

Gender, Reproductive Ageing, Adiposity, Fat Distribution and Cardiovascular Risk Factors in Spanish Women Aged 45-65

C. Bernis

INTRODUCTION

Cardiovascular disease, is now a days the leading cause of death for men and women both for developed and developing countries (Mackay and Mensah, 2004); For men and women, cardiovascular risk is known to increase with age, smoking, hypertension, blood lipids and glucose levels, and central obesity (Beck-Nielsen, 1990; Klag *et al.*, 1993; WHO, 2003). Despite that over the lifespan, approximately the same proportion of the female population as the male population dies of complications resulting from CVD, it has been traditionally considered as a middle-age “male” disease, the consequence has been for long, the exclusion of women from clinical trial and epidemiological studies, making extensive to women the results obtained for men. In the 1970s it was suggested that endogenous hormones protect against CVD in women, and that estrogen deprivation after menopause increased their cardiovascular risk (Kannel *et al.*, 1978). Since then, much has been published about the role of menopause in differential cardiovascular risk and about the mechanisms to explain why menopause is a risk factor for cardiovascular disease. These were mainly based on studies of the administration of exogenous estrogens, including combinations (Sullivan *et al.*, 1990; Stampfer and Colditz, 1991; Psaty *et al.*, 1993; WHO, 1996; Kannel and Wilson, 1995; Paganini-Hill, 2002), but recent randomised studies, including mainly elderly women on primary or secondary prevention, could not confirm this protective effect of a single combined regimen (Consensus Development Conference, 2003).

Consistent evidence demonstrating that menopause is significantly associated with earlier or more pronounced onset of cardiovascular disease in woman was controversial in late nineties (Sowers, 1996; Sowers and La Pietra, 1995; Rueda, 1998).

It has been traditionally argued that in addition to the effect of aging, menopause and endogenous sex hormones are strongly associated with cardiovascular risk factors around the time of

menopause (Shelley *et al.*, 1998; Portaluppi *et al.*, 1996) through with lipid modifications, (Bonithon-Kopp *et al.*, 1990; Jensen *et al.* 1990; Steevenson *et al.*, 1993; Hall *et al.*, 2002); whereas no consistent association has been found between menopause and other risk factors for cardiovascular diseases such as blood pressure or obesity, large prevention trials not only failed to confirm this protective effects (Staren and Omer, 2004, Lancet, 2003; Hulley *et al.*, 1998), but indicate that oral estrogens increases the risk of venous trombo-embolism (Oger y Scarabin, 1999).

The metabolic syndrome, which encompasses a range of conditions known to be CVD risk factors, (Jacobson *et al.*, 2004) also has a greater impact on the incidence of CVD in women than in men. Elevated triglyceride levels, and diabetes, have more of an impact on the risk picture for women than for men, especially in middle age, (Doteval *et al.*, 2004).

On the other hand, other results suggest that age and adiposity (measured through BMI), may be as important in determining the lipoprotein pattern and blood pressures as menopausal status (Wu *et al.*, 1990; Matthews *et al.*, 1994; Pasquali *et al.*, 1994; Sowers and La Pietra, 1995; WHO, 1996; Portaluppi *et al.*, 1997; Hall *et al.*, 2002).

In a previous paper, we explored the interaction between age, reproductive ageing and adiposity, in a consideration of their effects on the “classic” cardiovascular risk factors (Custodio *et al.*, 2003); our results showed that variation in cholesterol and ferritin is better explained by reproductive ageing, while that in glucose and triglycerides is better explained by changes in total and visceral adiposity. In this paper, besides age, menopausal status and adiposity markers, five different hormonal markers of reproductive ageing (FSH, LH, estradiol 17B, estrone and androstenedione) have been used to predict variation in CVRF (cholesterol, triglycerides, glucose, systolic and diastolic blood pressure) in a sample of 988 pre- and naturally postmenopausal Spanish women, aged 45-64 years. The objectives are:

a) to explore the relationship between the markers

- of reproductive ageing and cardiovascular risk factors, taking into account chronological age and adiposity indicators.
- b) to determine to what extent adiposity, fat distribution and weight change are independent predictors of cardiovascular risk factors.
 - c) to explore whether the effects of menopause on CVRFs, can be mediated by adiposity, fat distribution and weight change, which are known to affect the process of reproductive ageing, including the age at menopause.
 - d) to show how biological anthropologists can contribute to the understanding of the origins of the differences in health experiences between men and women, focusing on gender for explaining both sex differences, and interaction between biology and culture. Gender approach explains differences for medical perception of risk, real differences in risk and disease, different diagnosis and treatment.

MATERIAL AND METHODS

A cross-sectional sample of 998 women aged 45-65 years, both pre- and naturally postmenopausal (51.4%) from a deprived socioeconomic stratum was analysed. All women lived in Alcobendas, Madrid, and were participating in a preventive gynaecological health programme run jointly by the Health Councils of Alcobendas Town Council and of the Autonomous Government of Madrid, with the participation of the Anthropological Unit of the Universidad Autónoma de Madrid.

Between 1996 and 2000, all women from Alcobendas in the age range 45-65 years were invited to participate in the health program; all participants in the research program gave their signed, informed consent. Gynaecological examination, cytology, ovarian echography and mammography were performed in the Cantoblanco Hospital, where women were taken free of charge by municipal bus. Anthropometry and detailed surveys of socioeconomic characteristics, lifestyle, menstrual and reproductive history, and a 24-hour food recall were performed by trained members of the research team. Height, seated height (Harpender anthropometer) and weight were measured to the nearest 0.1 cm and 0.5 kg, respectively. Minimum waist and maximum hip circumference were measured to the nearest 0.1 cm. Tricipital, subscapular and suprailiac fat-

folds were measured with a Harpender calliper. More detailed methodological information can be found in Bernis et al. (2000), Custodio et al. (2002), Bernis et al. (2003) and Barroso (2003). Blood pressure (seated) was measured twice in each woman using a mercury sphygmomanometer, and the mean calculated.

Fasting blood samples were taken between 8.30 and 9.30 in the Cantoblanco Hospital (Madrid). All blood samples from premenopausal women were obtained between days 18 and 22 of their menstrual cycle. FSH, LH, E2, P, cholesterol, triglycerides and glucose were tested in 744 women. E1, androstenedione (T4-A) and growth hormone were tested in 244 frozen blood samples, randomly chosen to represent the proportion of pre-, peri- and postmenopausal women in the sample. Cholesterol, triglycerides and glucose levels were assessed using a Hitachi 717 chemical analyser. Total plasma cholesterol and triglycerides were evaluated using the TWIN Triglycerides GPO-PAP/Cholesterol CHOD/PAP enzymometric test (Roche Diagnostics GMBH, Mannheim, Germany). Glucose was determined using the hexokinase Gluco-quant Glucose/HK method (Roche Diagnostics GMBH, Mannheim). Plasma levels of FSH and LH were assessed by the AIA-PACK FER immunoenzymometric test (Toso Corporation, Tokyo, Japan).

The following variables were used to measure reproductive ageing: plasma levels of FSH, LH, E2, E1, T4-A, and menopausal status: premenopause: less than 12 months after last menstruation; postmenopause: 12 months or more after last menstruation. More detailed methodological and sample information can be found in Barroso (2003) and Bernis et al. (2003).

Separate multiple linear regressions were calculated for each of the five cardiovascular risk factors (total cholesterol, glucose, triglycerides, systolic and diastolic blood pressure) with respect to the explanatory capacity of the four groups of variables (age, reproductive ageing, adiposity, fat distribution and weight change, and smoking) summarised in Table 2.

A one-way ANOVA (GLM) was carried out for each of the five CVRFs, using the variables found to be of predictive value from the multiple regression models. For all CVRFs, age (age groups: 45-49, 50-54, 55-59 and 60-64) and weight change (no change or weight loss, 1-8 Kg increase, 9-21 kg, more than 21 kg increase) were introduced as factors, variables with predictive

value from regression models were introduced as covariables.

RESULTS

Table 1 summarises the basic information on the gonadotrophic and ovarian and extra ovarian hormones used as indicators of reproductive ageing in the analysis, classified by age group. Table 2 summarises the basic statistics for cardiovascular risk factors and adiposity indicators by age group; the F statistics and p-value from the one-way ANOVA carried out to compare mean values of different age groups are also shown. All cardiovascular risk factors and adiposity indicators showed a significant increase with age.

Table 3 summarises partial correlations coefficients, (age constant), between cardiovascular risk factors. Cardiovascular risk factors were quite independent of each other. Cholesterol is the only CVRF which correlates positively and significantly with all indicators of reproductive ageing used in the analysis, except androstenedione (A4-T).. C.

Table 1: Summary statistics for hormonal markers of reproductive ageing, by age group.

Age group	FSH	LH	E1	T4-A	E2
<i>45-49</i>					
Mean	35.45	15.07	42.52	1.39	54.14
StdDev	44.91	16.97	22.89	0.69	39.85
N	239	241	85	93	190
<i>50-54</i>					
Mean	84.29	25.66	29.72	1.28	24.33
StdDev	39.42	13.49	18.72	0.61	28.55
N	207	210	84	86	201
<i>55-59</i>					
Mean	91.58	25.44	27.04	1.26	12.18
StdDev	30.41	10.42	16.14	0.58	7.17
N	156	156	38	38	155
<i>>60</i>					
Mean	80.83	21.32	24.38	1.03	13.27
StdDev	27.30	9.68	10.21	0.42	11.83
N	134	134	40	41	134
<i>Total</i>					
Mean	69.30	21.37	32.85	1.28	27.82
StdDev	44.53	14.35	20.13	0.62	31.99
N					

None of the other CVRFs correlated significantly with hormonal markers.

Table 4 summarises partial correlation

Table 2: Mean levels of cardiovascular risk factors and adiposity levels by age group in Spanish women from Alcobendas (Madrid, Spain) aged 45-65 years

	Age groups					Differences between age groups (ANOVA)	
	45-49	50-54	55-59	>60	Total	F	P
Glucose	100.68±13.91 247	103.09±23.84 214	108.38±24.17 157	110.69±34.20 135	104.93±24.23 754	34.692	*
Cholesterol	217.60±38.86 224	229.03±33.89 210	238.69±39.26 153	235.02±36.64 130	228.64±37.96 718	11.836	*
Triglycerides	92.85±41.63 224	94.44±42.39 210	115.27±61.41 153	123.23±77.07 130	103.64±52.0 718	6.901	*
Systolic blood pressure	125.0±17.0 361	130.0±17.0 284	136.0±18.0 173	144.0±21.0 132	131.0±19.0 950	10.935	*
Diastolic blood pressure	80.0±11.0 361	83.0±11.0 283	85.0±12.0 173	87.0±12.0 132	3.0±12.0 950	8.860	*
Weight change	13.17±9.68 376	14.91±9.81 280	15.58±10.73 179	16.47±10.66 133	14.57±10.11 968	6.218	*
Tricipital fat-fold	23.7±6.9 391	25.1±7.0 301	25.0±7.1 196	25.1±14.4 144	24.52±6.931 032	3.897	*
Subscapular fat-fold	25.2±9.0 391	27.0±0.3 301	26.9±9.6 195	28.3±9.1 143	26.48±9.281 030	5.812	*
Suprailiac fat-fold	24.1±8.8 392	26.0±9.0 300	27.5±9.6 194	28.7±8.3 143	25.95±9.08 1029	6.218	*
Waist circumference	83.7±9.9 388	86.1±9.4 297	88.4±9.5 192	90.9±9.5 142	86.24±9.93 1019	3.897	*
Hip circumference	102.89.5 388	104.58.2 297	104.5±9.4 192	107.8±9.5 142	104.31±9.23 1019	5.812	*
Waist/hip ratio	0.81±0.06 388	0.82±0.06 297	0.85±0.06 192	0.84±0.07 142	0.83±0.0021 1019	10.882	*
BMI	27.36±4.15 393	28.19±3.95 301	28.573.85 196	29.65±4.09 145	28.15±4.01 1035	6.218	*

Table 3: Partial correlation coefficients (age constant) between cardiovascular. N=620.

	<i>CHOLEST</i>	<i>TRIGLY</i>	<i>GLUC</i>	<i>SBP</i>	<i>DBP</i>	<i>FSH</i>	<i>LHSA</i>	<i>ESTR</i>	<i>ANDRS</i>
TRIGLYC	0.3239***								
Glucose	NS	0.2097**							
SBP	NS	NS	NS						
DBP	NS	NS	NS	0.340***					
FSH	0.2638**	NS	NS	NS	NS				
LH	0.2221**	NS	NS	NS	NS	0.2470***			
Estrone	NS	NS	NS	NS	NS	-0.3734***	-0.2710***		
Androsten.	-0.1643*	NS	NS	NS	NS			0.2258***	
Estradiol	-0.1643*					-0.5768***	0.3807***	0.5959***	0.1757*

* p<0.01, **p<0.001, ***pH"0.000

Table 4: Partial correlation coefficients (age constant) between cardiovascular risk factors, markers of total fat and fat distribution.

	<i>Weight Change</i>	<i>TricfF</i>	<i>SubesfF</i>	<i>Waist C</i>	<i>Hip C</i>	<i>W/H</i>	<i>BMI</i>
Cholest	NS	NS	NS	NS	NS	NS	NS
Triglyc	0.239***	NS	0.253***	0.324***	0.097*	0.302****	0.208***
Glucose	0.1085*	NS	0.1274**	0.1419**	NS	0.1902	NS
SBP	0.2716***	NS	0.2245***	0.2563***	0.2301***	NS	0.2632***
DBP	0.3044***	0.1040*	0.1984***	0.3031***	0.2632***	NS	0.3010***

* p<0.01, **p<0.001, ***pH"0.000

coefficients (age constant), between each cardiovascular risk factor and the markers of adiposity, fat distribution, and weight change. All cardiovascular risk factors correlated positively with the markers of total fat, fat distribution, and weight change, apart from cholesterol, which was not correlated with adiposity in any case.

Table 5 shows the results of the five multiple stepwise regression analyses after accounting for age and menopausal status, which were performed to test: 1) the relative contribution of reproductive ageing after removing the effects of age, 2) the effects of adiposity, fat distribution and weight change after removing the effects of general and reproductive ageing. Our results show that the predictive variables included in the models explained a small but significant part of the total variance of the cardiovascular risk factors (from 6% for glucose, to 20% for triglycerides). Cholesterol seems to be more closely associated with reproductive ageing than the other CVRFs, as shown by the significant partial correlation coefficients for gonadotropic, ovarian and extra-ovarian hormones, and by the fact that the variation in cholesterol is predicted only by age and FSH. There was no significant relationship between estradiol, FSH, LH, estrone or androstenedione with triglyceride, SBP, DBP or glycaemia

Cardiovascular risk factors other than cholesterol are all predicted by age and weight change during reproductive life, while fat indica-

tors behaved differently for triglycerides and total fat (BMI). As for smoking, women who smoke have significantly elevated triglycerides. Menopausal status is not predictive of any cardiovascular risk factor after adjusting for age (Table 6).

Figures 1 and 2 have been obtained in the first two GLM analysis shown in table 5; represent, respectively, the variability of cholesterol and tryglicerid levels with age and weight change through reproductive life. Women who do not change weight or who lose weight during reproductive life, have significantly lower values of blood lipids. It is of particular note that these women exhibit no significant change of CVRF with age. Women who put on more than 20 kg have the highest values for CVRF, and show a pronounced and significant increase in CVRF with age.

DISCUSSION

In Spain, as in other Western countries, despite the favourable trend of recent years, cardiovascular diseases are still the main cause of death (in 1992, they represented 46.7% of all female deaths, of which 34.4% were due to cerebrovascular causes, and 20.5% were due to stroke). Women who develop CVD in middle age generally have higher overall risk factors than men (ie, multiple risk factors, such as those associated with the metabolic syndrome). The

Table 5: Relative contribution of reproductive ageing, age, adiposity, fat distribution and weight change.

Results of multiple linear regression analysis carried out on each of the 5 cardiovascular risk factors considered (CVRF)

Dependent variable: CVRF	AR ² (%)		Beta	Coeffic. SE	T	SIG.
Cholesterol (F=20.22; p=0.000)	9.0	Constant			9.912	0.000
		Age	0.870	0.359	2.426	0.016
		Fsh	0.229	0.043	5.364	0.000
Triglycerides (F=24.048; p=0.000)	16.5	Constant			-6.230	0.000
		Age	2.018	0.541	3.728	0.000
		W/H Ratio	36.362	0.280	7.004	0.000
		Weight Ch.	1.860	0.141	3.604	0.000
		Smokes?	20.947	6.511	3.148	0.002
Glucose (F=10.58; p=0.000)	5.9	Constant			2.290	0.022
		Age	0.408	0.223	1.831	0.068
		W/H Ratio	50.607	15.298	3.308	0.001
		Weight Ch	1909	0.774	2.460	0.014
Systolic bloodpressure (SBP)(F=30.94; p=0.000)	16.7	Constant			5.377	0.000
		Age	0.110	0.018	6.672	0.000
		Weight Ch	0.224	0.080	2.788	0.005
		Fsh	-0.0006	0.002	2.861	0.004
		Bmi	-0.0006	0.025	2.648	0.008
Diastolic bloodpressure (F= 25.180; p= 0.000)	14.5	Constant			7.840	0.000
		Age	4.072e-2	0.199	3.666	0.000
		Weigh Ch	0.049	0.196	3.803	0.000
		Bmi	3.841e-02	0.015	2.507	0.012

B1 Predictors: Age, Menopausal Status (Menopause No/Yes), B2 Predictors: FSH, E2, Waist/ Hip Ratio (W/H), Body Mass Index, Weight Change, Smokes?

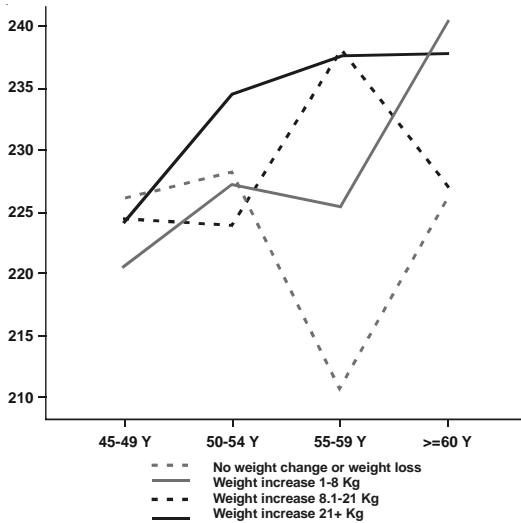


Fig. 1. Variation in triglycerides level, according to age and weight change (results of GLM, dependent variable: triglycerides; factors: age, weight change and tobacco use; covariables: waist/hip ratio, cholesterol, factors).

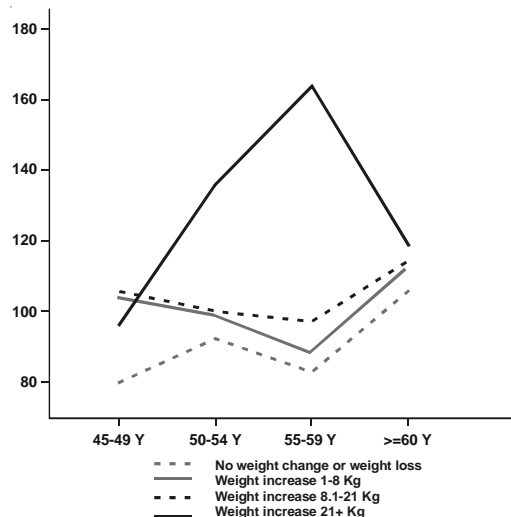


Fig. 2. Variation in cholesterol level according to age and weight change (results of GLM, dependent variable: cholesterol; factors: age and weight change; covariable: FSH).

features of the metabolic syndrome, including diabetes, hypertension, and hyperlipidemia, are also more prevalent in women with heart disease than in healthy women or in men with heart disease. Overt diabetes is associated with a greater increase in risk for atherosclerosis in women than in men. This effect may be because of the relatively more severe dyslipidemia seen in women with diabetes compared with men with diabetes, particularly on triglyceride levels. Triglycerides correlate significantly and positively with BMI, weight change along reproductive life, sub scapular fat fold, and waist and hip circumferences; also women who smoke have significantly more elevated triglycerides, which has been also found by other authors (Shelley et al., 1999). Cardiovascular risk profile of women in our sample is shown in table 6. Prevalence is higher than in other Spanish samples (Banegas et al., 1993, 1995; Ministerio de Sanidad y Consumo, 1995). Most of these women were born and grew up in rural areas, between 1934 and 1950, coinciding with the very harsh times of the Spanish Civil War, World War II, and both post-war periods (e.g., it was only in 1960 that the mean per capita calorie consumption surpassed 1800 Kcal in Spain (Graciani et al., 1996). Living conditions significantly improved, coinciding with their migration to Madrid, and with marriage, even though they still belonged to a low socio-economic group. On average they put on 15 kg during their reproductive life, this increase being

inversely correlated with their prereproductive BMI: slimmer women gained significantly more weight than stockier women (Montero et al., 2000).

Our results suggest that cholesterol is more related to reproductive aging and that the other cardiovascular risk factors are more related to adiposity, changes in adiposity and fat distribution, supporting the idea that "classic" risk factors are relatively independent of each other and that population variability could be explained by different set of factors (Stevenson, 1998).

In general, these results coincide with those of other authors, who have demonstrated overall that both total adiposity (measured by BMI) and visceral fat (measured either by waist circumference, waist/hip ratio, or suprailiac fat-fold), significantly increase CVRFs (Hartz et al., 1984; Ishida et al., 1997; Larsson 1984; van Pelt et al., 2001); Triglycerides also increased with BMI, and interestingly, show higher levels among smokers. The novelty of our results is that weight change during reproductive life is an independent factor, that interacts with age in predicting the levels of cardiovascular risk factors.

Recent results have shown that both for menopausal and fertile women, that diet and exercise induced a significant reduction of BMI, SBP, waist circumference, ratio T. Chol/HDL-C, and apoB (Santos, 2003). Also, lifestyle changes and pharmacological lipid-lowering therapy have been shown to favourably influence the natural course of atherosclerotic disease and reduce cardiovascular events in men and women (Bittner, 2002).

Our main conclusion is that weight change through reproductive age may be an important mediator of the observed increase of cardiovascular risk factors with age and also with menopause, since age at menopause has been shown to increase with total adiposity, and increased weight change during reproductive life. Lebrun et al. (2006) conclude that in elderly and late postmenopausal women, hormonal factors do not predict quality of life, results which also point out in this direction.

CONCLUSIONS

Considering our results and the following facts, it would seem wise to follow the WHO's (2003) advice: "(...) drug therapy should be considered only after serious attempts have been made to modify diet. Intervention trials have shown that reduction of blood pressure by 6 mm

Table 6: Cardiovascular risk profile of Spanish women living in Alcobendas, Madrid.

<i>Cardiovascular risk factors</i>	<i>N</i>	<i>Prevalence</i>
Hypercholesterolaemia (>=240 mg/dl)	216/617	35.0
Hypertriglyceridaemia (>=150 mg/dl)	87/617	14.1
Hyperglycaemia (>= 110 mg/dl)	134/647	20.7
Obesity (BMI>=30Kg/M ²)	207/849	24.4
Weight Increase (>20 Kg)	218/845	25.8
Waist/Hip Ratio (>0.85)	228/842	27.1
Systolic Hypertension (SBP>=150 mmHg)	90/836	10.8
Diastolic Hypertension (DBP<=95 mmHg)	104/835	12.5
Tobacco Use (Yes)	140/910	10.8
Diagnosed Diabetes	57/900	6.3
Treatment for Hypertension	132/787	16.8

Hg reduces the risk of stroke by 40% and of heart attack by 15%, and that a 10% reduction in blood cholesterol concentration will reduce the risk of coronary heart disease by 30%”.

1. Despite men and women share the same CV risk factors, they have differential exposure to them (Pollard, 1999)
2. The same exposure to a risk factor is more dangerous for women, for example, tobacco use has been shown to be more dangerous for women of all ages,
3. High blood triglycerides and blood pressure increases risk of atherosclerosis more in young women, compared to young men.
4. The same symptoms in men and women have been differently diagnosed and treated by medical doctors;
5. Menopause itself has not a direct effect on CVD, (McKay and Mensah, 2004)
6. weight control through diet and exercise is demonstrably very effective in reducing all CVR- factors (WHO, 2003),
7. epidemiological evidence for any cardio-protective effect of HRT is lacking (Consensus Development Conference, 2003)
8. Epidemiological evidence demonstrates that oral estrogens increases the risk of venous thromboembolism (Oger y Scarabin, 1999; McKay and Mensah, 2004; Canonico et al., 2006).

Extensive medicalization of women using RTH, is a good example of how normal biological functions for the female (such as menopause) have been essentially treated as a medical problem, disease-state, or risk factor for disease, and illustrates the necessity of focusing on the role of gender and the social construction of illness, as usually diagnosis and subsequent treatments for CVD have generally favoured men, but which have rarely advantaged women and even , as is the case, postmenopausal hormone therapy used mainly for CVD prevention has been found to increase the risk of HD.

REFERENCES

- Banegas , J.R., Villar F., Pérez de Andrés, C., Jiménez, R., Gil, E., Muñoz, J. and Juane, R.: Estudio epidemiológico de los factores de riesgo cardiovascular en la población española de 35 a 64 años. *Rev. San. Hig. Pub.*, **64**: 419-445 (1993).
- Banegas, J.R., Rodríguez, F., Graciani, A., Hernandez, R. and Rey Calero, J.: Trends in ischaemic heart disease mortality and its determinants in Spain 1940-1988. *European J. Public Health*, **5**: 50-55 (1995)
- Beck-Nielsen, H.: Impairment of glucose tolerance: Mechanism of action and impact on the cardiovascular system. *Am. J. Obstet. Gynecol.*, **163**: 292-5 (1990).
- Barroso, A.: *Envejecimiento reproductor en mujeres españolas desde una perspectiva ecológica y de ciclo vital*. Doctoral thesis. Madrid, Universidad Autónoma de Madrid. (2003).
- Bernis, C., Varea, C., Montero, P. and Arias, S.: Cambios en peso y masa corporal durante la etapa reproductora y post-reproductora en mujeres de la Comunidad de Madrid. pp.585-593. In : *Tendencias actuales de la Investigación en la Antropología Física Española*. Luis Caro , Humildad Rodríguez , Eduardo Sánchez , M. López Blanco M (Eds.). Ed. Universidad de León (2000).
- Bittner, V.: Lipoprotein abnormalities related to women's health. *The American Journal of Cardiology*, **90**, **Supplement 1**, **17**: 77-84 (2002)
- Canonico, M., Straczek, C., Oger, E., Plu-Bureau, G. and Scarabin, P.Y.: Postmenopausal hormone therapy and cardiovascular disease: an overview of main findings. *Maturitas*, **54**: 372-379 (2006).
- Castelo-Branco, C., Blümel, J.E., Roncagliolo, M.E., Haya, J., Bolf, D., Binfa, L., Tacla, X. and Colodrón, M.: Age, menopause and hormone replacement therapy influences on cardiovascular risk factors in a cohort of middle-aged Chilean women. *Maturitas*, **45(3)**: 205-212 (2003).
- Consensus Development Conference. On the route to combined evidence from OC and HRT/ERT. *Maturitas* **44(1)**: 69-82 (2003).
- Custodio, E., Bernis, C., Barroso, A., Montero, P. and Varea, C.: Riesgo cardiovascular en mujeres españolas de 45-68 años: el papel de la ferritina. *Antropo*, **4**: 1-15 (2003).
- Dotevall, A., Johansson, S., Wilhelmsen, L. and Rosengren, A.: Increased levels of triglycerides, BMI and blood pressure and low physical activity increase the risk of diabetes in Swedish women. A prospective 18-year follow-up of the BEDA study. *Diabetic Medicine*, **21(6)**: 615-622 (2004).
- Graciano, A., Rodríguez, F., Banegas, J.R., Hernandez, R. and Rey Calero, J.: *Consumo de alimentos en España del periodo 1940-1988*. Ed. Universidad Autónoma de Madrid (1996).
- Hall, G., Collins, A., Csemczyk, G. and Landgren, B.M.: Lipoproteins and BMI: A comparison between women during transition to menopause and regularly menstruating healthy women. *Maturitas*, **41**: 177-185 (2002).
- Hartz, A., Rupley, D.C. and Rimm, A.: The association of girth measurements with disease in 32.856 women. *American J. Epidemiology*, **19**: 71-80 (1984).
- Ishida, Y., Kanehisa, H., Carroll, J.F., Pollock, M.L., Graves, J.E. and Ganzarella, L.: Distribution of subcutaneous fat and muscle thicknesses in young and middle-aged women. *American Journal of Human Biology*, **9**: 247-255 (1997).
- Jacobson, T. A., Case, C. C., Roberts, S., Buckley, A., Murtaugh, K. M., Sung, J. C., Gause, D., Varas, C. and Ballantyne C. M.: Characteristics of US adults with the metabolic syndrome and therapeutic implications. *Diabetes, Obesity and Metabolism*, **6(5)**: 353 -362 (2004).
- Kannel, W.B., Hjortland, M.C. and McNamara, P.M.:

- Menopause and coronary heart disease. *Annals of Internal Medicine*, **89(2)**: 23-28 (1978).
- Kannel, W.B. and Wilson P.W. Risk factors that attenuate the female coronary disease advantage. *Arch. Intern. Med.*, **155**: 57-61 (1995).
- Klag, M.J., Ford, D.E. and Mead, L. A.: Serum cholesterol in young men and subsequent cardiovascular disease. *N Engl J Med.*, **20 Suppl 4**: 22-27 (1993).
- Knopp, R. H.: Risk factors for coronary artery disease in women. *The American Journal of Cardiology*. **89(Supplement 1)**: 28-34 (2002).
- Larsson, B., Svärdsudd, K., Welin, L., Wilhelmsen, L., Björntorp, P. and Tibblin, G.: Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *British Medical Journal*, **288**: 1401-1404 (1984).
- Lebrun, C., van der Schouw, Y., Jong, F. H., Pols, H., Grobbee, D. and Lamberts, S.: Relations between body composition, functional and hormonal parameters and quality of life in healthy postmenopausal women. *Maturitas*, **55**: 82-92 (2006).
- McKay, J. and Mensah, G. A.: *The Atlas of Heart Disease and Stroke*. World Health Organization, Geneva 112 pp. (2004).
- Matthews, K.A., Wing, R.R. and Kuller, L.H.: Influence of the perimenopause on cardiovascular risk factors and symptoms of middle-aged healthy women. *Arch. Intern. Med.*, **154**: 2349-2355 (1994).
- Ministerio de Sanidad y Consumo: *Indicadores de Salud: Tercera evaluación en España del programa regional europeo Salud para todos*. Secretaría General Técnica Centro de Publicaciones (1995).
- Montero, P., Bernis, C., Varela, C. and Arias, S.: Lifetime dietary change and its relation to increase in weight in Spanish women. *International Journal of Obesity*, **24**: 14-19 (2000).
- Oshaug, A.; Bugge, K.H.; Bjornnes, C.H.; Borch-Iohnsen, B. and Neslein, I-L.: Associations between serum ferritin and cardiovascular risk factors in healthy young men. A cross sectional study. *European Journal of Clinical Nutrition*, **49**: 430-438 (1995).
- Paganini-Hill, A.: Hormone replacement therapy and stroke: risk, protection or no effect. *Maturitas*, **42(1)**: 11-29 (2002).
- Pasquali, R., Casimirri, F., Morselli Labate, A.M., Tortelli, O., Pascal, G., Ancometani, B., Gatto, M.R.A., Flamia, R., Capelli, M. and Barbara, L.: VMH Collaborative Group: Body weight, fat distribution and the menopausal status in women. *Intl. Journal of Obesity*, **18**: 614-621 (1994).
- Van Pelt, R.E., Evans, E. M., Schechtman, K.B., Ehsani, A.A. and Kohrt, W.M.: Waist circumference vs body mass index for prediction of disease risk in postmenopausal women. *Intl. Journal of Obesity*, **25**: 1183-1188 (2001).
- Pollard, T.M.: Sex gender and cardiovascular disease. pp. 53-71. In: *Sex, Gender and Health*. T.M. Pollard and S.B. Hyatt (Eds.). Cambridge University Press, Cambridge (1999).
- Portaluppi, F., Pansini, F., Manfredini, R. and Mollica, G.: Relative influence of menopausal status, age and body mass index on blood pressure. *Hypertension*, **29**: 976-79 (1997).
- Psaty, B.M., Heckbert, S.R., Atkins, D., Siscovick, D.S., Koepsell, T.D., Wahl, P.W., Longstreth, W.T., Weiss, N.S., Wagner, E.H., Prentice, R. and Furberg, C.D.: A review of the association of estrogens and progestins with cardiovascular disease in postmenopausal women. *Archives of Internal Medicine*, **153**: 1421-1427 (1993).
- Rueda Martinez, J.R.: Menopausia frente a los nuevos mitos y la medicalización injustificada. *Atención primaria*, **22**: 23-29 (1998).
- Samsioe, G.: Cardiovascular disease in postmenopausal women. *Maturitas*, **30**: 11-18 (1998).
- Shelley, J. M., Green, A., Smith, A. M., Dudley, E., Dennerstein, L., Hopper, J. and Burger, H.: Relationship of Endogenous Sex Hormones to Lipids and Blood Pressure in Mid-Aged Women. *Annals of Epidemiology*, **8(1)**: 39-45 (1998).
- Sowers, M.F.: Longitudinal changes in body composition in women approaching the mid life. *Annals of Human Biology*, **23**: 253-265 (1996).
- Sowers, M.F. and La Pietra, M.T.: Menopause: its epidemiological and potential association with chronic diseases. *Epidemiologic Reviews*. **12(2)**: 287-302 (1995).
- Van der Graaf, Y., Kleijn, M.J.J. and van der Show, T.: Menopause and cardiovascular disease. *J. Psychosom. Obstet. Gynecol.*, **18**: 113-120 (1997).
- WHO: *Research on the Menopause in the 1990s*. WHO Technical Report 8, series 866. (1996).
- WHO. http://www.who.int/health_topics/cardiovascular_diseases/en/. (2003)
- Wu, Z., Wu, X. and Zhang, Y.: Relationship of menopausal status and sex hormones to serum lipids and blood pressure. *Intl. Journal of Epidemiology*. **19**: 297-301 (1990).

KEYWORDS Gender. Reproductive Aging. Menopause. Triglycerides. Weight Change

ABSTRACT Recent results on cardiovascular diseases (CVD), cardiovascular risk factors (CVRF) and THS as a protective factor for CVD in middle aged and elderly women are changing traditional ideas, rising new interest in the ways in which sex and gender interact with environmental and cultural contexts and demanding more research on health with a gender approach. In this paper, besides age, menopausal status and adiposity markers, five different hormonal markers of reproductive ageing have been used to predict variation in CVRF (cholesterol, triglycerides, glucose, systolic and diastolic blood pressure), in a sample of 988 pre- and naturally postmenopausal Spanish women, aged 45-64 years. Adiposity, fat distribution and weight change explain a significant part of the variability founded in CVRF. Our main conclusions are: a) Women who smoke have significantly more elevated triglycerides compared with non-smokers. B) Menopausal status is not predictive of any cardiovascular risk factor after adjusting for age. C) weight change through reproductive age may be an important mediator of the observed increase of cardiovascular risk factors with age and also with menopause, since age at menopause has been show to increase with total adiposity, and increased weight change during reproductive life. More elaborated gender approaches are needed to explain the

differences in medical perception of CVrisk, of CVdisease, for different diagnosis and treatment, and to understand the extensive use of hormone therapy for CVD prevention, despite recurrent evidences on its negative effects precisely on Heart.

Author's Address: Dr. C. Bernis, Universidad Autónoma de Madrid, Edificio de Biológicas, Departamento de Biología, Unidad de Antropología, 28049 Madrid, Spain
Fax: 00 34 91 4978344, E-mail: cristina.bernis @uam.es