Effects of Body Shape Correction and Resistance Exercise on the Vascular Elasticity and Inflammatory Response in Obese Middle-aged Women

Do-Jin Kim¹, Jong-Hyuck Kim*²

¹ Professor, Dept. of Rehabilitation Sports, Bucheon University, 25 Sinheung-ro 56 beon-gil, Bucheon-si Gyeonggi-do, 14632, Republic of Korea

²Professor, Dept. of Medical Beauty care, Jungwon University, 85 Munmu-ro, Goesan-eup, Goesangun Chungbuk, 367-700, Republic of Korea

taehab@hanmail.net ¹, jhkim4170@hanmail.net*²

Abstract

Background/Objectives: The purpose of this study is to investigate the effects of 12 weeks body correction and resistance exercise on vascular elasticity and inflammatory response reactions of obese middle-aged women, and provide basic data for improving obesity in efficient obese middle-aged women.

Methods/Statistical analysis: The subjects of this study were obese middle-aged women living in Seoul, Korea. The body shape correction exercise of the experimental group consisted of stretching the muscles around the spine around the stretching, using props and the like. In addition, resistance exercise was able to maintain the exercise intensity of more than 60% based on 1RM in consideration of the exercise intensity of the study subjects. Exercise intensity was adjusted in units of 4 weeks. 60 minutes three times per week for 12 weeks. Warm-up and cool-down exercises consisted of 10 minutes each and 40 minutes of main exercise. In the data processing, descriptive statistics were presented for each measurement item and a 2-way RGRM ANOVA was conducted to examine the interaction effects between groups.

Findings: The results have shown significant interaction effects in Vascular Elasticity(right and left hands, right and left feet) and the Inflammatory Response(CRP, IL-6).

Improvements/Applications: The purpose of this study was to investigate the effects of 12-weeks of body shape correction and resistance exercise on vascular elasticity and inflammatory response of obese middle-aged women. This study suggests that body correction and resistance exercise have positive effects on vascular elasticity and inflammatory response index. Therefore, 12 weeks of body correction and resistance exercise program proved that it can prevent and improve obesity and cardiovascular disease by effectively improving vascular elasticity and inflammatory response index. Considering these aspects, it is recommended to develop a variety of further exercise programs which combine body correction and resistance exercise.

Keywords: body shape correction exercise, Resistance Exercise, obese middle aged women, Vascular Elasticity, Inflammatory Response

1. Introduction

Obesity, one of the main causes of numerous diseases, refers to an unhealthy body condition which was made due to excess of fat in the body that has been accumulated more than necessary, resulting in an imbalance between calories consumed and calories ingested - because of lack of physical activity, excessive intake, or other genetic factors[1,2].

In 2016, 39% of adults worldwide were overweight and 13% were obese[3]. In addition, in Korea, according to the 2017 National Health Statistics, 34.8% of adults were obese based on the body mass index(BMI) of 25kg/m²-41.1% of men and 28.4% of women. Furthermore, 25.6% of women in their 40s and 31.7% of women in their 50s were obese- it showed that the older women were more likely to suffer from obesity[4].

As the age increases, visceral fat area and fat accumulation tend to increase[5]. Particularly from middle age, it is reported that the distribution of body fat tends to change from subcutaneous defense to visceral fat[6]. Unlike men, middle-aged women, body fat steadily increases from 40's to 60's, so obesity and weight management are very important for middle-aged women.

Obesity can be improved through applying various methods, such as exercise, which is a method of improving obesity by correcting energy by increasing calories consumed which is increasing metabolism. Exercise, along with dietary control, is the basis of obesity treatment, and is considered as an important means of maintaining lean mass as well as weight loss[7]. As explained, regular exercise is effective in reducing body fat and can prevent many diseases caused by obesity.

Physical activities can be further reduced not only because of body fat and weight gain of women, but also their weakening muscle strength. Still, physical activities are effective for health promotion, physical fitness improvement and prevention of chronic diseases[8].

The ACSM[9] emphasized participation of medium- and high-intensity physical activities every week for at least 30 minutes, if possible, and medium and high intensity physical activities are suggested as an exercise prescription to lower the risk of metabolic syndrome[10]. In addition, long-term resistance training has been reported to improve the health of middle-aged women due to metabolic risk factors, body composition and muscle strength[11].

Continuing body-correcting exercises which help restore body balance has the effect of preventing lower body edema and obesity as well as improving pain. In particular, Pilates' purposes have recently diversified beyond conventional rehabilitation treatment to an exercise which have numerous effects on body balance, posture correction, body care, and flexibility improvement[12], and also effective in strengthening muscle strength, muscular endurance, and improving musculoskeletal pain[13]. Therefore, it can be said that it is suitable to improve cardiovascular disease, metabolic disease and physical function of middle-aged women suffering from obesity.

Cardiovascular disease is the leading cause of death worldwide, ranking first with 31% of the world's

cause of deaths published by WHO[14]. In Korea, heart disease(10.8%) and cerebrovascular disease(8.0%) occupy the second and third place among the top ten causes of death. Furthermore, morality rates of both male and female due to cardiovascular diseases are also on the rise, with female mortality higher than males, depending on gender[15].

Weight loss through regular exercise is effective in reducing the risk of obesity and several metabolic diseases that can occur due to obesity[16]. Therefore, the purpose of this study is to investigate the effects of 12 weeks body correction and resistance exercise on vascular elasticity and inflammatory response reactions of obese middle-aged women, and provide basic data for improving obesity in efficient obese middle-aged women.

2. MATERIALS AND METHODS

2.1. Subject of study

In order to investigate the effects of 12 weeks of exercise and body resistance on vascular elasticity and inflammatory response index, 12 patients in the 40s and 50s were overweight and 12 in the control group(CG). The experimental group(EG) applied body correction and resistance exercise in parallel, and the control group maintained daily life<Table 1>.

Group \mathbf{N} Weight (kg) **Fat** (%) Age (yr) Height (cm) CG 157.78±3.98 12 49.63±2.95 62.10±2.99 31.04 ± 2.05 EG 12 48.51 ± 2.34 158.46 ± 4.14 62.59±3.16 30.33±2.55

Table 1: Physical Characteristic of Subjects (M±SD)

2.2. Treatment program

Body shape correction exercise of the experimental group consisted of stretching the muscles around the spine around the stretching, using props and the like. In addition, resistance exercise was able to maintain the exercise intensity of more than 60% based on 1RM in consideration of the exercise intensity of the study su bjects. Exercise intensity was adjusted in units of 4 weeks. 60 minutes three times per week for 12 weeks. Warm-up and cool-down exercises consisted of 10 minutes each and 40 minutes of main exercise. The exercise program is shown in <Table 2>.

Table 2: Exercise Program

Division	Exercise Program	Intensity	Time(min)
Warm Up	Joint Relaxation Stretching		10
Main Exercise	Correction exercise: single/double leg stretch, single/double leg circles, spine stretch forward, corkscrew, spine twist(10rep./3set)	1RM 60%	20

	Resistance exercise: squat to press, lying leg raise, stationary lunge with twisting pull-apart, triceps kickback(10rep./3set)	20
Cool Down	Joint Relaxation Stretching	10

2.3. Measurement method and equipment

The experimental and control groups underwent vascular elasticity tests and blood tests before and afte r 12 weeks of treatment. A 24-hour fasting time was maintained before blood tests, and blood was collected b y a nurse and referred to a medical corporation for analysis.

2.4. Data analysis

SPSS 21.0 was used for data analysis. Descriptive statistics for each measurement variable were presented to verify the treatment effects of the experimental and control groups. In addition, ANOVA was conducted to verify the effect on the experimental treatment. The significance level was verified at .05.

3. RESULTS

3.1. Vascular Elasticity

Significant differences were found in the right(p=.025) and left hands(p=.010), right(p=.002) and left feet(p=.005) in the experimental and control groups (p<05)<Table 3>.

Table 3: Vascular Elasticity

Factor	Group	Pre	Post	P			
Right hand(ms)	CG	193.20±5.44	194.05±6.77	Group*period:.025 Group:.093 Period:.002			
	EG	195.73±6.49	202.57±4.99				
Left hand(ms)	CG	192.53±5.94	192.89±5.20	Group*period:.010			
	EG	194.67±6.10	203.02±5.75	Group:.352 Period:.009			
Right foot (ms)	CG	291.34±7.89	292.45±6.36	Group*period:.002			
	EG	293.44±5.61	303.09±5.18	Group:.494 Period:.011			
Left foot (ms)	CG	292.77±6.64	291.87±7.34	Group*period:.005			
	EG	294.42±4.98	299.47±5.88	Group:.472 Period:.023			

3.2. Inflammatory Response

The experimental group and control group showed significant differences in CRP(p=.002) and IL-6(p=.011) (p<.05).<Table 4>.

P factor group Pre Post Group*period:.002 CG .31±.03 .31±.04 CRP(mg/dl) Group: .692 EG $.30 \pm .04$ $.25 \pm .03$ Period: .001 Group*period: .011 CG $5.03 \pm .79$ 5.01±.69 IL-6(pg/ml) Group: .521 EG $5.01 \pm .65$ $4.35 \pm .72$ Period: .015

Table 4: Inflammatory Response

4. DISCUSSION

This study was constructed to present the basic data of effective body correction and resistance exercise program for the improvement of health and prevention of cardiovascular disease in the obese middle-aged women by comparing and analyzing the differences in Vascular Elasticity and Inflammatory Response for 12 weeks. The following is a comparative analysis of the results of this study and previous studies.

As age increases, vascular function apt to decrease, and it ultimately leads to decreased vascular elasticity, resulting in various vascular diseases. In addition, when the arterial vessels are hardened, the elasticity of the arterial wall also tend to decrease, and as the arterial stiffness increases, left ventricular hypertrophy and decreased blood flow are known to increase the risk of cardiovascular disease[17].

Although the subjects and the exercise patterns are different, previous studies on the changes in vascular elasticity through exercise highly support this study by showing similar results for instance, Watts et al[18] reported that the vascular function of obese adolescents was improved by participating in 8-week circuit training. Tanaka et al[19] reported that three months of aerobic exercise (walking) improved arterial stiffness in middle-aged and elderly men. Lee[20] reported significant improvement in vascular elasticity as a result of Chinese pearl barley ingestion and 12-week suspension training for middle-aged women prior to menopause. Kim[21] reported significant changes in vascular elasticity of middle-aged women after 12 weeks of combined training, Chae[22] reported increased vascular elasticity as a result of 12 weeks of taekwondo exercise in older women, and Jeon[23] reported that 12 weeks of combined training in obese middle-aged women showed significant increase in vascular elasticity.

Looking at previous studies on changes in vascular elasticity through pilates and resistance exercise in obese middle-aged women, Kim, & Lee[24] reported that there was a positive effect on vascular elasticity of obese middle-aged women after 12 weeks of pilates and resistance exercise. In this study, in the similar way, 12 weeks of pilates and resistance exercise were conducted to groups of obese middle-aged women and brought significant differences in vascular elasticity of obese middle-aged women as well. As the previous study also showed the similar result, this study also suggests the effects of exercise on vascular elasticity in obese middle-aged women. These results suggest that regular exercise can increase blood flow due to positive changes in the

arterial blood system, thereby improving the oxidative capacity of each tissue cell. In addition to the increase in the amount of one-time ejection during the circulation of blood flow, the removal of wastes deposited on the inner wall of the blood vessels and the maintenance of vascular elasticity can lead to changes in arterial vessels by changing the blood flow rate, which has a positive effect on improving blood vessel function [25].

C-reactive protein(CRP) is a factor associated with inflammation, and is known as one of the new risk factors which formates plaques in blood vessel walls with CVD[26,27]. C-reactive protein(CRP) has been used as a clinical marker for cardiovascular diseases and has been discussed as an intervention subject[28]. One possible approach to improving CRP levels can be exercise, which is a low-cost non-pharmacological intervention available to most of the public[29].

Although the subjects and the exercise types and patterns are different, previous studies on the change of CRP through exercise showed that CRP decreased when conducting aerobic and resistance training. For instance, Martins et al[30] reported that 16 weeks of aerobic and resistance training in men and women decreased CRP in both aerobic and resistance training. Hayase et al[31] reported a decrease in CRP levels after a 10-week combined exercise of walking and resistance exercise among middle-aged obese men. Jorge et al[32] reported that there was a significant decrease in CRP as a result of 12 weeks of combined exercise in diabetics. Phillips et al[33] supported the findings that 12-week resistance exercise in postmenopausal obese women was effective in reducing inflammatory factors such as CRP, TNF-α and IL-6. On the other hand, Kadoglou et al[34] reported that the CRP did not change significantly after 12-weeks of complex exercise in patients with type 2 diabetes.

In this study, 12-weeks of pilates and resistance exercise were conducted to obese women who were in their middle age, and showed significant improvement in their CRP. These results suggest that, in addition to training, continuous physical activity has a positive effect on reducing CRP levels[35] and the 12-week body-correction and resistance exercise can protect the patients from cardiovascular diseases caused by acute inflammatory reactions, since exercises can decrease the inflammatory response, and ultimately can defense the body system from oxidative demage.

Interleukin-6(IL-6) has significant anti-inflammatory effects when aging, cardiovascular disease, and cancer occurs, due to its metabolic and anti-inflammatory immune functions[36]. Regular exercise improves anti-inflammatory function and has health benefits for patients with chronic diseases[37].

Although the subjects and the types of exercise are different, there were previous studies on the changes of IL-6 through exercise. For example, Hayase et al[31] reported a decrease in IL-6 concentration as a result of a 10-week combined exercise of walking and resistance exercise for middle-aged obese men.

Goldhammer et al[38] reported that il-6 concentrations of patients at risk of heart disease were reduced due to aerobic exercises. In addition, Phillips et al[33] also reported that 12 weeks of resistance exercise in postmenopausal obese women was effective in reducing inflammatory factors such as IL-6. Furthermore, six months of dietary control and aerobic exercise in postmenopausal obese women reported a significant decrease in IL-6[39]. On the other hand, Balducci et al[40] reported that a 12-week combined exercise of type 2 diabetes patients did not show any significant change in IL-6 and showed different results from this study.

In this study, 12-weeks of pilates and resistance exercise were conducted to obese middle-aged women,

and showed significant differences in IL-6. This study also proves the effects of exercise on IL-6 changes in obese middle-aged women. These results suggest that IL-6 was decreased due to the decrease of body fat and increase of lean body mass due to combined exercise[41]. Therefore, it is thought that Pilates and resistance exercise do have positive effects on improving inflammatory markers by increasing muscle strength and regulating IL-6. As a result, Pilates and resistance exercise for 12-weeks may help to improve inflammatory markers in obese middle-aged women.

5. Conclusion

The purpose of this study was to investigate the effects of 12-weeks of body shape correction and resistance exercise on vascular elasticity and inflammatory response of obese middle-aged women. This study suggests that body correction and resistance exercise have positive effects on vascular elasticity and inflammatory response index. Therefore, 12 weeks of body correction and resistance exercise program proved that it can prevent and improve obesity and cardiovascular disease by effectively improving vascular elasticity and inflammatory response index. Considering these aspects, it is recommended to develop a variety of further exercise programs which combine body correction and resistance exercise.

REFERENCES

- [1] Ferrucci, L. Sarcopenic obesity: definition, cause and consequences. Current Opinion in Clinical Nutrition and Metabolic Care. 2008;11(6):693-700.
- [2] LeMone P, Burke K, Dwyer T, Levett-Jones T, Moxham L, & Reid-Searl K. Medical-surgical nursing: Pearson Higher Education AU. 2015.
- [3] World Health Organization. Fact sheet on obesity and overweight. Retrieved from http://www.who.int/news-room/fact-sheets/detail/obesity-and- overweight. 2018.
- [4] Ministry of Health and Welfare. 2017 National Health Statistics. Retrieved from https://knhanes.cdc.go.kr/ knhanes/sub04/sub04_03.do?classType=7. 2018.
- [5] Tchernof A, & Després JP. Pathophysiology of human visceral obesity: an update. Physiological reviews. 2013;93(1):359-404.
- [6] Preis SR, Massaro JM, Robins SJ, Hoffmann U, Vasan RS., Irlbeck T, & Fox CS. Abdominal subcutaneous and visceral adipose tissue and insulin resistance in the Framingham heart study. Obesity, 2010;18(11):2191-2198.
- [7] Drenowatz C, Prasad VK, Hand GA, et al. Effects of moderate and vigorous physical activity on fitness and body composition. Journal of Behavioral Medicine. 2016;39(4):624-632.
- [8] Centers for Disease Control and Prevention. Physical Activity and Health: The Benefits of Physical Activity [Internet]. CDC; 2018 [cited 2018 May 1]. Available from: https://www.cdc.gov/physicalactivity/basics/pa-health/index.htm. 2018.
- [9] American College of Sports Medicine. ACSM's resource manual for Guidelines for exercise testing and prescription, 7th. Lippincott Williams & Wilkins. 2014.
- [10] Kaur, J. A comprehensive review on metabolic syndrome. Cardiology research and practice. 943162.

2014.

- [11] Botero JP, Shiquemoto GE, Prestes J, Marin CT, Do Prado WL, Pontes CS, Guerra RL, Ferreia FC, Baldissera V & Perez SE. Effects of long term periodized resistance training on body composition, leptin, resistin and muscle strength in elderly postmenopausal women. The Journal of sports medicine and physical fitness. 2013;53(3):289-94.
- [12] Siler, Brooke. The pilates body. Broadway Books, New York. NY. 2000.
- [13] Curnow D, Cobbin D, Wyndham J, & Choy SB. Altered motor control, posture and the Pilates method of exercise prescription. Journal of bodywork and movement therapies. 2009;13(1):104-111.
- [14] World Health Organization. Fact sheet on cardiovascular diseases(CVDs) Retrieved from https://www.who.int/news-room/fact-sheets/detail/ cardiovascular-diseases-(cvds). 2017.
- [15] National Statistical Office of Korea. Statistics for cause of death in 2017. Retrieved from http://kosis.kr/statisticsList/ statistics List Index. do? menuId=M_01_01&vwcd=MT_ZTITLE & parmTabId=M_01_01 & parentId=D.1;D1.2;D11.3;#D11.3. 2018.
- [16] Foright RM, Presby DM, Sherk VD, Kahn D, Checkley LA, Giles ED, Bergouignan A, Higgins JA, Jackman MR, Hill JO, MacLean PS. Is regular exercise an effective strategy for weight loss maintenance? Physiology and Behavior. 2018;188:86-93.
- [17] Kingwell BA, Medley TL, Waddell TK, Cole TJ, Dart AM, & Jennings GL. Large artery stiffness: Structural and genetic aspects. Clinical and Experimental Pharmacology and Physiology. 2001;28(12):1040-1043.
- [18] Watts K, Beye P & Siafriskas A. Exercise training normalizes vascular dysfunction and improves central adiposity in obese adolescent. Journal of the American College of Cardiology. 2004;43(10):1823-1827.
- [19] Tanaka H, Dinenno FA, Monahan KD, Clevenger CM, DeSouza CA. & Seals DR. Aging, habitual exercise and dynamic arterial compliance. Circulation. 2000;102(11):1270-1285.
- [20] Lee CK. Effects of suspension training and adlay intake on health-related fitness, blood lipid profile and vascular compliance in middle-aged women. Pusan National University. master's thesis. 2015.
- [21] Kim YM. Effects of aerobic exercise combined with resistance exercise on pulse wave velocity and health-related physical fitness in obese middle-aged women. Sungkyunkwan University. master's thesis. 2005.
- [22] Chae SI. Study on the effect of functional fitness, body composition and vascular compliance before and after 12 weeks Taekwondo training in elder women. Hanyang University. master's thesis. 2011.
- [23] Jeon JH. Effects of 12weeks combined training on vascular compliance, insulin resistance and body composition in middle-aged obese women. The Korean Journal of Sport. 2013;11(1):357-374.
- [24] Kim YJ, Lee JY. Effect of Pilates and Resistance Exercises on Vascular Compliance, Body Composition in obese middle-aged Women. Official Journal of the Korean Society of Dance Science. 2015;32(2):115-126.
- [25] Jacquet L, Vancaenegem O, Pasquet A, Matte P, Poncelet A, Price J, Gurne O, & Noirhomme P. Exercise capacity in patients supported with rotary blood pumps is improved by a spontaneous increase of pump flow at constant pump speed and by a rise in native cardiac output. Artificial Organs. 2011;35(7):682-690.
- [26] Benedini S, Caimi A, Alberti G, Terruzzi I, Dellerma N, La Torre A, et al. Increase in homocysteine levels after a half-marathon running: A detrimental metabolic effect of sport? Sport Sciences for Health. 2010; 6(1):35-41.

- [27] von Känel R, Mausbach BT, Dimsdale JE, Mills PJ, Patterson TL, Ancoli-Israel S, et al. Ways of coping and biomarkers of an increased atherothrombotic cardiovascular disease risk in elderly individuals. Cardiovasc Psychiatry Neurol. 2012; 2012:875876.
- [28] Corrado E, Rizzo M, Aluigi L, Patti AM, Coppola G, Muratori I, Caccamo G, Balasus F, Novo S. Prediction of vascular events in subjects with subclinical atherosclerosis and the metabolic syndrome: the role of markers of inflammation. International angiology. 2012; 31(3):219–226.
- [29] Kelley GA, Kelley KS. Effects of aerobic exercise on C-reactive protein, body composition, and maximum oxygen consumption in adults: a meta-analysis of randomized controlled trials. Metabolism. 2006; 55(11):1500–1507.
- [30] Martins RA, Neves AP, Coelho-Silva MJ, Verissimo MT, & Texeira AM. The effect of aerobic versus strength-based training in high-sensitivity C-reactive protein in older adults. European Journal of Applied Physiology. 2010;110(1):161-169.
- [31] Hayase H, Nomura S, Abe T, & Izawa T. Relation between fat distributions and several plasma adipocytoki ness after exercise training in premenopausal and post menopausal women. Journal of physiological anthropology and applied human science. 2002;21(2):105-113.
- [32] Jorge ML, MP, de Oliveira VN, Resende NM, Paraiso LF, Calixto A, Diniz ALD, & Jorge PT. The effects of aerobic, resistance, and combined exercise on metabolic control, inflammatory markers, adipocytokines, and muscle insulin signaling in patients with type 2 diabetes mellitus. Metabolism. 2011;60(9):1244-1252.
- [33] Phillips MD, Patrizi RM, Cheek DJ, Wooten JS, Barbee JJ, Mitchell JB. Resistance training reduces subclinical inflammation in obese, postmenopausal women. Medicine and science in sports and exercise. 2012;44(11):2099-2110.
- [34] Kadoglou NP, Vrabas IS, Kapelouzou A, Lampropoulos S, Sailer N, Kostakis A, & Angelopoulou N. The impact of aerobic exercise training on novel adipokines, apelin and ghrelin, in patients with type 2 diabetes. Medical Science Monitor. International Medical Journal of Experimental and Clinical Research. 2012;18(5):290-295.
- [35] Wannamethee SG, Lowe GD, Whincup PH, Rumley A, Walker M, & Lennon L. Physical activity and hemostatic and inflammatory variables in elderly men. Circulation. 2002;105(15):1785-1790.
- [36] Roubenoff R, Parise H, Payette HA, Abad LW, Agostino RD, Jacques PF, Wilson PW, Dinarello CA, Harris TB. Cytokines, insulin-like growth factor 1, sarcopenia, and mortality in very old community-dwelling men and women: the Framingham Heart Study", Am J Medicine. 2003;115(6):429–435.
- [37] Wilund KR. Is the anti-inflammatory effect of regular exercise responsible for reduced cardiovascular disease? Clinical Science. 2007;112(11):543-555.
- [38] Goldhammer E, Tanchilevitch A, Maor I, Beniamini Y, Rosenschein U, & Sagiv M. (2005). Exercise training modulates cytokines activity in coronary heart disease patients. International Journal of Cardiology. 2005;100(1):93-99.
- [39] Ryan AS, Nicklas BJ, Berman DM, & Elahi D. Adiponectin levels do not change with mode rate dietary induced weight loss and exercise in obese postmenopausal women. International Journal of Obesity. 2004;27(9):1066-1071.

International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 7, 2020 ISSN: 1475-7192

[40] Balducci S, Zanuso S, Nicolucci A, Fernando F, Cavallo S, Cardelli P, & Fallucca F. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. Nutrition, Metabolism and Cardiovascular Diseases. 2010; 20(8):608-617.

[41] Dekker MJ, Lee S, Hudson R, Kilpatrick K, Graham TE, Ross R, & Robinson LE. An exercise intervention without weight loss decreases circulating interleukin-6 in lean and obese men with and without type 2 diabetes mellitus. Metabolism. 2007;56(3):332-338.