



Original/*Obesidad*

Lipid profile response to weight loss program in overweight and obese patient is related with gender and age

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Abstract

Introduction: the risk of developing cardiovascular disease (CVD) increases with age, however CVD is markedly higher in men than in no-menopausal women. There are few interventions where compare the different effects to lose weight on lipid profile between men and women.

Objective: the aim of this study was to compare the response on the lipid profile by gender after a weight loss program, and determine whether there are differences by age group.

Methods: one hundred eighty (96 women and 84 men) overweight and obese participants (BMI 25–34.9 kg/m²) aged 18–50 years were randomised into treatment groups. The intervention period was 22 weeks (in all cases 3 times/wk of training for 22 weeks and 2 weeks for pre and post evaluation). All subjects followed a hypocaloric diet (25-30% less energy intake). Energy intake, body composition) and blood lipid profile were recorded at baseline and after of treatment.

Results: the response of HDL varied between men and women (p = 0.001). While in women it decreased (HDL: -2.94%, p = 0.02), HDL was elevated in men (HDL: 5% p = 0.02). After intervention men achieved decrease significantly LDL values a 6.65% more than women (p = 0.01). For TG concentrations there were significant differences between men and women in baseline however, only men had a significant change in post-training measured (p = 0.001). TC showed significant differences between men and women in baseline (p = 0.013). After intervention, men and women showed a significant decreased to TC (p = 0.01).

INFLUENCIA DEL GÉNERO Y LA EDAD EN LA RESPUESTA DEL PERFIL LIPÍDICO TRAS UN PROGRAMA DE PÉRDIDA DE PESO EN PERSONAS CON SOBREPESO Y OBESIDAD

Resumen

Introducción: el riesgo de desarrollar una enfermedad cardiovascular (ECV) se incrementa con la edad; sin embargo, el riesgo de ECV en edad fértil es mayor en hombres que en mujeres. Son pocas las intervenciones en las que se comparan las diferencias entre hombres y mujeres que un programa de pérdida de peso tiene sobre el perfil lipídico.

Objetivo: comprobar el cambio en el perfil lipídico entre hombres y mujeres tras un programa de pérdida de peso, comparando las diferencias por género y categoría de edad.

Métodos: ciento ochenta participantes (96 mujeres y 84 hombres) con sobrepeso y obesidad (IMC 25–34.9 kg/m²) con edades comprendidas entre los 18-50 años fueron repartidos de forma aleatoria en los diferentes grupos de intervención. El período de intervención fue de 22 semanas y 2 semanas para la evaluación pre y post. Todos los sujetos siguieron una dieta equilibrada hipocalórica (25-30% de restricción calórica) y un programa de ejercicio 3 veces/semana. Antes y después de la intervención todos los grupos fueron evaluados de los cambios en el perfil lipídico, la composición corporal y la ingesta diaria.

Resultados: hubo diferencias significativas en el cambio de HDL entre hombres y mujeres (p = 0,001). Mientras que en las mujeres disminuyó (HDL: -2,94%, p = 0,02), en los hombres hubo un aumento de la concentración de HDL (HDL: 5% p = 0,02). Después de la intervención los hombres lograron disminuir significativamente el LDL un 6,65% más que las mujeres (p = 0,01). Para concentraciones de TG hubo diferencias significativas entre hombres y mujeres al inicio de la intervención; sin embargo, solo los hombres tuvieron una mejoría significativa tras la intervención (p = 0,001). El TC mostró diferencias significativas entre hombres y mujeres preintervención (p = 0,013). Tras la intervención, los hombres y las mujeres mostraron una significativa disminución de TC (p = 0,01).

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Conclusion: men achieve a positive greater change on lipid profile than women. In addition, the favorable lipid profile response decreases with increasing age.

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Key words: *Lipoprotein. Gender. Overweight. Obese. Weight loss treatment. Clinical trial.*

Abbreviations

ACSM: American College of Sport Medicine.
BMI: Body mass index.
CF: Tascular fitness.
DEE: Daily energy expenditure.
DXA: Dual-energy x-ray absorptiometry.
E: Endurance training group.
HDL: High density lipoprotein.
HPA: Habitual physical activity.
HR: Heart rate.
HRR: Heart rate reserve.
HULP: University Hospital La Paz.
ICCr: Intraclass correlation coefficient.
LDL: Low density lipoprotein.
MetS: Metabolic Syndrome.
PA: Diet and physical activity recommendations group.
PRONAF: Programas de Nutrición y Actividad Física para el tratamiento del sobrepeso y la obesidad.
RM: Repetition maximum.
RPE: Rate of perceived exertion.
S: Strength training group.
SE: Combine training group.
TC: Total cholesterol.
TG: Triglycerides.
VO₂: Oxygen uptake.

Introduction

There is a marked difference in cardiovascular disease (CVD) risk between sexes. Over the last decade, compelling evidence supports the idea that the different impact of CVD in men and women may be, at least in part, related to the cardiovascular and metabolic effects of sex steroid hormones¹. Epidemiologically, the incidence of CVD is higher in men than in premenopausal women². CVD incidence and mortality among men have shown to be 3 fold and 5 fold greater than in women, respectively³. However after the menopause, the risk of CVD increases in women⁴. Blood lipid profile is considered an independent cardiovascular risk factor⁵. Many cohort studies attempt to explain these gender differences, and the influence that age may have on lipid profile change^{1,3,6}. Premenopausal women show lower concentrations of total cholesterol (TC), low-density lipoprotein cholesterol

Conclusión: los hombres obtuvieron un cambio más favorable en las variables del perfil lipídico con respecto a la mujeres. Además, la respuesta al perfil lipídico favorable disminuye con el aumento de la edad.

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Palabras clave: *Perfil lipídico. Género. Edad. Obesidad. Sobrepeso. Pérdida de peso. Ensayo clínico.*

(LDL), and plasma triglycerides (TG), and higher high-density lipoprotein cholesterol (HDL) values than men, partially due to effects of estrogen⁷. In both sexes, the risk of CVD increases markedly with age. In most populations, TC increases as age increases. In men, this increase usually levels off around the age of 45 to 50 years, whereas in women, the increase continues sharply with postmenopause³.

Clinical trials have already shown the relevant role of healthy habits as balance diet, no smoke and regular physical activity to protect and decrease CVD risk⁸⁻¹⁰. However, most of these lifestyle or weight loss interventions do not analyze or compare the different response of lipid profile in men and women and age groups. PRONAF Study¹¹ was designed as a weight loss intervention for men and women allowing comparison of the lipid profile changes obtained. It also allows to study the effect of age on the response of the lipid profile after intervention.

Therefore, the aim of this study was to measure the response of the lipid profile between men and women after weight loss program with calorie restriction diet and exercise. A secondary aim was to determine whether there are differences by age group in the change on lipid profile.

Material and methods

Study design

The PRONAF study is a large study *Nutrition and Physical Activity for Obesity* (the PRONAF study according to its Spanish initials), whose aim was to investigate the effects of different types of physical activity and nutrition programs for the treatment of overweight and obesity. Data collection took place from 2008 to 2011 in the Region of Madrid, Spain. This study was an intervention trial of 24 week duration. The study was performed twice, one year apart, first in the overweight group (January 2009 - July 2010) and then in the obese group (January 2010 - July 2011). The measurements took place in the first week (baseline values) for all subjects before starting training, and after 22 weeks of training in week 24 (post-training values). Detailed descriptions of the PRONAF sampling and recruitment approaches, standardisation and

harmonisation processes, inclusion criteria, data collection, intervention program, statistic analyses and quality control activities were published previously¹¹.

Study sample

The study sample population consisted of 173 overweight and obese participants (94 women and 79 men) (overweight participants: body mass index [BMI] 25–29.9 kg/m², obese participants: BMI 30–34.9 kg/m²), all middle-aged (range 18–50 years). Baseline characteristics of the participants are summarized in Table I. All subjects were healthy, normoglycaemic, non-smokers, but led sedentary lifestyles. All female subjects had regular menstrual cycles. The exclusion criteria covered all physical and psychological diseases that may have precluded the performance of the requested strength or endurance training, and the consumption of any medication known to influence physical performance or the interpretation of the results. Subjects with a background of systematic strength or endurance training (moderate to high intensity training more than once a week) in the year before the study started were also excluded. In agreement with the guidelines of the Declaration of Helsinki regarding research on human subjects, all participants signed an institutionally approved document of informed consent. All subjects were carefully informed about the possible risks and benefits of the study, which was approved by the Human Research Review Committee of the La Paz University Hospital (HULP). HULP code PI-643.

Subjects who fulfilled the inclusion criteria and passed a baseline physical examination were stratified by age and sex and randomly assigned in four intervention groups. The intervention groups are extensively described in Zapico et al.¹¹. For the presented work, the sample was classified by sex and age in responders or no-responders groups. Responders were defined as those who achieved a decrease in body weight higher

than 5% and no-responders those who achieved less than 5%¹². Also, participants were assigned into 3 age groups: 18–29 years group, 30–39 years group and 40–50 years group.

Intervention program

Exercise training program. The different exercise groups followed the corresponding, supervised training program, which consisted in all cases of training 3 times/wk for 22 weeks¹¹. All training sessions were carefully supervised by certified personal trainers. An adherence to training of 90% was demanded.

Hypocaloric diet program. Diet prescription was performed for all patients by expert dieticians in the Nutrition Department of HULP. All groups underwent an individualized and hypocaloric diet (between 1200 and 3000 kcal). Diet was lowered a 25–30% from daily energy expenditure (DEE) measured using SenseWear Pro Armband™ data.

Data collection

The analyses and measurements were made at baseline and at the end of the study period:

Blood analysis. All blood samples were taken after 12 h fast between 7:00 and 9:00 a.m. at baseline and post-training intervention (week 1 and week 24). All post-training samples were obtained 72 hours after the last training day to avoid acute effects of training on blood lipids. All blood samples were drawn from the antecubital vein and handled according to standardized laboratory practice at HULP. Serum biochemicals (total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) were determined using enzymatic methods with Olympus reagents by automated spectrophotometry performed on Olympus AU 5400 (Olympus Diagnostica, Hamburg, Germany).

Table I
Baseline data of the participants (n=173)

	Overweight n=84		Obesity n=96	
	Women n=47	Men n=34	Women n=47	Men n=45
Age (years)	37.29 ± 8.25	37.42 ± 8.02	39.02 ± 7.74	38.79 ± 7.99
Body Weight (kg)	73.5 ± 5.87	88.21 ± 8.13	88.33 ± 10.1	102.04 ± 8.94
Height (m)	1.62 ± 0.06	1.75 ± 0.07	1.64 ± 0.07	1.77 ± 0.06
BMI (kg/m ²)	28.01 ± 1.32	28.57 ± 1.12	32.41 ± 1.85	32.4 ± 1.90
Body fat (%)	43.28 ± 3.62	33.8 ± 4.63	47.11 ± 3.49	38.17 ± 4.02
Body fat free mass (kg)	40.25 ± 4.3	55.99 ± 5.47	44.3 ± 4.71	58.63 ± 8.96
Bone mineral density (g/cm ²)	1.18 ± 0.1	1.26 ± 0.09	1.21 ± 0.11	1.3 ± 0.1

Results are shown as Mean ± SD.

Note. BMI, Body Mass Index. Body fat, Body fat free mass and Bone mineral density calculated by Dual-energy x-ray absorptiometry (DXA).

Menstrual cycle was controlled by diary to define the follicular and luteal phases when blood samples were taken¹³.

Body composition. Body composition was assessed by dual-energy x-ray absorptiometry DXA (GE Lunar Prodigy; GE Healthcare, Madison, WI, GE Encore 2002, version 6.10.029 software) and was used to measure total body fat (%) and body fat free (kg) mass.

Anthropometric measures included height (stadiometer SECA; range 80-200cm), body mass (BC-420MA, Bio Lógica, Tecnología Médica SL) and body mass index (BMI) calculated as [body weight (kg)/(height (m))²].

Statistical analysis

SPSS version 15.0 for Windows was used for statistical analyses (SPSS Inc., Chicago, Illinois, USA). Standard statistical methods were used for the calculation of the means and standard deviation. To analyze the effects on lipid profile used a threshold of a 5% weight loss was taken into account to consider the sample as responders or non-responders¹².

The effects of gender (men vs. women) and age (18-29 vs. 30-39 vs. 40-50 groups) on blood lipid profile were tested using four-way repeated-measures analysis of variance (ANOVA).

Multivariate analysis of variance (MANOVA) was used to compare within gender and age the delta percentage on lipid profile. Bonferroni's post-hoc test was employed to locate specific differences. Relationships among the android fat, gynoid fat, and changes in the dependent variables were determined by using Pearson correlation coefficients. The delta percentage was calculated through the standard formula: % change =

$[(\text{post-test score} - \text{pre-test score})/\text{pre-test score}] \times 100$. The significance level was set at $\alpha=0.05$.

Results

Table II shows changes in plasma lipid and lipoprotein concentrations in four groups (men and women responders and men and women no-responders) before and after the intervention period. For HDL levels there were significant differences between men and women of responders and no-responders in baseline and post-training. Women responders decreased significantly HDL concentrations, whereas men responders obtained a significant increase for HDL values. In baseline, LDL values showed differences between men and women of the responders group ($p=0.001$) but not in no-responders group. After intervention, men responders and no-responders improved LDL concentrations, showed a significant decrease ($p=0.001$; $p=0.009$). For TG concentrations there were significant differences between men and women responders in baseline and trend to significant in post-training ($p=0.08?$). Only the men responders improved significantly the TG values after intervention. TC showed significant differences between men and women responders in baseline. After intervention, men and women responders and men no-responders showed a significant decreased to TC. The 62.5% in men and the 61.7% achieved or remained to non-atherogenic values. The effects size to lipid profile variables was: HDL: 0.017, LDL: 0.062, TG: 0.001, CT: 0.028.

Table III shows baseline and post-training blood lipid profile values for gender and age groups (18-29; 30-39; 40-50). HDL decreased significantly from the baseline to post-training period in women responders

Table II
Changes on blood lipid profile in man and women

		Responders					No responders				
		Baseline		Post-training		p-value	Baseline		Post-training		p-value
		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
HDL (mg/dL)	Men	46.23 ± 9.50	48.17 ± 10.07	0.02	43.93 ± 6.23	44.86 ± 7.37	0.60				
	Women	55.65 ± 11.20 *	53.88 ± 10.57 *	0.02	52.70 ± 9.83 *	52.10 ± 11.22 *	0.69				
LDL (mg/dL)	Men	142.75 ± 30.79	125.11 ± 29.25	0.01	134.07 ± 20.66	120.86 ± 13.52	0.01				
	Women	124.21 ± 29.29 *	120.36 ± 27.75	0.08	126.53 ± 26.13	126.21 ± 22.90	0.94				
TG (mg/dL)	Men	132.31 ± 66.80	110.40 ± 48.04	0.01	126.71 ± 55.41	119.14 ± 56.72	0.52				
	Women	100.18 ± 37.00 *	96.43 ± 44.34	0.46	112.00 ± 64.39	99.65 ± 45.63	0.21				
CT (mg/dL)	Men	215.80 ± 36.75	193.38 ± 34.58	0.01	200.79 ± 24.66	187.86 ± 15.84	0.01				
	Women	200.50 ± 36.06 *	192.08 ± 34.14	0.04	198.60 ± 37.37	195.30 ± 32.49	0.53				

Results are shown as Mean ± SD. (Men responders n=65; women responders n=74; men no responders n=14; women no responders n=20) HDL, higher high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, plasma triglycerides; TC, total cholesterol.

*Differences within gender.
p value to change intragroup.

and no-responders of the 40-50 age group. For the 30-39 group there were significant differences in baseline and post-training HDL values between men responders and women responders. In baseline, the men responders of 40-50 group obtained significant differences with the same women age group in HDL levels. For post-training LDL values the women responders of 19-29 group showed significant differences with 30-39 group and 40-50 group. In baseline, the men responders of 18-29 group obtained significant differences with 40-50 group for LDL concentration. Also, the participants responders of 40-50 group showed significant differences between men and women. After intervention, men no-responders 18-29 group and men responders 30-39 group and 40-50 group achieved significant improvements for LDL levels. TG values showed significant differences in baseline measure between women no-responders of the 18-29 group and the 30-39 group. In post-training moment, men responder of the 18-29 obtained significant differences to TG concentrations with the 30-39 group. There were significant differences between men and women responders of the 30-39 group in baseline. After intervention, women no-responders of the 18-29 group decreased significantly TG values. Also, men responders of the 40-50 group improved significantly TG concentrations. For TC concentrations, women responders of the 18-29 group showed significant differences with the 30-39 and 40-50 groups in post-training. Men responders of the 18-29 group obtained significant differences to TC with the 40-50 group in baseline and post-training values. In baseline, there were significant differences between men and women responders of the 40-50 group. After intervention, men responders of the 30-39 and 40-50 groups improved significantly the TC concentrations.

Figure 1 shows % change on blood lipid profile by sex.

Figure 2 shows % change on blood lipid profile by sex and age.

Discussion

The main finding of the present study was that men appeared to have a better response of the lipid profile than women to a weight loss intervention program such as the PRONAF Study. On the other hand, with age, the favorable response on lipid profile is markedly diminished.

Guidelines established by the National Cholesterol Education Program (NCEP) promote exercise and weight loss for the treatment of abnormal lipoprotein levels¹⁴. To improve cardiometabolic health in men and women, the literature suggests that healthy diet, weight loss, exercise and physical activity are key to prevent and treat the development of these diseases¹⁵. However, despite men and women present different response to the treatments, there are not individualized recommendations.

The results of the present work showed different significant changes in HDL between men and women. In baseline, HDL concentration was significantly greater in women than men. However, after intervention this difference was lower because men obtained a significant improvement and women decreased significantly. Different studies reported in their results that HDL can increase¹⁶, decrease^{17,18}, or remain stable¹⁹ with weight loss. In women, the reduction in fat intake leads to decrease HDL concentration^{9,20,21}. Our results are in agreement with these studies. After intervention, both men and women achieved an average of 10% weight loss (data no showed). This reduction represents the main reason for the improvement on the lipid profile levels^{22,23}.

For LDL, TG and TC concentrations the PRONAF Study participants achieved general improvements after intervention. Lipid profile values decreased up to values considered as no-atherogenic. Similar interventions also agree with our outcomes^{9,10,24-28}. However, it is not that clear to discuss what happens when sex differences are studied, because there are not clinical trials comparing treatment efficacy and impact between men and women. Nevertheless, we found interventions which applied hormone therapy to improve cardiovascular risk factors in men and women^{1,29}. In these interventions considered to apply different doses for men and women, due to androgens and estrogens influence in the change in cardiovascular risk factors, often in a sex-specific manner^{1,29}.

In this regard, there is controversy to consider the different cardiovascular risk factors by sex. Regiz-Zagrosek et al.⁷ reported that it should be considered in a gender-specific manner what factors can affect more in men than in women and vice versa. They emphasize the need to study gender-specific pathophysiology analysis in response to exercise⁷.

When the response on lipid profile is compared by sex after weight loss intervention in our study, men achieved a better change than women. In the literature, we found reviews and epidemiological studies that try to explain the gender-specific differences to lipid profile abnormalities treatment. There are several factors that can affect men and women differently. Fat distribution is different in men than in women. Peripheral adiposity with gluteal fat accumulation characterizes premenopausal women⁷. However, the male pattern is android obesity⁷. This body distribution is very important because the shift from peripheral to visceral obesity has a number of negative consequences. First, visceral fat is an important source of free fatty acids and inflammatory mediators which are directly delivered to the liver via the portal vein. This contributes to develop lipid abnormalities⁷. Visceral adipocytes differ from peripheral adipocytes in their lipolytic activity^{30,31}. Moreover, fat tissue interferes with hormone metabolism, even more as growth and aging takes place. White fat is the major source of estrogens in elderly women and

Table III
Changes on blood lipid profile in man and women by age groups

	Men responders						Women responders						Men no responders						Women no responders														
	Post-training			p-value	Post-training			p-value	Baseline			p-value	Post-training			p-value	Baseline			p-value	Post-training												
	Mean	SD	Mean		SD	Mean	SD		Mean	SD	Mean		SD	Mean	SD		Mean	SD	Mean		SD	Mean	SD	Mean	SD								
HDL (mg/dL)	43.75 ± 4.77	47.25 ± 5.06	51.85 ± 10.13	0.82	54.38 ± 9.55	51.85 ± 10.13	0.17	41.50 ± 6.45	42.25 ± 10.87	0.13	55.75 ± 4.35	54.25 ± 10.11	0.65	44.38 ± 9.02	46.43 ± 10.05	55.82 ± 11.17 *	0.16	45.50 ± 6.89	46.88 ± 6.24	0.55	51.57 ± 15.75	56.43 ± 15.41	0.55	47.86 ± 10.38	49.39 ± 10.90	53.46 ± 10.46	0.17	42.50 ± 0.71	42.00 ± 1.41	0.91	52.22 ± 5.49	47.78 ± 6.51	0.04
LDL (mg/dL)	148.69 ± 28.69 a	130.49 ± 22.67	124.74 ± 25.81 a	0.01	126.59 ± 26.74 *	124.74 ± 25.81 a	0.53	130.00 ± 9.90	108.00 ± 2.83	0.10	126.78 ± 28.20	123.22 ± 23.98	0.56	143.38 ± 31.35	123.57 ± 37.34	123.82 ± 28.38 a	0.18	135.13 ± 16.57	128.75 ± 12.67	0.33	117.17 ± 23.30	130.00 ± 14.53	0.09	148.69 ± 28.69 a	130.49 ± 22.67	124.74 ± 25.81 a	0.01	134.00 ± 34.09	111.50 ± 4.65	0.02	140.00 ± 25.59	127.25 ± 34.71	0.17
TG (mg/dL)	133.90 ± 71.92	125.14 ± 56.72 a	103.45 ± 60.54	0.36	100.41 ± 30.77 *	103.45 ± 60.54	0.74	115.25 ± 45.41	111.75 ± 56.72	0.82	92.00 ± 40.07 a	87.29 ± 35.06	0.77	93.88 ± 28.50	68.88 ± 65.94 a	100 ± 54.37	0.60	137.50 ± 78.24	115.25 ± 65.94	0.31	174.75 ± 101.01	118.75 ± 58.47	0.01	139.92 ± 68.14	111.03 ± 54.45	98.00 ± 38.30	0.34	151.00 ± 66.47	156.50 ± 54.45	0.85	99.67 ± 48.22	100.78 ± 49.22	0.94
TC (mg/dL)	180.38 ± 34.61	166.50 ± 27.89 b	167.00 ± 37.72	0.06	179.62 ± 36.14	167.00 ± 37.72	0.06	198.50 ± 38.13	176.75 ± 10.40	0.07	224.00 ± 29.62	205.25 ± 39.14	0.11	214.71 ± 41.24 a	192.33 ± 42.38	199.00 ± 32.38 a	0.01	201.38 ± 20.47	195.00 ± 15.75	0.44	180.00 ± 41.64	194.86 ± 33.80	0.09	224.31 ± 29.93	199.97 ± 28.19	203.26 ± 35.80 *	0.01	203.00 ± 24.04	181.50 ± 14.85	0.07	201.78 ± 32.42	191.22 ± 31.75	0.08

Results are shown as Mean ± SD. (Men responders n=65, women responders n=74, men no responders n=14, women no responders n=20).

* Differences between men responders and women responders of the same age group and intervention time.

a Differences with group 18-29.

b Differences with 30-39.

p value to change intragroup.

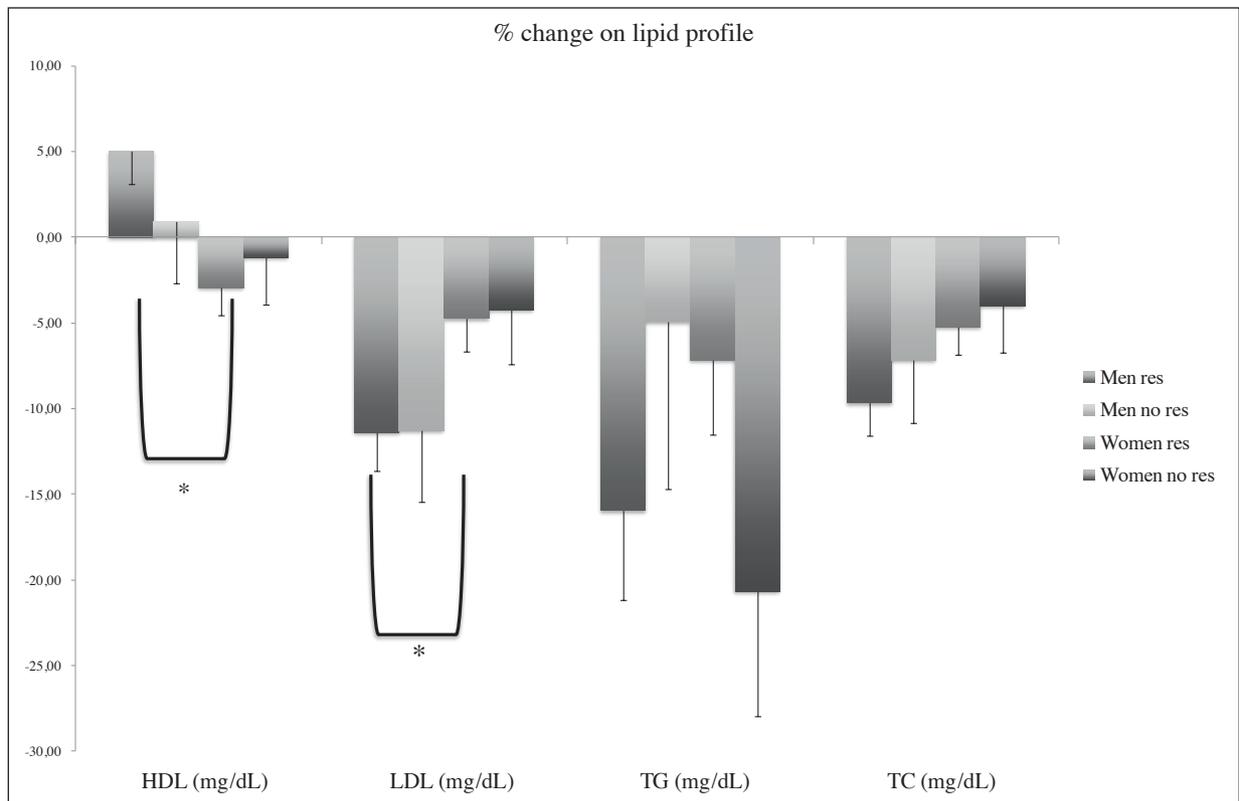


Fig. 1.—% change (mean – SD) on lipid profile by gender.

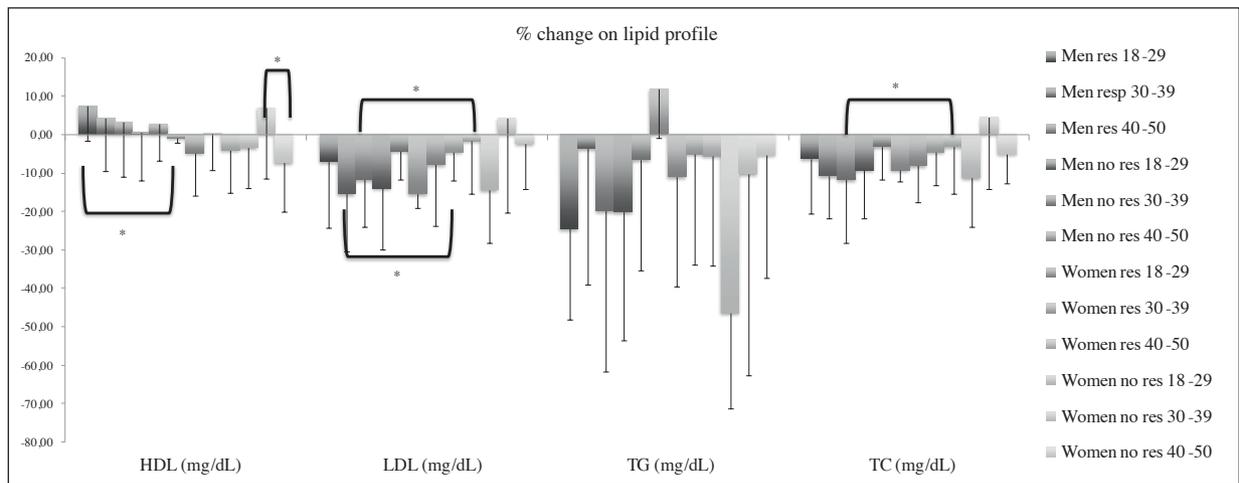


Fig. 2.—% change (mean-SD) on lipid profile by gender and age group. *: differences between gender of same age group.

men, because testosterone is converted there to estradiol in women and men. The conversion is related to adipocytes functions⁷. Due to increased age, there is an increment in the visceral fat accumulation^{7,32}. This can explain why the PRONAF Study participants obtained less improvement as age increases. When the concentration and sizes of lipoprotein particles has been studied, the results showed higher atherogenic values in the older age group⁶.

After analyzing these factors there is still discrepancy in the pathophysiologic mechanics that determine the gender differences. It is a fact that the development of atherosclerosis is influenced by gender and that the acute vasodilating effects of estrogens have been attributed as protector in the development of atherosclerosis¹.

The baseline values in our participants showed a higher cardiometabolic risk in men than in women. The

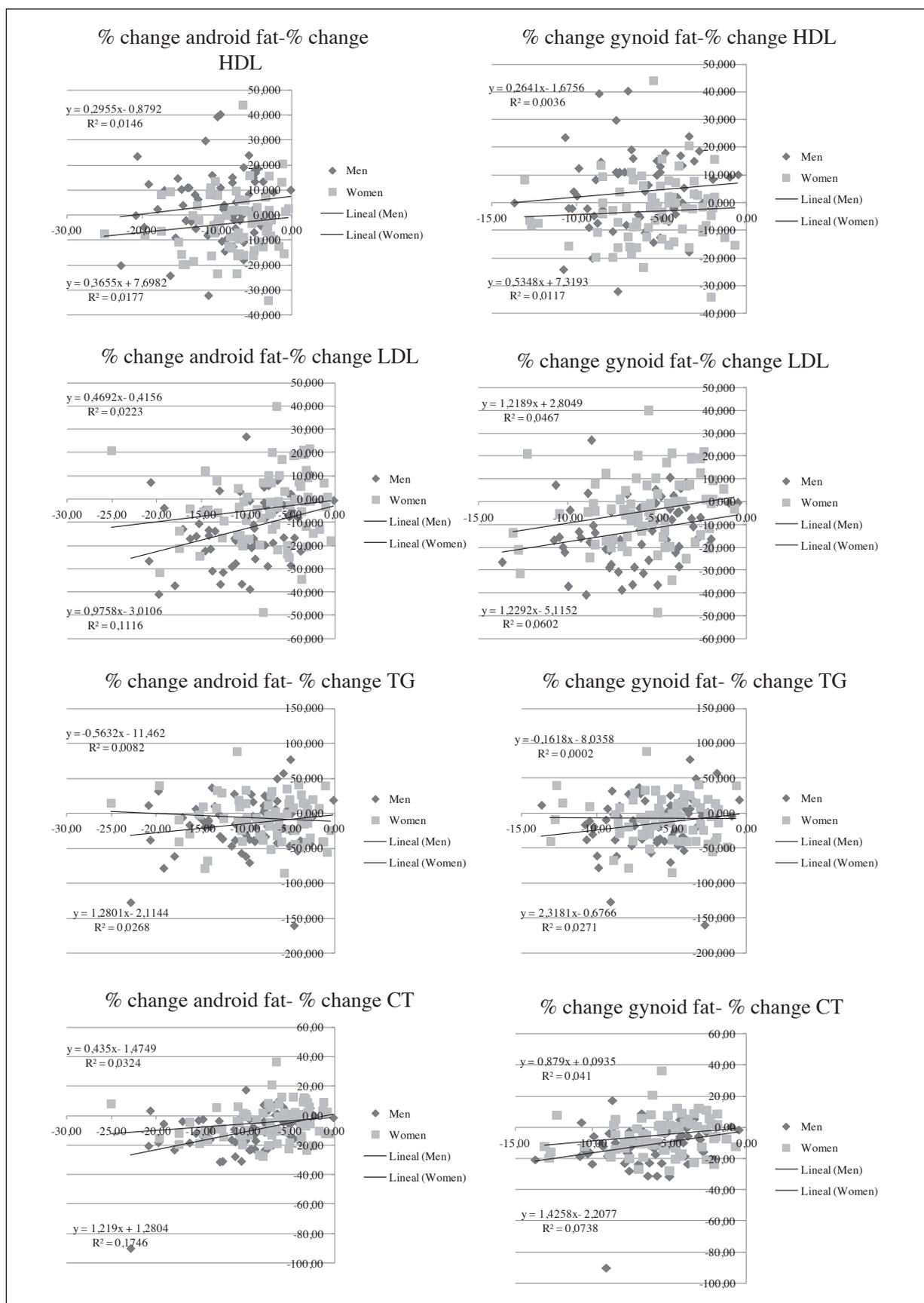


Fig. 3.—Relationship between percentage change of android and gynoid fat and percentage change of lipid profile variables.

partially sex-dependent differences between fat distribution patterns may provide an explanation of why android obesity in men is linked to more atherogenic values (Fig. 3). Thereby, the reduced tendency to accumulate fat at intraabdominal sites may be one of the primary metabolic differences underlying the reduced risk of CVD and Metabolic Syndrome. This may help to explain physiologically why the male participants who start with more atherogenic values have a better response to the weight loss treatment.

Figure 3. Relationship between percentage change of android and gynoid fat and percentage change of lipid profile variables.

Also, circulating lipids are different, are differently regulated, and have different significance in women and men^{7,32}. The estrogen effect in women is a greater activity in lipoprotein transport and removal of LDL and VLDL from the plasma than do men. This may explain the differences in baseline values between women and men in our study. The decrease in visceral fat leads to decrease LDL and TC concentrations and CVD risk. Such factors are responsible of the gender differences and may explain the better response of lipid profile in men than in women. In figure 3 can see a greater decrease in the android fat in men than in women.

Some of the findings described previously have direct clinical implications. Physicians should recognize the different effects of exercise and diet in the treatment of overweight and obesity in men and women. In PRONAF study the exercise mode showed no significant difference^{22,23}. Despite it is necessary to analyze cardiovascular risk factors, to consider the risk by sex and to choose the most appropriate treatment. In Europe, we need to develop specific aspects in our guidelines to cover cardiovascular risk management in women, as has been accomplished in USA³³.

A point of interest of the PRONAF Study is that is the first randomized controlled intervention study performed in Spanish overweight and obese adults without any other associated disease with the aim of losing weight and improving several health related parameters by means of combining caloric restriction and controlled training programs. This allows to compare and to discourse about the different response by groups of intervention, gender and/or age. And thus, to support the clinical practice for cardiovascular risk factors treatment. Unfortunately, the main limitation could be the low statistical power due to sample size to get significant differences.

Conclusion

In conclusion, the present results showed that men achieved a positive greater change on lipid profile than women. Moreover, the favorable lipid profile response decreases with increasing age. Therefore, we should consider gender characteristics in order to decide the

most appropriate treatment to enhance overweight, obesity and associated diseases. Health is a social matter and it is interesting to know which is the lowest cost and efficient treatment that ensures long-term positive changes. PRONAF Study analysis included a followed up data collection and results showed that participants maintain favorable improvements after one year finish intervention³⁴. These results are still being analyzed to throw light on the variables that can influence more weight loss interventions. It is necessary to consider the non modifiable characteristics of the sample (sex, age, genetic factors), as covered in this study. Future research is required in order to investigate the role of other non modifiable factors including genetics in PRONAF Study.

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Conflict of interest statement

The authors have no conflicts of interest.

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