Clinical Characteristics change and the Heart Rate variability of Subjects with Metabolic Syndrome in the Weight Loss Program

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Abstract—The purpose of this study was to evaluate whether a weight loss program, including nutrition education and physical fitness, has a positive effects on heart rate variability (HRV) in subjects with metabolic syndrome. Twelve female volunteers with metabolic syndrome, who aged between 30 and 60 years, and resided at Jiantan, Taiwan, were studied. All subjects participated in the weight loss program for 3 months comprised of the nutrition education and aerobic exercise (three times a week). The blood tests and HRV of subjects were determined, and the data were analyzed statistically using dependent sample *t*-test. The results of this study showed that the average of the waist circumference and the level of fasting plasma glucose and total cholesterol was significantly reduced in all subjects after having a 3-month weight loss program (*P*<0.05). Moreover, the three parameter values (total power, high frequency and low frequency) of HRV in those subjects increase significantly, compared to their baseline values (*P*<0.05). In our study, we concludes that a 3-month weight loss program combined with the nutrition education and aerobic exercise improves the body composition, the value of fasting glucose, the level of total cholesterol and the function of autonomic nervous system in the subjects with metabolic syndrome.

Keywords—weight-control program; metabolic syndrome; heart rate variability; nutrition education; aerobic exercise

I. INTRODUCTION

Metabolic syndrome (MetS, also known as Syndrome X) is characterized by a cluster of metabolic risk factors including elevated blood pressure and sugar levels, insulin resistance or glucose intolerance, and blood fat disorders [8]. The concept of metabolic syndrome has existed since 1920s and it was firstly described by Kylin, a Swedish Physician, as the syndrome involving hypertension, hyperglycaemia, hyperuricaemia and gout [17]. In 1988, the metabolic syndrome was firstly recognized as a unique clinical entity because Reaven proposed Syndrome X which described the association of multiple risk factors for cardiovascular diseases and insulin resistance [25].

Resnick *et al.* has shown that metabolic syndrome (MetS) is a predictor of cardiovascular diseases and diabetes [26]. In their study, 2283 nondiabetic American Indians (AI) without cardiovascular diseases and diabetes were examined. The incidence of diabetes and CVD in the nondiabetic AI with MetS was 1.9-fold and 1.35-fold, respectively, higher than that in whom without MetS after over 7 years of following-up [26]. In another population-based study, Trevisan *et al.* illustrated that the mortality from all causes, CVD, coronary diseases is 1.95-fold, 2.49-fold, and 3.01-fold in men and 2.54-fold, 15.91-fold and 17.75-fold in women with MetS, compared to those in men and women without MetS after age-adjusted models [31]. Thus, MetS leads to increase the incidence of chronic diseases and significantly associated with a high risk of CVD mortality [11].

Weight-loss intervention is the key to improve some or every aspects of metabolic syndrome [9, 29]. Rosenbaum *et al.* proposed that the combination of increased frequency of exercise and reduced intake of energy can be more efficient to achieve the goal of weight-loss [27]. In the study of a 6-month weight-loss program including dietary modifications and exercise training was introduced to 95 obese participants. Among them, the average weight, BMI and all risk factors of MetS was significantly reduced in 63 participants and the rate of MetS in the subjects before and after the study was declined from 54% to 37% [4].

Not only MetS is commonly used to predict the CVD, but also heart rate variability (HRV) was found to be associated with CVD. HRV analysis is a noninvasive method to evaluate the effect of the autonomic nervous system on heart-bets. HRV is an independent and strong predictor of acute myocardial infarction mortality [3, 12]. During 1960-1990, 878 Dutch men, aged 40-60 years, were studied and followed to examine the mortality of all causes using HRV method [7]. They showed that the mortality from all causes in the middle-age and elderly men with low HRV increases by 1.4-fold and 2.1-fold, compared to that in those with high HRV [7]. Furthermore, it is proposed that low HRV may be predictive of the risk of death because the value of HRV is lower in people who are obesity, MetS, diabetes and hypertension than that in the healthy people [13]. Hence, the intervention study of physical activity may benefit the function of autonomic nervous system as well as improve the autonomic disturbances after weight reduction.

To sum up, MetS correlates closely with chronic diseases. Moreover, it has been shown that the function of autonomic nerves system of healthy or obese subjects can be improved by the intervention of exercises and weight reduction. However, it is little known that whether the weight-loss program together with physical activities influence the function of autonomic nerves system in subjects with MetS. Therefore, in the present study, we investigated the effects of weight-loss program comprising nutrition and exercise on the clinical characteristics and HRV in the subjects with MetS.

II. MATERIALS AND METHODS

A. *Subjects*

Sixty-six volunteers were recruited from Jian-Tan community (Zhoungshan District, Taipei). Participants were aged between 30 and 60 years with body mass index (BMI) $\geqq$24, and none of them had cardiovascular diseases. The nature, purpose, and the potential risks of this study were explained to all subjects before participation in the study. The study protocol was approved by Ethics committee, National Taiwan Sport University, and all subjects gave written informed consent. At the beginning of the 3-month study period, all participants underwent a physical examination, blood analysis, HRV test and MetS diagnosis. Participants who had incomplete data for variables defining the MetS and poor attendance at the exercise training sessions of the study were excluded. After all exclusions, 12 female subjects with MetS were eligible.

B. *Definitions of Metabolic Syndrome*

The metabolic syndrome was defined according to the criteria of Bureau of Health Promotion, Department of Health, ROC (Taiwan) [5]. From baseline examination, MetS was diagnosed when at least 3 of the following criteria were met: a) central obesity (waist circumference $\geqq$ 90 cm in men or $\geqq$ 80 cm in women); b) hypertriglyceridemia ($\geqq$ 150 mg/dL); c) low high-density lipoprotein cholesterol (HDL-C; < 40 mg/dL in men or < 50 mg/dL in women); d) high blood pressure ($\geqq$ 130/85 mm Hg or use of antihypertensive medication); and e) impaired fasting glucose ($\geqq$ 100 mg/dL, or use of diabetes medication).

C. *Weight-Loss Intervention*

Weight-loss intervention consisted of nutrition education and aerobic exercise training program. Nutrition education program was given by professional nutritionists. The purpose of this program was to instruct the participants in the strategies of dietary modulations, focusing on making healthy food choices, understanding and estimating caloric content of foods, and using dietary record. All participants received seven 60-minute sessions of the nutrition education program. The following topics were included in the program: a) healthy diet b) healthy eating on festivals and special occasions, c) weight-loss and eating out, d) weight-loss through balanced diet, e) estimating your caloric intake, f) the use of dietary record, and g) calcium-rich diet.

All aerobic exercise training sessions were supervised by an exercise physiologist and were conducted at the National Taiwan Sport University. The exercise training session was conducted for one hour, two times per week for 3 months. In brief, a 5-minute warm-up session was conducted in a fitness studio, followed by a 50-minute aerobic exercise and a 10-minute cold-down period. Participants were exercising at 55-89% of the maximum heart rate, corresponding to their maximum heart rate, or 12-16 of the score of rating of perceived exertion (RPE) [1]. In addition, participants used the talk test to monitor their exercise intensity levels during each exercise session. Participants were excluded when they were absent in the exercise training sessions for more than 3 times. Apart from 2 times per week exercise sessions in the fitness studio, participants were also encouraged to do more exercise individually at home. Therefore, exercise frequency should be at least 3 times per week during the 3-month intervention.

D. Laboratory Measurements

Blood samples were taken from participants at the beginning and the end of the 3-month nutritional and exercise intervention period. The participants were asked to fast for a minimum of 10 hours before the blood sampling, which was conducted in the morning from 08:00 to 10:00. Five milliliters of venous blood sample were collected from each participant. Venous blood samples were then transferred to centrifuge tubes immediately and spun for 10 minutes at 1500×g. After centrifugation, plasma samples were collected and stored at –20°C until analysis. Plasma lipid profiles, such as total cholesterol (TC), triglyceride (TG) and HDL-cholesterol (HDL-C), were determined using standard enzymatic methods. Furthermore, plasma glucose levels were estimated using the glucose oxidase autoanalyzer method (Life Scan II, California, USA).

E. Heart Rate Variability Test

After the blood sampling, participants were maintained at rest for 15 minutes and the HRV test was carried out in a climatically controlled room at 22–23°C. All participants were advised to have normal night’s sleep and not to consume caffeinated and alcoholic beverages 24-hour before the HRV test. The procedures for HRV test have been explained elsewhere in detail [16, 18]. HRV was analyzed using frequency domain method. Parameters of frequency domain analysis were total power (TP), very low frequency (VLF), low frequency (LF), high frequency (HF), HF and LF power in normalized units, and LF/HF ratio, as has been described previously [15]. The HF band considers the frequencies between 0.15~0.4Hz to reflect mainly parasympathetic activity, while the LF band considers the frequencies between 0.04 Hz and 0.15 Hz to reflect mainly sympathetic activity. Furthermore, LF and HF were estimated in normalized units and the LF to HF ratio was estimated as a measure of autonomic balance (sympathetic to parasympathetic) [30].

F. Anthropometric Measurements

Waist circumference was measured at the minimum circumference between the lower border of the rib cage and the superior border of the iliac crest using an anthropometric table, while the participants were wearing light clothing. Bioelectrical impedance analysis (BIA) was used to estimate body composition. The estimate was obtained using a Tanita TBF-521 body composition analyzer digital scare following manufacturer's recommended protocol and the body weight was measured at the same time (Tanita Corporation, Arlington Heights, IL, USA).

Body Mass Index (BMI, in kg/m^2) was also calculated. Before body composition measurements were taken, participants were asked not to have hard exercise or lots of water, and wear socks. Systolic and diastolic blood pressure was measured on seated participants, after a 5-min rest, using an Omron HEM-712C automatic blood pressure monitor (Omron Healthcare, Inc, Bannockburn, IL, USA) and an adapted cuff size.

G. Statistical Analyses

Data are presented as means ± SD. Statistical analysis were performed using SPSS Software Version 12. Comparisons of data between pre- and post-intervention were made by dependent *t*-test. Statistical significant was assigned at $P < 0.05$.

III. RESULTS

The 12 subjects whose data make up this study had means ± SD age of 51.66 ± 9.24 years and height of 158.39 ± 4.54 cm (data not shown). The physical characteristics and blood tests of the participants at baseline and after the 3-month intervention period were outlined in Table I. Significant reductions in weight, BMI, percentage of body fat and waist circumference were seen in the participants after the 3-month nutrition and exercise intervention (weight pre 69.71 ± 8.50 kg, weight post 65.09 ± 8.30 kg; BMI pre 27.76 ± 2.88, BMI post 26.29 ± 3.20; % body fat pre 34.53 ± 5.40%, % body fat post 31.38 ± 5.57, all above variables $P = 0.0001$; waist pre 88.03 ± 9.34 cm, waist post 83.58±9.78 cm, $P = 0.001$). As expected, the effects of the weight loss interventions on body composition and metabolic risk factors have been demonstrated previously [22]. Regarding the effects of the nutrition and exercise intervention on the plasma lipid parameters, only TC level significantly decreased from 218.19 ± 35.98 to 190.25 ± 14.45 mgdL^{-1} ($P = 0.01$) in the participants. Furthermore, the fasting glucose of participants was significantly reduced after the intervention compared to the baseline ($P = 0.02$; Table I). However, there was no significant difference in both systolic and diastolic blood pressure after the 3-month nutrition and exercise training programs when compared with the baseline levels ($P > 0.05$; Table I).

Table II depicts the results of the HRV analysis in participant before and after the study. Weight-loss program via nutrition education and exercise training significantly affected VLF, LF, HF, and TP values in participants after the 3-month intervention period. A significant increasing of VLF (from 5.44 ± 0.93 ms^2 to 6.35 ± 1.16 ms^2, $P = 0.03$), LF (4.68 ± 0.95 ms^2 to 5.41 ± 0.65 ms^2 $P = 0.02$), HF (from 4.39 ± 1.35 ms^2 to 5.24 ± 0.81 ms^2, P =0.01), and TP (from 6.28 ± 0.79 ms^2 to 7.07 ± 0.89 ms^2, $P = 0.01$) were noted at the end of the intervention. However, no changes were observed in the other HRV parameters (i.e., LF or HF power in normalized unit, and LH/HF ratio) ($P > 0.05$; Table II).

IV. DISCUSSION

The result of this study indicated that the three-month intervention of both nutrition education (focusing on dietary counseling) and physical activity (three times per week) were effective to lower the MetS parameters, such as the percentage of body fat, BMI, waist circumference, and the levels of the TC and fasting glucose. However, there were no significant changes found in the diastolic and systolic blood pressures, and the levels of TG and HDL-C. Our finding suggested that the strategy aimed at reducing weight through the introduction to the nutrition education and physical activity benefiting the alteration of the body composition indices for the participants with MetS.

The results were consistent with previous studies, indicating that the counseling on diet and exercise training greatly improve the body composition of obese adults [20, 23]. In addition, our findings revealed a marked decrease in BMI and waist circumference, suggesting that our approach to reducing the weight of participants with MetS can be a good strategy to result in losing abdominal visceral fat. MetS is a complex cluster of cardiometabolic abnormalities, and the loss of abdominal visceral fat may improve MetS because abdominal visceral fat is one of the risk factors to identify MetS [28]. In contrast, the increase of abdominal visceral fat has been found to correlate with the increase of cardiometabolic risks [28]. Although the level of abdominal visceral fat is not estimated in this study, all anthropometric measures such as BMI, the percentage of body fat, and waist circumference, have been commonly used as predictors of abdominal visceral fat [14, 24]. Among those predictors, waist circumference has been identified as the best one [24]. Therefore, it can be deduced that the abdominal visceral fat of MetS participants in our study may be reduced by three-month weight loss intervention.

Obesity and the raise of plasma lipids, such as triglyceride and cholesterol, are the risks of CVD which can be moderated by weight loss. Body weight has been considered as a significant factor in determining the synthesis of blood cholesterol in the context of obesity [32] and overweight is positively associated with the cholesterol synthesis rate [21]. Our finding showed that the intervention of nutrition education and aerobic exercise led to decreases in weights and total cholesterol levels in the participants with MetS. This finding is consistent with the observation showing that the decline in total cholesterol level is attributed to weight loss [6]. However, the mechanism through which weight loss decreases the blood cholesterol level remains to be clearly illustrated. Nevertheless, few explanations have been addressed by different research groups. One study proposes that despite both liver and adipose tissue being able to synthesize cholesterol, the excess dietary cholesterol may suppress the capacity of cholesterol synthesis in the adipose tissue [32]. Hence, in this condition, the synthesis of cholesterol may be more likely to take place in the liver or intestine [32]. Another research by Bennion and Grundy indicates that the wegiht loss has been found to cause an elevated secreation of cholesterol in bile acid resulting in lowering blood cholesterol levels [2]. Addiotnally, the elevated level of blood triglyceride is linked to excess weight [10]. In our study, there was no significant reduction in the levels of TC (from 134.19±40.11mg/dL to 105.31±31.20mg/dL). This finding is opposite to the results reported by Lokey and Tran [19], finding the decreases in the levels of TC and TG following a weight loss program. This discrepancy might be accounted for by the differences in the degree of weight loss or the participants. The weight loss in people with MetS, to some extent, requires further investigations on the improvement of their concentrations on TC and TG.

In conclusion, this study demonstrates the substantial improvements in weights, body fat percentages and waist circumferences in the subjects with MetS following three-month lifestyle intervention. A structured, energy-restricted diet and a regular aerobic exercise (three times per week) are incorporated into the intervention. Further, the improvement is also noticeable in levels of total cholesterol and fasting glucose. Additionally, the intervention results in significant increases in TP, HF and LF indices of HRV suggesting an improvement in the function of ANS of the participants with MetS. We conclude that lifestyle intervention of the dietary restriction and aerobic exercise has beneficial effects on the risk factors of CVD and the function of ANS in the MetS subjects.

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TABLE I. Population clinical characteristics at baseline and after a weight loss program in metabolic syndrome subjects

	Pre-intervention	**Post-intervention**	***P* value**
Weight（kg）	69.71±8.50	65.09±8.30	.000*
BMI (kg/m^2)	27.76±2.88	26.29±3.20	.000*
Body fat (%)	34.53±5.40	31.38±5.57	.000*
Waist (cm)	88.03±9.34	83.58±9.78	0.00*
SBP (mmHg)	123.81±16.03	128.88±23.37	0.35
DBP (mmHg)	75.50±9.08	79.50±9.81	0.06
FG (mg/dL)	118.38±20.08	108.19±17.10	0.02*
HDL-C (mg/dL)	39.00±6.35	39.80±6.51	0.70
TG (mg/dL)	134.19±40.11	105.31±31.20	0.09
TC (mg/dL)	218.19±35.98	190.25±14.45	0.01*

* represent significantly differences between pre- and post-intervention measurements (P<0.05). SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose.

TABLE II. Changes of HRV parameters pre- and post- intervention

	Pre-intervention	**Post-intervention**	***P* value**
VLF (ms^2)	5.44 ± 0.93	6.35 ± 1.16	0.03*
LF (ms^2)	4.68 ± 0.95	5.41 ± 0.65	0.02*
HF (ms^2)	4.39 ± 1.35	5.24 ± 0.81	0.01*
TP (ms^2)	6.28 ± 0.79	7.07 ± 0.89	0.01*
LF%	47.56 ± 19.65	43.87 ± 15.85	0.91
HF%	34.61 ± 15.60	37.26 ± 12.76	0.52
LF/HF	0.30 ± 1.09	0.16 ± 0.77	0.65

* represent significantly differences between pre- and post-intervention measurements (P<0.05).