximal exercises. The results showed there was no change before and after the exercise period and the researchers stated that 8 weeks of aerobic training does not have an

effect on Cys C and kidney performance¹⁸. Baxman et al (2008) studied body configuration and activities effect on urinary creatinine and Cys C. They reported that Cys C is not affected by physical activity which is the same as our results¹⁹. On the other hand Pechter et al (2003) analyzed Cys C serum level after 12 -week of regular low-intensity aquatic exercise. They reported that aquatic exercise decreases Cys C and creatinine²⁸.

Table 2: Comparative analysis of covariance the variables in females with kidney transplants

Variables	Test stages	F value	P value
Cys C(ng/ml)	Pre and post test	10.55	0.06
	Between groups	/002	0.899
FBS(mg/dl)	Pre and post test	5.54	0/026*
	Between groups	0.113	0.699
HDL(mg/dl)	Pre and post test	12.83	0.003*
	Between groups	3.01	0.163
TG(mg/dl)	Pre and post test	88.76	0.002*
	Between groups	6.01	0.031*
WC (cm)	Pre and post test	9.05	0.08
	Between groups	9.77	0.768
SBP(mmHg)	Pre and post test	65.12	0.024*
	Between groups	0.122	0.621
DBP	Pre and post test	12.46	0.081
	Between groups	.1.01	0.896

P sig <0.05

The difference between results of Pechter et al study and our study could be for the difference between the intensity and duration of exercise, and also because our subjects were patients with KT and Pechter et al were renal patients. Also their exercise was aquatic exercise and ours was land exercise. It seems water immersion improve renal function, probably due to an improvement in renal hemodynamics associated with decreases in vasopressor and increases in vasodepressor hormones^{29,30}.

Also our analyzed shows that aerobic training is associated with lower risk of Mets among females with KT. A number of studies have showed correlations between metabolic syndrome and CKD³¹. Chen *et al* (2004) found that having metabolic syndrome results in a 2-fold higher chance of developing CKD compared with the general population³².

According to our study aerobic training appeared to have beneficial effects on individual components of Mets including TC, TG, HDL and FBS as well as systolic blood pressures. However some studies have shown effect only on some of Mets components³³.

Although our results were not significant in either group. One of the reasons could be the use of drugs like anti-immune system for organ transplantation, such as cyclosporine, as most studies state that Cyclosporine has side effects such as increase TC and TG levels³⁴.

Another common issue after transplantation is the increase in blood pressure²⁰.

High blood pressure results in nephrosclerosis, through dependent on or independent mechanism. In patients suffering from high blood pressure and urinary protein excretion, GFR declines which means that even a slight increase in blood pressure can expose these patients to kidney damage^{27, 35, 36}. Our results are consistent with study of Pechter et al (2003). They reported that a 12-week low-intensity aquatic exercise program in 26 patients with mild to moderate chronic kidney disease resulted in decreased blood pressure, decreased proteinuria, and a slight improvement in GFR^{28,37}.

A possible mechanism for the effect of aerobic exercises on blood pressure reduction is through its effect on reducing body weight, which is justified by the performance and structure changes in vascular system, Renin-angiotensin system modifications and sympathetic nervous system reduction³⁸.

Blood glucose increase after transplant operation is more. The results of studies including current study show physical activity decreases blood glucose, so can say physical activity play an effective and efficient role in blood glucose reduction^{39, 40}. It is worth highlighting that regular physical activity is critically important for prevention of

the Mets and its components in both early life and later life. Evidence is beginning to accumulate in the epidemiological literature which suggests that participation in physical activity may alter all metabolic risk factors as well as KT.

CONCLUSION

Eight weeks of aerobic exercise does not have a significant effect on Cys C on females with KT, while decreases Met S components. Thus, according to the fact that the Met S components increase after the transplant and can have negative effects on kidney performance in long-term, therefore, according to the results of the study can say aerobic exercise effect on these components. It seems that Syc C is also affected by aquatic activity, and the land activity has no effect on Syc C, however there should be more studies with various exercise types, duration and intensity in order to present proper solutions for patients, as well as increasing the knowledge.

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