



Original / Deporte y ejercicio

## A home-based treadmill training reduced epicardial and abdominal fat in postmenopausal women with metabolic syndrome

Gabriel Fornieles González<sup>1</sup>, Miguel Ángel Rosety Rodríguez<sup>1</sup>, María Antonia Rodríguez Pareja<sup>2</sup>, Antonio Díaz Ordóñez<sup>3</sup>, Jesús Rosety Rodríguez<sup>4</sup>, María Teresa Pery Bohorquez<sup>1</sup>, Francisco Brenes Martín<sup>3</sup>, Antonio Escribano Ocon<sup>5</sup>, Manuel Rosety Rodríguez<sup>1</sup>, Francisco Javier Ordóñez Muñoz<sup>5</sup>, Rocío Toro Cebada<sup>1</sup> and Ignacio Rosety Rodríguez<sup>1</sup>

<sup>1</sup>Universidad de Cádiz. <sup>2</sup>Hospital Asociado Universitario Jerez de la Frontera. <sup>3</sup>Universidad de Cádiz, Departamento de Medicina. <sup>4</sup>Hospital Universitario Puerta del Mar, Cádiz. <sup>5</sup>Centro Estudios Olímpico Cádiz, Universidad de Cádiz. España.

### Abstract

**Introduction:** The current study was designed to determine the effect of home-based treadmill training on epicardial and abdominal adipose tissue in postmenopausal women with metabolic syndrome (MS). A secondary objective was to identify significant correlations between imaging and conventional anthropometric parameters.

**Material and methods:** Sixty postmenopausal women with MS volunteered for the current trial. Thirty were randomly assigned to perform a supervised home-based 16-week treadmill training program, 3 sessions/week, consisting of a warm-up, 30-40 min treadmill exercise (increasing 5-minutes each 4-weeks) at a work intensity of 60-75% of peak heart rate (increasing 5% each 4-weeks) and cooling-down. Epicardial fat thickness (EFT) was assessed by echocardiography. Abdominal fat mass in the lumbar regions L1-L4 and L4-L5 was determined by dual X-ray absorptiometry.

**Results:** Epicardial fat thickness and abdominal fat percentages were significantly improved after the completion of the training program. Another striking feature of the current study was the moderate correlation that was found between EFT and waist circumference (WC).

**Conclusion:** Home-based treadmill training reduced epicardial and abdominal fat in postmenopausal women with MS. A secondary finding was that a moderate correlation was found between EFT and WC. While current investigations are promising, future studies are still required to consolidate this approach in clinical application.

(Nutr Hosp. 2014;30:609-613)

DOI:10.3305/nh.2014.30.3.7129

Key words: *Metabolic syndrome. Postmenopausal. Epicardial adipose tissue. Abdominal adipose tissue. Exercise.*

**Correspondence:** Gabriel Fornieles González.  
Universidad de Cádiz.  
E-mail: gabriel.fornieles@uca.es

Recibido: 12-XI-2013.  
1.ª Revisión: 5-I-2014.  
1.ª Revisión: 5-III-2014.  
Aceptado: 29-VI-2014.

### EL ENTRENAMIENTO DOMICILIARIO EN TAPIZ RODANTE REDUCE LA GRASA EPICÁRDICA Y ABDOMINAL EN MUJERES POSMENOPÁUSICAS CON SÍNDROME METABÓLICO

#### Resumen

**Introducción:** El presente estudio se diseñó para conocer la influencia de un programa de entrenamiento aeróbico domiciliario en la masa grasa epicárdica y abdominal de mujeres postmenopáusicas con síndrome metabólico (SM). Un segundo objetivo fue identificar correlaciones significativas entre las variables antropométricas ensayadas.

**Material y Método:** Participaron voluntariamente un total de 60 mujeres postmenopáusicas con diagnóstico de SM que se distribuyeron aleatoriamente en el grupo de intervención (n=30) o control (n=30). El programa de intervención, desarrollado en el domicilio, consistió en un entrenamiento en tapiz rodante de 16 semanas, 3 sesiones/semana. La parte principal se realizó a una intensidad del 60-75% FCmax (incrementando 5% cada 4 semanas) durante 30-40 minutos (incrementando 5-minutos cada 4-semanas). La masa grasa epicárdica se determinó mediante ecocardiografía. La masa grasa abdominal de las regiones de interés L1-L4 y L4-L5 se determinó mediante densitometría.

**Resultados:** Se observó un descenso significativo tanto de la masa grasa epicárdica como abdominal tras completar el entrenamiento. Se identificó una correlación moderada entre la masa grasa epicárdica y el perímetro de la cintura de las participantes que podría facilitar su seguimiento clínico.

**Conclusión:** Un programa de entrenamiento de resistencia redujo la masa grasa epicárdica y abdominal. Futuros estudios en esta línea son aún necesarios.

(Nutr Hosp. 2014;30:609-613)

DOI:10.3305/nh.2014.30.3.7129

Palabras clave: *Síndrome metabólico. Postmenopausia. Masa grasa epicárdica. Masa grasa abdominal. Ejercicio.*

## List of abbreviations:

BMI: Body mass index.  
CRF: Cardiorespiratory fitness.  
CT: Computed tomography.  
DEXA: Dual energy X ray absorptiometry.  
EAT: Epicardial adipose tissue.  
EFT: Epicardial fat thickness.  
EKG: Electrocardiogram.  
HDL-cholesterol: high density lipoprotein cholesterol.  
LDL-cholesterol: Low-density lipoprotein cholesterol.  
LVDD: Left ventricular diastolic dysfunction.  
MRI: Magnetic resonance imaging.  
MS: Metabolic syndrome.  
NCEP-ATPIII: National Cholesterol Education Program. Adult Treatment Panel-III.  
ROI: Region of interest.  
SBP: Systolic blood pressure.  
TNF- $\alpha$ : Tumor necrosis factor-alpha.  
TG: Triglycerides.  
VAT: Visceral adipose tissue.  
VO<sub>2</sub>max: Maximal oxygen consumption.  
WC: Waist circumference.

## Introduction

The Framingham Heart Study<sup>1</sup> and the Multi-Ethnic Study of Atherosclerosis<sup>2</sup> identified epicardial adipose tissue (EAT) as independent risk marker for cardiovascular and coronary heart disease in general population. Similar results have been found by Fernandez-Munoz<sup>3</sup> in adult women with metabolic syndrome (MS). In this respect, an EAT value  $\geq 5$  mm showed a good sensitivity and specificity for predicting MS in the Venezuelan population<sup>4</sup>. These findings may be explained, at least in part, given that the embryological origin of EAT is similar to intra-abdominal visceral adipose tissue<sup>5</sup>. In a more detailed way, EAT has been shown to function as an endocrine organ secreting various adipocytokines, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and leptin, that may play a key role in the pathogenesis of MS<sup>6</sup>. Furthermore, EAT is contiguous with the myocardium without fascia boundaries resulting in local effects<sup>7</sup>. In fact, EAT has been significantly correlated with left ventricular diastolic dysfunction (LVDD), even after adjusting for other cardiometabolic risk factors such as age, systolic blood pressure, body mass index (BMI), blood glucose and low-density lipoprotein cholesterol (LDL-cholesterol) in subjects with MS<sup>8</sup>. Similarly, EAT is an independent predictor of blunted heart rate recovery, a novel cardiovascular risk factor, in patients with MS<sup>9</sup>. Lastly, Killcasian et al.<sup>10</sup> reported that increased EAT was associated with cardiac functional changes in healthy women too.

Accordingly, there is a compelling need to monitor epicardial adipose tissue not only for diagnostic pur-

poses, but also for therapeutic interventions<sup>11</sup>. In this respect,

Karadag et al.<sup>12</sup> found that EAT measurement by echocardiography was an efficient method in the determination of visceral adiposity in patients with MS. In addition, Willens et al.<sup>13</sup> reported that a loss of 40 kg (26%) of body weight after bariatric surgery was accompanied by a 24% reduction in pericardial fat in severely obese patients. With regard to pharmacological interventions, pioglitazone, simvastatin or combination treatment substantially reduced the expression of pro-inflammatory genes in EAT of coronary patients with MS<sup>14</sup>.

A recent meta-analysis confirmed the need for gender-specific approaches and outcomes of obesity treatment in general and more specific in the treatment of abdominal obesity<sup>15</sup>. In this line, to date, no studies have been focused on reducing EAT by performing an intervention program based on regular exercise despite previous focused on other outcomes showed promising results in this group<sup>16,17,18</sup>. Therefore, the current study was designed to determine the effect of a short-term, home-based treadmill training program on epicardial and abdominal adipose tissue in adult women with metabolic syndrome. A secondary objective was to identify significant correlations between imaging and conventional anthropometric parameters in this population group.

## Material and methods

Sixty adult women with MS volunteered for the current trial (table I). All participants met the following inclusion criteria: (1) postmenopausal; (2) 45-55 year-old; (3) diagnosis of MS according to the update criteria established by the National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (ATP-III); (4) Medical approval for physical activity participation. On the other hand, exclusion criteria were: (1) Participation in a training program in the 6 months prior to their participation in the trial; (2) Not completing at least 90% of the training sessions.

Participants were randomly allocated to the intervention or control group using a concealed method.

Thirty were randomly assigned to perform a supervised, home-based 16-week treadmill training program, 3 sessions per week, consisting of a warm-up (10-15 min), 30-40 min treadmill exercise (increasing 5 minutes seconds each four weeks) at a work intensity of 60-75% of peak heart rate (increasing by 5% each four weeks) measured during a maximal treadmill test, and cooling-down (5-10 min). In order to ensure that the training workload was appropriate, all participants from intervention group wore a wireless wearable heart rate monitor (Sport Tester PE3000, Polar Electro, Kempele, Finland).

The control group included 30 age, sex and BMI matched postmenopausal women with MS who did not take part in any training program.

**Table I**

*Anthropometric, biochemical and clinical characteristics of postmenopausal women enrolled in the intervention and control groups at baseline.*

	<i>Intervention</i>	<i>Control</i>	<i>P value</i>
<b>Age years</b>	49.2± 3.8	51.4± 3.3	>0.05
<b>BMI (kg/m<sup>2</sup>)</b>	30.6±3.1	31.1± 3.5	>0.05
<b>WC (cm)</b>	98.7± 4.3	100.1± 4.7	>0.05
<b>c-LDL (mg/dl)</b>	128.4± 13.9	132.6± 14.6	>0.05
<b>c-HDL (mg/dl)</b>	48.3± 6.2	47.8± 6.0	>0.05
<b>Triglycerides (mg/dl)</b>	161.8± 15.6	164.2± 16.1	>0.05
<b>Glycaemia (mg/dl)</b>	111.2± 7.6	113.1± 6.9	>0.05
<b>SBP (mm Hg)</b>	134.8± 10.5	136.4± 10.2	>0.05
<b>DBP(mmHg)</b>	85.3± 8.4	87.7± 8.9	>0.05

Note: WC: Waist circumference. c-LDL: Low density lipoprotein cholesterol. c-HDL: High density lipoprotein cholesterol. SBP: Systolic blood pressure. DBP: Diastolic blood pressure.

Two experienced observers assessed EAT by transthoracic two-dimensional echocardiography (GE-Vivid 7 system; GE-Vingmed Ultrasound AS; Horten, Norway) according to standard techniques stated by the American Society of Echocardiography<sup>19</sup>. In a more detailed way, epicardial fat thickness (EFT) was measured in end diastole on the free wall of the right ventricle from the parasternal long- and short-axis views, as previously described by Iacobellis et al.<sup>20</sup>. Intra-observer and inter-observer variability of EAT thickness quantification was analyzed using the inter-class correlation coefficient.

Abdominal fat mass was determined using a Lunar DPX-L type DEXA (dual energy X ray absorptiometry). This device has been widely used in the literature because the software it uses greatly facilitates the radiologist's task of defining the regions of interest (ROI) for the study of body fat mass. The ROI envisaged in our study were the lumbar regions L1-L4 and L4-L5. To avoid bias when delineating ROI, it is crucial that the patient is positioned correctly in parallel to the scanner table. This procedure exposes subjects to a minimum radiation of between 0.015 to 0.06 *mrem*, depending on the antero-posterior diameter of the person undergoing the examination, equivalent to between 1% and 10% of a chest radiograph.

In order to determine physical fitness before and after the intervention, all participants performed a continuous maximal incremental test, using the standard Bruce treadmill protocol until exhaustion, at the Sports Medicine Laboratory. Gas exchange data were collected throughout the test using a breath-by-breath metabolic system. The electrocardiogram (EKG) was continuously recorded using a 12 lead stress analysis system. In this respect, the criteria we used to determine the maximal oxygen consumption (VO<sub>2</sub>max) was the maximal O<sub>2</sub> value at plateau despite increasing workload (< 2 ml/kg/min in-

crease in VO<sub>2</sub> between progressive stages). Furthermore, it should be pointed out that all participants, including the control group, underwent a pre-training session to be familiarized with the correct use of the treadmill.

Written informed consent was obtained from all participants. Furthermore, the current protocol was approved by an Institutional Ethics Committee. The results were expressed as mean (SD). The Shapiro-Wilk test was used to assess whether data were normally distributed. To compare the mean values, a one-way analysis of variance (ANOVA) with post-hoc Bonferroni correction to account for multiple tests was used. Pearson's correlation coefficient (r) was used to determine potential associations among tested parameters. Finally, Cohen's d statistics were used for determining mean effect sizes as follows: small d >0.2 and < 0.5; medium d > 0.5 and <0.8; large d > 0.8.

## Results

Physical fitness, expressed as VO<sub>2</sub>max, was significantly improved (26.6±1.5 vs. 29.2±1.7 ml/kg/min; p=0.0396) in the intervention group. Similarly, abdominal and epicardial fat mass were significantly improved after the completion of the training program. These results are listed in table II. Similarly, WC was significantly reduced in the intervention group (98.7±4.3 vs 95.0±3.9 cm; p=0.037). Furthermore, significant correlations were found between WC and both EFT (r=0.57; p=0.028) and abdominal (L1-L4 [r=0.68; p=0.10]; L4-L5 [r=0.63; p=0.022]) adipose tissue. It should be pointed out that intra-observer reproducibility for EFT thickness measurements was excellent with a correlation coefficient of 0.98, while the inter-observer data showed a coefficient of 0.96. Lastly, neither sports-related injuries nor withdrawals from the program were reported during the entire study period.

**Table II**  
*Influence of aerobic training on epicardial and abdominal fat mass in sedentary postmenopausal women with metabolic syndrome.*

	INTERVENTION GROUP		CONTROL GROUP		
	Pre-test	Post-test	Baseline	Final	Cohen's d
<b>EFT</b>	7.3 ± 0.8	6.4 ± 1.1 <sup>a,b</sup>	7.5 ± 1.0	7.7 ± 1.2	0.78
<b>ROI LI-L4</b>	38.9 ± 3.6	35.9 ± 4.0 <sup>a,b</sup>	39.5 ± 3.9	39.8 ± 4.1	0.97
<b>ROI L3-L4</b>	40.4 ± 4.1	37.5 ± 3.9 <sup>a,b</sup>	40.7 ± 4.1	41.2 ± 4.3	0.88

Note: EFT: Epicardial fat thickness expressed in mm. ROI LI-L4: Fat mass percentage in region of interest LI-L4; ROI L3-L4: Fat mass percentage in region of interest L3-L4 <sup>a</sup>p<0.05 versus pre-test; <sup>b</sup>p<0.05 versus control group (final).

Finally, no significant changes in any of the tested outcomes were found in the control group.

## Discussion

The clinical relevance of the present results is related to the major relevance of visceral adipose tissue (VAT) in the pathogenesis of MS. As was hypothesized, a home-based training reduced both epicardial and abdominal fat mass in postmenopausal women with MS. In a previous study, Brinkley et al.<sup>21</sup> found that a mixed protocol based on caloric restriction and aerobic exercise reduced pericardial fat in postmenopausal women. Similarly, Fu et al.<sup>22</sup> reported that dietary education and exercise intervention for 3 months significantly reduced EAT in non-diabetic obese men with MS. It should be emphasized that our training program was not combined with a highly controlled dietary intervention so that it may be considered more feasible and practical for participants. Lastly, a recent systematic review and meta-analysis<sup>15</sup> showed that an exercise program without hypocaloric diet has the potential to reduce visceral adipose tissue. Furthermore, these authors also concluded that combining aerobic training with strength training does not result in a higher decrease of visceral adipose tissue<sup>15</sup>.

Anyway, these findings are of particular interest given that women who lose more fat are more likely to lower blood pressure, glucose, and triglyceride levels to resolve MS<sup>23</sup>.

Furthermore, the present protocol lasted just 16 weeks in contrast to the 6-month exercise intervention designed by Jonker et al.<sup>24</sup> to reduce paracardial fat volume in patients with type 2 diabetes mellitus.

Another striking feature of the current study was the moderate correlation that was found between EFT, measured by echocardiography, and waist circumference (WC). These results are consistent with previous data reported by Vicennati et al.<sup>25</sup> in obese women and Cetin et al.<sup>26</sup> in patients with type 2 diabetes. Therefore, these findings support WC is widely accepted as an indicator of visceral abdominal fat (VAT) and by extension, cardiometabolic risk. Anyway, it should be also pointed

out EAT assessment scores over WC regarding both accuracy and reproducibility<sup>19</sup>. In addition, Sengul et al.<sup>27</sup> reported EAT was associated with increased carotid intima-media thickness, a potential indicator of subclinical atherosclerosis, in patients with metabolic syndrome.

Lastly, a systematic review reported by Rabkin<sup>28</sup> found that EAT correlates significantly with each of the components of the MS such as systolic blood pressure (SBP) and plasma levels of triglycerides (TG) and high-density lipoprotein cholesterol (HDL-cholesterol). Similarly, EAT was significantly associated with parameters of inflammation in obese subjects<sup>29</sup>.

Finally, the treadmill training improved physical fitness in postmenopausal women with MS. Recent studies had also reported EAT was associated with poor cardiorespiratory fitness in overweight and obese male adults<sup>30</sup>. In a previous study, Arsenault et al.<sup>31</sup> concluded that after matching individuals with similar body mass index values but with high or low cardiorespiratory fitness (CRF), men with low CRF were characterized by more visceral adipose tissue accumulation.

The present study has some limitations that should be considered. The small sample size may also limit the generalization of the results. Another major weakness was the relatively short duration of the exercise intervention in that there was no follow-up to determine whether the positive effects induced by treadmill training were maintained. Accordingly there is a clear need for large longitudinal studies to determine whether correction of epicardial and abdominal fat mass improves clinical outcomes of postmenopausal women with MS.

On the other hand, regarding the strengths, the excellent adherence rate suggested the training program was effective and easy to follow-up. This was of particular interest given that it may finally give them the confidence to continue exercising after the trial finishes. Furthermore, EAT volume was obtained by a safer and easier technique such as transthoracic echocardiography when compared to computed tomography (CT) and/or magnetic resonance imaging (MRI)<sup>32,33</sup>.

In conclusion, home-based treadmill training reduced epicardial and abdominal fat in postmenopausal women with MS. A secondary finding was that a mo-

derate correlation was found between EAT and WC. While current investigations are promising, future studies are still required to consolidate this approach in clinical application.

### Conflict of interest

Authors would like to express there is no conflict of interest to declare.

### References

1. Lehman SJ, Massaro JM, Schlett CL, O'Donnell CJ, Hoffmann U, Fox CS. Peri-aortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. *Atherosclerosis* 2010; 210:656–661.
2. Ding J, Hsu FC, Harris TB, Kritchevsky SB, Szklo M, Ouyang P, et al. The association of pericardial fat with incident coronary heart disease: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* 2009; 90:499–504.
3. Fernández-Muñoz MJ, Basurto-Acevedo L, Córdova-Pérez N, Vázquez-Martínez AL, Tepach-Gutiérrez N, Vega-García S, et al. Epicardial Adipose Tissue Is Associated With Visceral Fat, Metabolic Syndrome, and Insulin Resistance in Menopausal Women. *Rev Esp Cardiol* 2014; 67:436–441.
4. Lima-Martínez MM, Paoli M, Donis JH, Odreman R, Torres C, Iacobellis G. Cut-off point of epicardial adipose tissue thickness for predicting metabolic syndrome in Venezuelan population. *Endocrinol Nutr* 2013; 60: 570–6.
5. Marchington JM, Mattacks CA, Pond CM. Adipose tissue in the mammalian heart and pericardium: structure, foetal development and biochemical properties. *Comp Biochem Physiol B* 1989; 94:225–32.
6. Gormez S, Demirkan A, Atalar F, Caynak B, Erdim R, Sozer V, et al. Adipose tissue gene expression of adiponectin, tumor necrosis factor- $\alpha$  and leptin in metabolic syndrome patients with coronary artery disease. *Intern Med* 2011; 50:805–10.
7. Hatem SN, Sanders P. Epicardial adipose tissue and atrial fibrillation. *Cardiovasc Res* 2014; 102:205–13.
8. Park HE, Choi SY, Kim M. Association of epicardial fat with left ventricular diastolic function in subjects with metabolic syndrome: assessment using 2-dimensional echocardiography. *BMC Cardiovasc Disord* 2014; 14: 3
9. Sengul C, Duman D. The association of epicardial fat thickness with blunted heart rate recovery in patients with metabolic syndrome. *Tohoku J Exp Med* 2011; 224:257–62.
10. Kilicaslan B, Ozdogan O, Aydin M, Dursun H, Susam I, Ertas F. Increased epicardial fat thickness is associated with cardiac functional changes in healthy women. *Tohoku J Exp Med* 2012; 228:119–24.
11. Payne GA, Kohr MC, Tune JD. Epicardial perivascular adipose tissue as a therapeutic target in obesity-related coronary artery disease. *Br J Pharmacol* 2012; 165: 659–669.
12. Karadag B, Ozulu B, Ozturk FY, Oztekin E, Sener N, Altuntas Y. Comparison of epicardial adipose tissue (EAT) thickness and anthropometric measurements in metabolic syndrome (MS) cases above and under the age of 65. *Arch Gerontol Geriatr* 2011; 52:e79–84.
13. Willens HJ, Byers P, Chirinos JA, Labrador E, Hare JM, de Marchena E. Effects of weight loss after bariatric surgery on epicardial fat measured using echocardiography. *Am J Cardiol* 2007; 99:1242–5.
14. Grosso AF, de Oliveira SF, Higuchi Mde L, Favarato D, Dallan LA, da Luz PL. Synergistic anti-inflammatory effect: simvastatin and pioglitazone reduce inflammatory markers of plasma and epicardial adipose tissue of coronary patients with metabolic syndrome. *Diabetol Metab Syndr* 2014; 6:47.
15. Vissers D, Hens W, Taeymans J, Baeyens JP, Poortmans J, Van Gaal L. The Effect of Exercise on Visceral Adipose Tissue in Overweight Adults: A Systematic Review and Meta-Analysis. *PLoS One* 2013; 8:e56415.
16. Rosety-Rodríguez M, Díaz-Ordoñez A, Rosety I, Fornieles G, Camacho-Molina A, García N, et al. Aerobic training improves antioxidant defense system in women with metabolic syndrome. *Medicina (B Aires)* 2012; 72:15–8.
17. Rosety-Rodríguez M, Fornieles G, Camacho-Molina A, Rosety I, Díaz AJ, Rosety MA, et al. A short-term training program reduced acute phase proteins in premenopausal women with metabolic syndrome. *Nutr Hosp* 2013; 28:1604–9.
18. Stensvold D, Slørdahl SA, Wisløff U. Effect of exercise training on inflammation status among people with metabolic syndrome. *Metab Syndr Relat Disord* 2012; 10:267–72.
19. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; 2:358–67.
20. Iacobellis G, Assael F, Ribaudo MC, Zappaterreno A, Alessi G, Di Mario U, et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. *Obes Res* 2003;11:304–10.
21. Brinkley TE, Ding J, Carr JJ, Nicklas BJ. Pericardial fat loss in postmenopausal women under conditions of equal energy deficit. *Med Sci Sports Exerc* 2011; 43:808–14.
22. Fu CP, Sheu WH, Lee IT, Tsai IC, Lee WJ, Liang KW, et al. Effects of weight loss on epicardial adipose tissue thickness and its relationship between serum soluble CD40 ligand levels in obese men. *Clin Chim Acta*. 2013; 421:98–103.
23. Joseph LJ, Prigeon RL, Blumenthal JB, Ryan AS, Goldberg AP. 2011. Weight loss and low-intensity exercise for the treatment of metabolic syndrome in obese postmenopausal women. *J Gerontol A Biol Sci Med Sci* 2011; 66:1022–9.
24. Jonker JT, de Mol P, de Vries ST, Widya RL, Hammer S, van Schinkel LD, et al. Exercise and type 2 diabetes mellitus: changes in tissue-specific fat distribution and cardiac function. *Radiology* 2013; 269:434–42.
25. Vicennati V, Cavazza C, Garelli S, Nayak K, Goyal A, Diaz LS. Anthropometric, hormonal and nutritional correlates of epicardial fat in obese women. *Endocrine Abstracts* 2012; 29:1233.
26. Cetin M, Cakici M, Polat M, Suner A, Zencir C, Ardic I. Relation of epicardial fat thickness with carotid intima-media thickness in patients with type 2 diabetes mellitus. *Int J Endocrinol* 2013; 769175.
27. Sengul C, Cevik C, Ozveren O, Oduncu V, Sunbul A, Akgun T, et al. Echocardiographic epicardial fat thickness is associated with carotid intima-media thickness in patients with metabolic syndrome. *Echocardiography* 2011; 28:853–8.
28. Rabkin SW. The relationship between epicardial fat and indices of obesity and the metabolic syndrome: a systematic review and meta-analysis. *Metab Syndr Relat Disord*. 2014; 12:31–42.
29. Gaborit B, Kober F, Jacquier A, Moro PJ, Cuisset T, Boullu S, et al. Assessment of epicardial fat volume and myocardial triglyceride content in severely obese subjects: relationship to metabolic profile, cardiac function and visceral fat. *Int J Obes (Lond)* 2012; 36:422–30.
30. Kim MK, Tanaka K, Kim MJ, Matsuo T, Tomita T, Ohkubo H, et al. Epicardial fat tissue: relationship with cardiorespiratory fitness in men. *Med Sci Sports Exerc* 2010; 42:463–9.
31. Arsenaault BJ, Lachance D, Lemieux I, Alméras N, Tremblay A, Bouchard C. Visceral adipose tissue accumulation, cardiorespiratory fitness, and features of the metabolic syndrome. *Arch Intern Med* 2007; 167:1518–25.
32. Kunita E, Yamamoto H, Kitagawa T, Ohashi N, Oka T, Utsumomiya H, et al. Prognostic value of coronary artery calcium and epicardial adipose tissue assessed by non-contrast cardiac computed tomography. *Atherosclerosis*. 2014; 233:447–53.
33. Verhagen SN, Visseren FL. Perivascular adipose tissue as a cause of atherosclerosis. *Atherosclerosis* 2011; 214:3–10.