

A HOSPITAL-BASED THERAPEUTIC LIFESTYLE PROGRAM FOR WOMEN WITH METABOLIC SYNDROME

Hei-Jen Jou^{1,2}, I-Ping Hsu³, Hui-Ting Huang⁴, I-Li Liu⁵, Pei-Li Chien⁵, I-Chen Li⁵,
Yi Ching Chen⁵, Shih-Ming Chen^{1*}

Departments of ¹Obstetrics and Gynecology, ⁴Internal Medicine, and ⁵Preventive Medicine,
Taiwan Adventist Hospital, ²Department of Obstetrics and Gynecology, National Taiwan University Hospital, and
³Health Education Resource Center, Bureau of Health Promotion, Taipei, Taiwan.

SUMMARY

Objective: The aim of the present study is to evaluate the effect of a hospital-based therapeutic lifestyle program on women with metabolic syndrome (MetS).

Materials and Methods: We conducted a therapeutic lifestyle program for women with MetS. They all received a low calorie, balanced diet and participated in a regular aerobic exercise program for 8 weeks. Anthropometric indices, blood pressure, and biochemical data were collected. A paired *t* test was used for statistical analysis. A *p* value of less than 0.05 was considered statistically significant.

Results: Forty-four women took part in the program. All the components of MetS had decreased significantly by the end of the program and 25% of women no longer had MetS at the end of the program.

Conclusion: The therapeutic lifestyle program with diet control and regular exercise improves most markers of MetS except for levels of high density lipoprotein cholesterol. Therapeutic lifestyle intervention may be the best way of reducing the risk of cardiovascular disease in women with MetS [*Taiwan J Obstet Gynecol* 2010;49(4): 432–437].

Key Words: aerobic exercise, low calorie diet, metabolic syndrome, therapeutic lifestyle program, weight control

Introduction

The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) first provided a working definition of metabolic syndrome (MetS). MetS represents a combination of risk factors for cardiovascular disease (CVD), including atherogenic dyslipidemia, elevated blood pressure (BP), elevated glucose, a prothrombotic state, and a proinflammatory state [1]. People with MetS are at high risk for diabetes and

coronary heart disease, with an increased mortality rate from CVD [2,3]. The diagnostic cutoffs for MetS in the ATP III criteria were subsequently modified in the 2000 World Health Organization Asia Pacific Guideline for ethnic differences in the risk of diabetes and CVD [4]. The diagnosis of MetS for Taiwanese people was based on the definition from the Bureau of Health Promotion in Taiwan in 2005 [5]. The prevalence of MetS varies according to the definition, age, sex and area. The age-adjusted prevalence of MetS among adults from the United States was 23.7% according to ATP III criteria [6] and the prevalence of MetS was 14.3% (16.1% in men, 13.8% in women) in Taiwan [7]. The large numbers of residents with MetS has become an important issue with respect to health care policy.

MetS is a progressive disorder which is strongly associated with obesity and a sedentary lifestyle. The key to treating the abnormalities of MetS involves lifestyle modification with weight reduction, increase in physical



ELSEVIER

*Correspondence to: Dr Shih-Ming Chen, Department of Obstetrics and Gynecology, Taiwan Adventist Hospital, 424, Section 2, Ba-De Road, Taipei 105, Taiwan.
E-mail: jouheijen@gmail.com
Accepted: March 10, 2009

activity and a healthy diet. To date, only a few studies have focused on the effect of lifestyle intervention on MetS. Furthermore, most studies were based on data from western countries with quite different lifestyles and ethnic characteristics compared with the Taiwanese. The aim of the present study was to investigate the effects of a hospital-based lifestyle program in women with MetS from Taiwan.

Materials and Methods

Subjects

A prospective pilot study was conducted to observe the effects of a hospital-based therapeutic lifestyle program on women with MetS. Subjects were recruited from the Department of Internal Medicine and Department of Obstetrics and Gynecology from the Taiwan Adventist Hospital and from the community near the hospital. A questionnaire was conducted for each subject at the beginning of the study to determine current medical status. The exclusion criteria included severe systemic diseases such as coronary heart disease or stroke or long-term medication for chronic diseases. Subjects who could not take part in an aerobic exercise program due to high risk of adverse effects were also excluded. The present study was approved by the Institutional Review Board of Taiwan Adventist Hospital.

Collected data included age, medical condition, anthropometric indices, and biochemical results of the subjects. Anthropometric indices, BP and physical fitness were measured every week. Blood samples were obtained at the beginning and the end of the program.

Anthropometric indices

Body weight was measured to the nearest 0.1 kg while the subjects were wearing light clothing and height was measured to the nearest 0.1 cm. Body mass index (BMI) was then calculated using weight and height measurements. Waist circumference (WC) was measured to the nearest 0.1 cm at the midway point between the lowest margin of the rib cage and the iliac crest. BP was measured on the right arm of the subject using an automatic BP monitor after 15 minutes rest.

Biochemical tests

After an overnight fasting period of at least 8 hours, levels of fasting glucose, total-cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase, aspartate aminotransferase, γ -glutamyltransferase and triglyceride (TG) were measured using commercial kits on an

automated analyzer (Synchron CX9; Beckman Coulter Co., Fullerton, CA, USA) in the hospital laboratory.

Fasting insulin levels were also determined using commercial kits on an automated analyzer (Access Immunoassay System; Beckman Coulter Co.) in the same laboratory. Homeostasis model assessment for insulin resistance (HOMA-IR) was used to evaluate insulin resistance as described by Matthews et al [8]. Insulin resistance was defined as a HOMA-IR ≥ 3.0 [9].

Physical fitness test

The physical fitness of subjects was evaluated at the beginning of the study at Taiwan Adventist Hospital, and the parameters measured included cardiovascular endurance, flexibility, muscular endurance and resting heart rate. Cardiovascular endurance was measured by a 3-minute Step-Test. The Sit-and-Reach test was used to measure flexibility, and the 1-minute sit up test was used to measure muscular endurance.

Criteria for MetS

The definition for MetS in the present study was in accordance to the MetS criteria from the Bureau of Health Promotion in Taiwan. Women who met at least three of the following five component risk factors were diagnosed as having MetS: (1) a WC greater than 90 cm; (2) a systolic BP greater than 130 mmHg or a diastolic BP greater than 85 mmHg; (3) a fasting glucose level greater than 100 mg/dL; (4) a TG level greater than 150 mg/dL; and (5) a HDL-C level lower than 50 mg/dL.

The therapeutic lifestyle program was an 8-week project which included diet control and an aerobic exercise program. The subjects received a 1-hour lecture regarding healthy diet every week. Subjects were asked to record their diet for 2 days every week, including one weekday and 1 day on the weekend, to evaluate the content of their diet. A suggested diet was provided by nutritionists according to body weight, physical condition, history of disease of the subjects, and after reviewing the diet diary. The calories were controlled within 1,200–1,800 calories every day according to the formula: total calories = weight (kg) \times 40 kcal (for heavy worker) or 35 kcal (for medium workers) or 30 kcal (for light workers) – (500–1000) kcal. The suggested diet contained 55–58% carbohydrates, 14–20% protein and 25–28% fat. It was suggested that subjects use complex instead of simple carbohydrates, using buckeye as a source of oil, and avoiding foods rich in saturated fatty acids or containing trans-fatty acids. Subjects also received a group lecture alternating with aerobic exercise and yoga for 1 hour every week and were asked to exercise at the gym for at least 180 minutes per week.

Statistical analysis

Results were expressed in terms of means and standard deviations for continuous variables and frequencies for categorical variables. Two-tailed tests of hypotheses were used to compare the results between the beginning and the end of the study. All statistical analyses were performed using SPSS software (version 15.0; SPSS Inc., Chicago, IL, USA). A *p* value less than 0.05 was considered statistically significant.

Results

From January 2008 to December 2008, 44 women with MetS completed the therapeutic lifestyle program. Table 1 lists the basic characteristics of the subjects at the beginning of the study. The mean age of the subjects was 43.5 (range, 19–61 years). The mean body weight was 77.4 kg (range, 54.3–122.3 kg). Mean BMI was 30.2 (range, 21.8–45.6). According to the definition specifically for Taiwanese, 8 (18.2%) were overweight and 32 (72.7%) were obese. The incidence for abnormal WC, BP, fasting glucose level, HDL-C and TG were 100% (*n*=44), 72.7% (*n*=32), 47.7% (*n*=21), 86.4% (*n*=38) and 56.8% (*n*=25), respectively, at the beginning of the program. Only 36

subjects received liver function tests and fasting insulin measurement.

The results are in Table 2. Mean body weight had decreased by 3.8% by the end of the program, which was significantly different. Marked improvement was found in most components of MetS except HDL-C. The percentage reduction of WC, systolic BP, diastolic BP, fasting glucose, HDL-C and TG was 5.3%, 8.5%, 4.7%, 6.9%, 5.6% and 16.3%, respectively.

In addition to the components of MetS, total-cholesterol, LDL-C and HOMA-IR decreased significantly, and a decrease in the fasting insulin concentration

Table 1. Basic characteristics of the women with metabolic syndrome at baseline level

	Mean ± SD
Age (yr)	43.5 ± 11.3
Body height (cm)	160.3 ± 6.2
Body weight (Kg)	77.4 ± 14.1
BMI (kg/m ²)	30.2 ± 5.2
Subjects with metabolic syndrome (<i>n</i>)	
3 criteria	23
4 criteria	14
5 criteria	7

SD=standard deviation; BMI=body mass index.

Table 2. Comparison of anthropometric measures, blood pressure, and blood biochemistry at baseline and 8 weeks after lifestyle intervention

	Baseline	8 wk	Difference (%)	<i>p</i>
Body weight (kg) (<i>n</i> =44)	77.4 ± 14.1	74.5 ± 13.2	3.8	<0.001
BMI (<i>n</i> =44)	30.2 ± 5.2	29.0 ± 4.9	3.8	<0.001
WC (cm) (<i>n</i> =44)	97.0 ± 11.0	91.9 ± 10.4	5.3	<0.001
Blood pressure (mmHg) (<i>n</i> =44)				
Systolic	137.6 ± 19.1	125.9 ± 16.1	8.5	<0.001
Diastolic	81.0 ± 11.2	77.2 ± 11.1	4.7	0.006
Insulin sensitivity				
Fasting sugar (mg/dL) (<i>n</i> =44)	105.0 ± 22.7	97.8 ± 11.3	6.9	0.013
Fasting insulin (μU/mL) (<i>n</i> =36)	12.5 ± 9.8	10.0 ± 7.6	20.0	0.053
HOMA-IR (<i>n</i> =36)	3.2 ± 2.6	2.4 ± 1.9	24.4	0.031
Lipid profile (<i>n</i> =44)				
T-Chol (mg/dL)	201.4 ± 38.2	184.3 ± 29.5	8.5	<0.001
HDL-C (mg/dL)	42.1 ± 9.6	39.7 ± 8.0	5.6	0.001
LDL-C (mg/dL)	128.1 ± 31.2	118.4 ± 25.2	7.6	0.005
TG (mg/dL)	156.0 ± 72.3	130.7 ± 58.3	16.3	0.005
Liver function (<i>n</i> =36)				
AST (U/L)	29.5 ± 12.9	25.5 ± 8.9	13.7	0.006
ALT (U/L)	38.8 ± 30.0	30.1 ± 19.9	22.5	0.001
γ-GT (U/L)	32.4 ± 19.6	25.8 ± 16.0	20.4	0.002

BMI=body mass index; WC=waist circumference; HOMA-IR=homeostasis model assessment for insulin resistance; T-Chol=total cholesterol; HDL-C=high density lipoprotein cholesterol; LDL-C=low density lipoprotein cholesterol; TG=triglyceride; AST=aspartate aminotransferase; ALT=alanine aminotransferase; γ-GT=γ-glutamyltransferase.

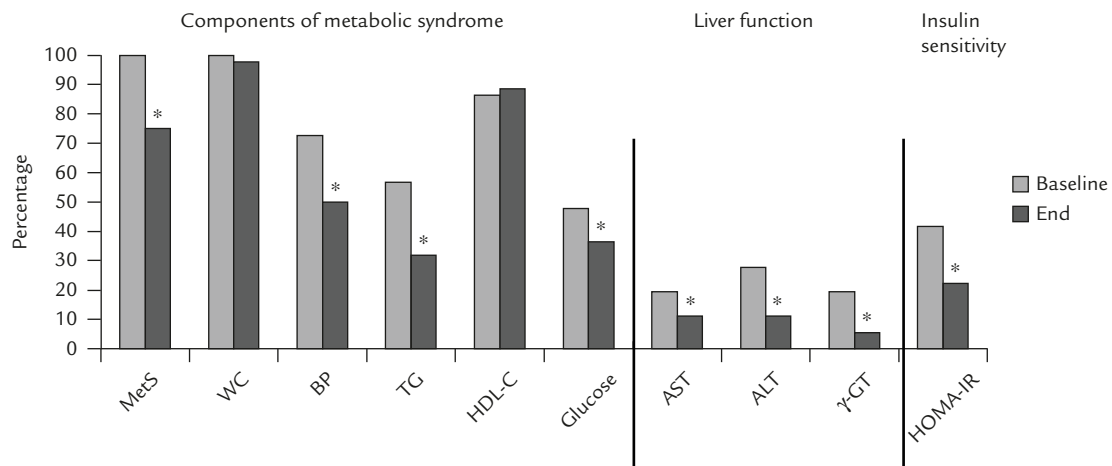


Figure. Percentage of subjects with abnormal values for each parameter at the baseline and at the end of the study, $*p < 0.05$. MetS=metabolic syndrome; WC=waist circumference; BP=blood pressure; TG=triglyceride; HDL-C=high density lipoprotein cholesterol; AST=aspartate aminotransferase; ALT=alanine aminotransferase; γ -GT= γ -glutamyltransferase; HOMA-IR=homeostasis model assessment for insulin resistance.

was marginally significant. Marked improvement in liver function, including aspartate aminotransferase, alanine aminotransferase, and γ -glutamyltransferase, was observed in these 36 women.

The Figure shows the percentage of subjects with abnormal values for each parameter at the baseline and at the end of the study. Significant reduction in the percentage of abnormal values was noted in most parameters except WC and HDL-C. The percentage of subjects with an abnormal HDL-C concentration had increased by 5.6% at the end of the study.

Discussion

The present study attempted to investigate the effects of a hospital-based lifestyle program on women with MetS in an Asian population. Our findings showed that up to a 25% reduction of the incidence of MetS was obtained after an 8-week, short-term program with a low calorie balanced diet and regular aerobic exercise. The lifestyle program improved almost all components of MetS, including WC, BP, fasting glucose and TG. Significant improvement in insulin sensitivity and liver function was also observed.

The prevalence of obesity and related comorbidities has increased rapidly in Taiwan [10]. The prevalence of obesity increased from 13.2% in the 1993–1996 Nutritional and Health Surveys in Taiwan to around 17% in 2005 [10]. Contributing to this obesity epidemic may be high fat diets and sedentary lifestyles [11]. Asians appear to be more susceptible to accumulating excess abdominal fat and developing the health consequences of obesity, even at lower BMIs [4]. Chinese

people with MetS are much more likely to develop CVD [12].

There are surprisingly few published studies of lifestyle intervention regarding MetS. Esposito et al demonstrated dietary intervention with a Mediterranean-style diet had a 48% net reduction of MetS after 2 years when compared with the control diet [13]. In the Diabetes Prevention Program randomized trial, lifestyle intervention was more successful in reducing the incidence of MetS than treatment with metformin and the placebo [14]. After a mean follow-up period of 3.2 years, 38% of the lifestyle intervention group and 18% of the placebo group no longer had MetS [14]. In a randomized controlled trial involving 375 participants by Bo et al, the absolute risk reduction for MetS was 31% after a 12 month lifestyle intervention when compared with the control group [15]. Lifestyle intervention may significantly reduce the prevalence of MetS and also reduce the risk of CVD in the long run [16].

The present study revealed that the lifestyle program lowered systolic BP and diastolic BP by 8.5% and 4.7%, respectively. Previous studies have also demonstrated the effect of lifestyle intervention in lowering BP [17–20].

Although most of the studies involved diets with relatively high protein content [17–19], diets with low protein content were also effective in reducing BP [20]. The present study reveals that a low-calorie diet with 55–58% carbohydrate, 14–20% protein and 25–28% fat accompanied with regular exercise can effectively improve hypertension in subjects with MetS.

This lifestyle program results in a significant reduction of TG concentrations by 16.3% and a 7.6% decrease in mean HDL-C levels. Previous studies have demonstrated

changes in HDL-C were unremarkable when lifestyle intervention was greater than 6 months [15,21,22]. However, regular aerobic exercise over 6 months may significantly increase HDL-C [23]. The decreased HDL-C concentrations in the present study was probably due to decreased dietary intake. Additionally, an 8-week exercise program may not be enough to achieve a favorable effect on HDL-C levels, with a prolonged period of intervention required.

Insulin resistance is a result of accumulation of intracellular lipid metabolites in skeletal muscle and hepatocytes and plays a key role in the pathophysiology of MetS [24]. Previous studies have revealed that a lifestyle intervention greater than 6 months might effectively reduce fasting glucose levels in individuals with MetS [15,16] while a short-term (10 weeks) intervention could not significantly reduce the fasting glucose level in pre-menopausal women with MetS [25]. The diet control, intensity of exercise and duration of intervention were all important factors for the results. The present study revealed a lifestyle intervention, even one as short as 8 weeks, might effectively reduce fasting glucose levels and improve insulin sensitivity in Taiwanese women with MetS. Although the mechanism is not understood well, exercise might play a key role in effecting insulin concentrations [26,27]. The present study revealed that even a modest weight reduction of 3.8% (2.9 kg) may effectively reduce the fasting glucose level and HOMA-IR by 6.9% and 24.4%, respectively.

Our data also revealed significant improvement in liver biochemistry and decreases in the percentage of people with an abnormal liver function after lifestyle intervention. These results confirm our previous report on subjects with non-alcoholic fatty liver disorders (NAFLD) [28]. NAFLD has become the most common cause of abnormal liver function in Taiwan [29]. Although liver ultrasound or biopsies were not done to prove the existence of fatty liver in the present study, a previous study has demonstrated the close association between MetS and NAFLD [30]. Therefore, the therapeutic lifestyle program can effectively improve comorbidity of MetS, such as NAFLD, in addition to components of MetS.

A major limitation of this study was its lack of control group. However, it has been revealed that obesity and metabolic abnormalities could not be improved without active intervention. The differences between the beginning and the end of the study were enough to demonstrate the efficacy of the lifestyle program on the women with MetS. The second major limitation was that the follow-up in the present study was limited to 8 weeks. Therefore, the long term effects of the program remained to be determined.

In conclusion, this study provides important evidence that therapeutic lifestyle intervention, even as short as 8 weeks, may effectively correct the metabolic abnormalities in women with MetS. The treatment of MetS in women will become one of the major challenges for primary physicians as the prevalence of obesity and MetS increases in Taiwan. Therapeutic lifestyle intervention should be provided as the first line treatment for MetS. Although more well-designed and large-scale studies are needed to obtain further evidence, we believe the present study provides useful information for the treatment of MetS in Taiwan.

References

1. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143–421.
2. Chen K, Lindsey JB, Khera A, et al. Independent associations between metabolic syndrome, diabetes mellitus and atherosclerosis: observations from the Dallas Heart Study. *Diab Vasc Dis Res* 2008;5:96–101.
3. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002;288:2709–16.
4. Gill TP. Cardiovascular risk in the Asia-Pacific region from a nutrition and metabolic point of view: abdominal obesity. *Asia Pac J Clin Nutr* 2001;10:85–9.
5. Bureau of Health Promotion. The Criteria of metabolic syndrome. Available from http://www.bhp.doh.gov.tw/BHPnet/Portal/Them_Show.aspx?Subject=200712250023&Class=2&No=200712250123. [Date accessed: January 30, 2009]
6. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002;287:356–9.
7. Hwang LC, Bai CH, Chen CJ. Prevalence of obesity and metabolic syndrome in Taiwan. *J Formos Med Assoc* 2006;105:626–35.
8. Matthews D, Hosker J, Rudenski A, Naylor B, Treacher D, Turner R. Homeostasis model assessment: insulin resistance and B-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–9.
9. Cortez-Pinto H, Camilo ME. Non-alcoholic fatty liver disease/non-alcoholic fatty liver disease steatohepatitis (NAFLD/NASH): diagnosis and clinical course. *Best Pract & Res Clin Gastroenterol* 2004;18:1089–104.
10. Pan WH, Lee MS, Chuang SY, Lin YC, Fu ML. Obesity pandemic, correlated factors and guidelines to define, screen and manage obesity in Taiwan. *Obes Rev* 2008;9(Suppl 1):22–31.

11. Huang KC. Obesity and its related diseases in Taiwan. *Obes Rev* 2008;9(Suppl 1):32-4.
12. Nestel P, Lyu R, Low LP, Sheu WH, Nitiyanant W, Saito I, Tan CE. Metabolic syndrome: recent prevalence in East and Southeast Asian populations. *Asia Pac J Clin Nutr* 2007;16:362-7.
13. Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA* 2004;292:1440-6.
14. Orchard TJ, Temprosa M, Goldberg R, et al. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome. *Ann Intern Med* 2005;142:611-9.
15. Bo S, Ciccone G, Bal Di C, et al. Effectiveness of a lifestyle intervention of metabolic syndrome. A randomized controlled trial. *J Gen Intern Med* 2007;22:1695-703.
16. Ilanne-Parikka P, Eriksson JG, Lindström J, et al. Finnish Diabetes Prevention Study Group. Effect of lifestyle intervention on the occurrence of metabolic syndrome and its components in the Finnish Diabetes Prevention Study. *Diabetes Care* 2008;31:805-7.
17. Sargrad KR, Homko C, Mozzoli M, Boden G. Effect of high protein vs high carbohydrate intake on insulin sensitivity, body weight, hemoglobin A1c, and blood pressure in patients with type 2 diabetes mellitus. *J Am Diet Assoc* 2005;105:573-80.
18. Appel LJ, Sacks FM, Carey VJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA* 2005;294:2455-64.
19. Hodgson JM, Burke V, Beilin LJ, Puddey IB. Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons. *Am J Clin Nutr* 2006;83:780-7.
20. Muzio F, Mondazzi L, Harris WS, Sommariva D, Branchi A. Effects of moderate variations in the macronutrient content of the diet on cardiovascular disease risk factors in obese patients with the metabolic syndrome. *Am J Clin Nutr* 2007;86:946-51.
21. Villareal DT, Miller BV 3rd, Banks M, Fontana L, Sinacore DR, Klein S. Effect of lifestyle intervention on metabolic coronary heart disease risk factors in obese older adults. *Am J Clin Nutr* 2006;84:1317-23.
22. Lien LF, Brown AJ, Ard JD, et al. Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension* 2007;50:609-16.
23. Stewart KJ, Bacher AC, Turner K, et al. Exercise and Risk Factors Associated with Metabolic Syndrome in Older Adults. *Am J Prev Med* 2005;28:9-18.
24. Petersen KF, Shulman GI. Etiology of insulin resistance. *Am J Med* 2006;119:S10-6.
25. Lofgren IE, Herron KL, West KL, et al. Weight loss favorably modifies anthropometrics and reverses the metabolic syndrome in premenopausal women. *J Am Coll Nutr* 2005;24:486-93.
26. Jennings GL, Nelson L, Nestel P, Korner P, Burton D, Bazelmans J. The effects of changes in physical activity on major cardiovascular risk factors, haemodynamics, sympathetic function and glucose utilization in man: a controlled study of 4 levels of activity. *Circulation* 1986;73:30-40.
27. Cox KL, Burke V, Morton AR, Beilin LJ, Puddey IB. Independent and additive effects of energy restriction and exercise on glucose and insulin concentrations in sedentary overweight men. *Am J Clin Nutr* 2004;80:308-16.
28. Chen SM, Liu CY, Li SR, Huang HT, Tsai CY, Jou HJ. Effects of therapeutic lifestyle program on ultrasound-diagnosed non-alcoholic fatty liver disease. *J Chin Med Assoc* 2008;71:551-8.
29. Chen CH, Huang MH, Yang JC, Nien CK, Yang CC, Yeh YH, Yueh SK. Prevalence and etiology of elevated serum alanine aminotransferase level in an adult population in Taiwan. *J Gastroenterol Hepatol* 2007;22:1482-9.
30. Hsiao PJ, Kuo KK, Shin SJ, et al. Significant correlations between severe fatty liver and risk factors for metabolic syndrome. *J Gastroenterol Hepatol* 2007;22:2118-23.