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Fibrinolysis and lipoprotein(a) in women with coronary artery disease. Influence of hormone replacement therapy

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Background and Objectives. The incidence of coronary artery disease (CAD) is higher in post-menopausal than in pre-menopausal women. Epidemiological studies suggest that hormone replacement therapy (HRT) decreases the risk of cardiovascular disease in post-menopausal women. HRT could modify the cardiovascular risk via several mechanisms, including modifications in the fibrinolytic system and lipoprotein (a) levels. Our study was aimed at investigating some of these modifications.

Design and Methods. In the cross-sectional part of the study we evaluated several components of the fibrinolytic system, coagulation inhibitors and lipid profile in pre-menopausal (n=15) and post-menopausal women (n=64) with CAD and compared these parameters with those of healthy pre-menopausal (n=31) and post-menopausal women (n=88). The prospective part of the study analyzed the effect of HRT with transdermal estrogen with or without progestogen in post-menopausal women with CAD.

Results. Pre- and postmenopausal women with CAD showed significant lower fibrinolytic activity and higher plasminogen activator inhibitor type 1 (PAI-1) levels than their control groups. Lp(a) levels were higher in pre-menopausal women with CAD than in healthy pre-menopausal women. In post-menopausal women with CAD, HRT induced a significant decrease in PAI-1 and Lp(a) levels. No significant differences were observed in any parameter studied between the groups treated with transdermal estrogen with and without progestogen.

Interpretation and Conclusions. CAD is associated with a decrease in fibrinolytic activity, possibly due to an increase in PAI-1 levels. An increase in fibrinolytic activity and a decrease in PAI-1 and Lp(a) levels were observed in CAD women receiving transdermal HRT and these changes may have a favorable impact on the risk of new cardiovascular events in post-menopausal CAD women.

Key words: fibrinolysis, Lp(a), coronary artery disease, hormone replacement therapy

An increase in the incidence of coronary heart disease has been found in post-menopausal women,[1–3] and epidemiological data suggest that hormone replacement therapy (HRT) can reduce the risk of cardiovascular disease and mortality in post-menopausal women.[3-7] The beneficial effects of HRT on cardiovascular risk could be due to several mechanisms, including modifications of the plasma concentrations of lipoproteins, glucose and insulin, and of blood pressure and the hemostatic system.[2,8-13]

Modifications of the hemostatic system may play a role in the pathogenesis of coronary heart disease.[14] A fibrinolytic hypofunction due to an increase in plasminogen activator inhibitor-1 (PAI-1) has been detected in coronary ischemic disease,[14-17] and this increase in PAI-1 has been found to constitute a risk factor for recurrent myocardial infarction.[14,15] An increase in factor VII, fibrinogen and PAI-1 has been reported in post-menopausal women.[18-20] Moreover, total cholesterol, low-density lipoprotein and lipoprotein (a) [Lp(a)] levels have also been found to rise in post-menopausal women.[20-22] These alterations could contribute to the increased risk of cardiovascular disease seen in post-menopausal women.

Lp(a) is a variant of the low-density lipoprotein (LDL) in which apoprotein B-100 is covalently linked to a single apolipoprotein (a) [apo(a)].[23, 24] Increased levels of Lp(a) have been considered an independent risk factor linking the pathophysiologic processes of atherosclerosis and thrombosis in coronary artery disease.[25,26] However, the mechanism behind these processes is not completely understood. Lp(a) could compete *in vitro* with plasminogen for its binding to fibrin and might thereby significantly impair physiologic fibrinolysis and promote thrombosis.[26,27]

Observational studies in women with coronary disease show that users of estrogen replacement therapy have a lower risk of reinfarction, CHD-related death, and coronary restenosis.[28-30] In contrast, the results of a large randomized clinical trial (HERS report)[31] indicate that HRT (oral estrogen plus progestogen) did not reduce coronary heart disease events in post-menopausal women with

established coronary disease. It must, however, be taken into account that in the HERS trial the participants were older than in previous studies and they were treated only with oral estrogen plus progestogen.

A beneficial effect of HRT on plasma lipids in hypercholesterolemic post-menopausal women with CAD has been reported,[32] but the lipid levels recommended for secondary prevention were not achieved. However, to our knowledge no studies have been reported on the effect of HRT on the fibrinolytic system and coagulation inhibitors in post-menopausal women with CAD.

The aim of the present study was to evaluate several components of the fibrinolytic system, coagulation inhibitors and lipid profile, including Lp(a) levels, in premenopausal and post-menopausal women with CAD and compare them with the same parameters in healthy women and to analyze the effect of HRT (transdermal estrogen with or without progestogen) on these parameters in post-menopausal women with CAD.

Design and Methods

Clinical groups

The CAD post-menopausal group consisted of 64 women in post-menopause (for at least 1 year) aged from 39 to 63 years, with a mean value of 55±5 years. The cardiac diagnoses were myocardial infarction or angina pectoris with positive coronariography. The group comprised 50 women without diabetes mellitus (DM) and 14 women with DM. None of the women had any hormonal preparation during the eight weeks prior to the study. All the CAD patients with hypercholesterolemia (n=23) were receiving cholesterol-lowering therapy (statins). Patients who had had a myocardial infarction or unstable angina in the 3 months preceding the study, or with severe uncontrolled hypertension or on anticoagulants were excluded from the study.

The CAD premenopausal group consisted of 15 women aged from 31 to 50 (42±6 years) with regular menstruation, not receiving hormonal treatment.

The healthy post-menopausal group comprised 88 women in post-menopause (for at least 1 year) aged 36 to 65 (52±6 years). None of the women had any hormonal preparation during the eight weeks prior to the study. None of the women had a history of thromboembolism, severe metabolic, endocrinologic or gastrointestinal disease, neoplasm or uncontrolled hypertension.

The healthy premenopausal group comprised 31 healthy women aged from 19 to 51 (39±9 years) with regular menstruation, not receiving hormonal treatment.

This study was a 1-year, randomized clinical trial designed to analyze the effect of hormone replacement therapy with transdermal estrogen on fibrinolytic parameters, coagulation inhibitors and lipid profile in CAD post-menopausal patients. The women were randomly divided into two groups of 32 women (with and without HRT). The different parameters were evaluated in the HRT group before and 3-4 months, and 12 months after the start of HRT. Nine women from the group with HRT withdrew from the study between the 4th and 12th month of follow-up because of lack of motivation. Nine women in the group without HRT withdrew from the study before the 12th month of follow up, because of lack of compliance. The results were compared with the post-menopausal women from the CAD group without HRT, in whom the parameters were evaluated before beginning the study and 12 months later. Both groups were matched for age, DM, hypercholesterolemia and cardiovascular disease. Similar percentages of patients with DM (22% vs 18%) or hypercholesterolemia (43% vs 36%) were included in the group with and the group without HRT.

In the group with HRT, 20 women received transdermal estradiol (Menorest 50, Rhône-Poulenc Rorer, 0.05 mg/day) plus medroxyprogesterone acetate (2.5 mg/day) and 12 women who had had a hysterectomy received transdermal estradiol. Any other treatment that any patient was receiving remained the same while under HRT as before the hormone therapy. Women with a history of breast or endometrial cancer were excluded from the study, as were those with previous thromboembolic disease. All the women had a normal mammography, normal cervical smear and normal liver function tests.

Informed consent was obtained from all the women before sample extraction.

Blood collection

Venous blood samples were obtained between 8 and 10 am, after 12-hour overnight fasting. Subjects remained in a sitting position for 20 minutes before venipuncture. Blood samples were anticoagulated with 0.13 mmol/L trisodium citrate (9:1, vol:vol, blood:anticoagulant), and were immediately centrifuged at 1,500 x g for 30 min at 4°C. Plasma was snap-frozen in small portions and stored at -80°C until the assays were performed in series (within 6 months). Blood serum was used to determine the lipid profile and estradiol levels.

Methods

Fibrinolytic and coagulation inhibitor parameters

Euglobulin lysis time (ELT) was assayed as previously described,[33] using fresh plasma. The intra-assay variability was 3%. Determination of tissue type plasminogen activator (t-PA) antigen was performed with a commercially available enzyme-linked immunosorbent assay (Imulyse t-PA, Biopool). The assay detects free and complexed t-PA with similar efficiency. The intra-assay and inter-assay variabilities were 4% and 6%, respectively. PAI-1 antigen was quantified by a commercially available ELISA assay (Tint Elize PAI-1, Biopool). The assay detects active and latent (inactive) forms of PAI-1 and complexed PAI-1 with the same efficiency. The intra-assay and inter-assay variabilities were 3% and 7%, respectively.

The PAI-1 activity assay was performed as previously described.[34] One unit of PAI activity is defined as the amount that inhibits 1 IU of single chain t-PA in 15 minutes at room temperature under the conditions used. The intra-assay and inter-assay variabilities were 6%

Table 1. Fibrinolytic parameters, coagulation inhibitors, glucose, triglycerides, total cholesterol, lipoprotein(a) [Lp(a)], estradiol levels and body mass index (BMI) in post and premenopausal women with coronary artery disease (CAD) in comparison with healthy groups.

	Group 1 CAD post-menop (n=64)	*Group 2 healthy post-menop (n=88)*	*Group 3 CAD pre-menop (n=15)*	*Group 4 healthy pre-menop (n=31)*	*Statistical significance*			
					1 vs 2	*1 vs 3*	*2 vs 4*	*3 vs 4*
ELT (min)	208±57	173±52	198±51	152±58	*p*<0.001	NS	NS	*p*<0.05
PAI-1 ag (ng/mL)	35±17	28±17	27±18	15±8	*p*<0.05	NS	*p*<0.001	*p*<0.01
PAI-1 ac (U/mL)	24±14	12±10	23±11	11±8	*p*<0.001	NS	NS	*p*<0.01
t-PA ag (ng/mL)	15±6	10±11	14±5	5±1	*p*<0.01	NS	*p*<0.05	*p*<0.001
Plasminogen (%)	103±13	101±16	99±10	93±12	NS	NS	*p*<0.05	NS
Protein C (%)	121±31	119±20	111±21	106±14	NS	NS	*p*<0.01	NS
Protein S (%)	131±34	119±24	108±14	113±14	*p*<0.05	*p*<0.05	NS	NS
Antithrombin (%)	102±9	108±22	104±9	108±14	NS	NS	NS	NS
Glucose (mg/dL)	115±54	88±11	91±8	83±7	*p*<0.001	*p*<0.05	*p*<0.05	*p*<0.01
Triglycerides (mg/dL)	127±58	106±58	117±59	76±29	NS	NS	*p*<0.01	p<0.01
Cholesterol (mg/dL)	221±40	234±37	207±30	201±35	NS	NS	*p*<0.001	NS
Lipoprotein(a) (mg/dL)	18	27	18	11				
	12 (1-66)	19 (1-104)	15 (1-50)	8 (3-27)	*p*<0.05	NS	*p*<0.001	NS
Estradiol (pg/ML)	8±7	27±27	90±82	86±70	*p*<0.001	*p*<0.001	*p*<0.001	NS
BMI (kg/m^2)	28.2±5.1	25.3±3.2	24.6±3.5	22.0±2.4	*p*<0.001	*p*<0.01	*p*<0.001	NS

Values are expressed as mean ±SD. Lp(a) data were expressed as mean, median and (range). CAD= coronary artery disease. ELT= euglobulin lysis time.PAI-1= plasminogen activator inhibitor type 1. t-PA=tissue type plasminogen activator. NS=not significant.

and 10%, respectively.

Functional plasminogen activity and antithrombin were measured by a chromogenic substrate method.[16,33] The intra- and interassay coefficients of variation were 5% and 9% for the plasminogen method and 6% and 10% for the antithrombin assay, respectively. Protein C[35] and total protein S[36] antigen were determined by ELISA assays as indicated before.

The fibrinogen level was determined by a standard coagulation method.[37]

Table 2. Mean of fibrinolytic system, coagulation inhibitors, glucose, lipids and estradiol levels in postmenopausal women with coronary artery disease during the study (with or without hormone replacement therapy).

	WITH HRT					*WITHOUT HRT*		
	Baseline (1) (n=32)	*After 3-4 m (2) (n=32)*	*After 12 m (3) (n=23)*	**Statistical significance*		*Baseline (4) (n=23)*	*After 12 m (5) (n=23)*	**Statistical Significance 4 vs 5*
				1 vs 2	*1 vs 3*			
ELT (min)	225±41	207±35	201±41	*p*<0.01	*p* <0.05	196±54	187±68	*p* <0.01
PAI-1 ag (ng/mL)	40±17	34±13	34±15	*p* <0.05	*p* <0.05	29±14	31±17	NS
PAI-1 ac (ng/mL)	27±13	21±15	23±11	*p* <0.05	*p* <0.05	18±13	19±16	NS
t-PA ag (ng/mL)	14±4	14±5	16±7	NS	NS	15±4	13±5	NS
Plasminogen (%)	104±16	103±12	102±13	NS	NS	98±9	102±18	NS
Fibrinogen (mg/dL)	324±82	315±58	309±73	NS	NS	324±82	315±58	NS
Protein C (%)	121±26	117±23	102±21	NS	*p* <0.01	127±34	121±32	NS
Protein S (%)	130±28	131±29	122±34	NS	NS	121±29	125±36	NS
Antithrombin (%)	102±8	104±12	102±12	NS	NS	105±7	106±10	NS
Glucose (mg/dL)	114±39	113±39	120±59	NS	NS	106±46	113±58	NS
Triglycerides (mg/dL)	126±55	140±62	126±53	NS	NS	108±40	101±40	NS
Total cholesterol (mg/dL)	222±39	213±34	203±45	NS	*p* <0.05	223±38	225±37	NS
LDL cholesterol (mg/dL)	141±32	136±25	127±39	NS	*p* <0.05	149±40	150±33	NS
HDL cholesterol (mg/dL)	51±11	50±10	47±10	NS	NS	54±14	55±10	NS
Lipoprotein(a) (mg/dL)	18	16	10			17	16	
	12 (0.1-66)	12 (0.1-55)	8 (0.1-31)	NS	*p* <0.01	12(0.1-56)	12 (0.1-40)	NS
Estradiol (mg/dL)	8±7	15±10	21±14	*p*<0.001	*p* <0.001	10±7	6±5	NS

*Values are expressed a mean ±SD. Lp(a) data were expressed as mean, median, and (range). *Paired t test.*

Study of plasma Lp(a) levels and isoforms

Lp(a) levels were determined with an ELISA kit [Macra Lp(a), Terumo] as previously described.[33] The assay uses a monoclonal antibody against apo(a) that does not cross-react with plasminogen, and a second polyclonal antibody directed against the apo(a) portion of Lp(a). The assay recognizes all apo(a) isoforms with the same efficiency and does not cross-react with HDL-cholesterol, LDL-cholesterol or VLDL-cholesterol. High total cholesterol or LDL- cholesterol levels do not interfere with the Lp(a) determination.[38] The intra-assay and inter-assay variabilities were 3% and 8%, respectively.

The apo(a) phenotype was determined by agarose gel electrophoresis using the method described by Kamboh *et al.*[39] with slight modifications, followed by immunoblotting as previously described.[40]

Other laboratory parameters

Total cholesterol and triglycerides were determined by an enzymatic technique using an autoanalyzer (RA-1000 autoanalyzer, Bayer Diagnostic). High-density lipoprotein (HDL-cholesterol) was quantified by spectrophotometry after selective precipitation with heparin and manganese, also using a RA-1000 autoanalyzer. Low-density lipoprotein (LDL-cholesterol) was calculated by Friedewald's formula. Glucemia was determined by an automated method (DAX Techicon).

Estradiol was measured by a commercially available enzyme-immunologic test (Enzymun-test Oestradiol, Boehringer Mannheim Immunodiagnostic).

Body mass index (BMI) was calculated from weight in kilograms divided by the square of height in meters.

Statistical analysis

Levels of significance between the two groups were determined by Student's t-test and the Mann-Whitney non-parametric U test. Comparisons between different groups were performed by ANOVA and multiple comparison tests. The χ^2 test was used to compare percentages. The paired *t* test was used to compare the effect of HRT, except in the case of Lp(a), when the Kruskal-Wallis test was used. The correlation coefficient between variables was calculated using Spearman's rank test. Values of $p<0.05$ (two-tailed, where applicable) were considered to be statistically significant. All values are presented as mean±SD; Lp(a) data are expressed as the mean, median and (range). All these tests were performed using the statistical package SPSS Release 6.0 for Windows (SPSS Inc., Chicago, USA).

Results

Fibrinolytic parameters and coagulation inhibitors in women with CAD

Table 1 shows the several fibrinolytic parameters and coagulation inhibitors studied in our clinical groups. A significant decrease in fibrinolytic activity, evidenced by a prolongation of ELT and probably due to an increase in PAI-1, was observed in post-menopausal women with CAD in comparison with in healthy post-menopausal women (post-menopause: CAD vs healthy: ELT: 208 ±57 min vs 173±52 min, $p<0.001$; PAI-1 antigen: 35±17 ng/mL vs 28±17 ng/mL, $p<0.05$) (Table 1). Moreover fibrinolytic activity was significantly lower and PAI-1 levels significantly higher in CAD premenopausal women than in healthy premenopausal women (premenopause: CAD vs healthy: ELT: 198±51 min vs 152±58 min, $p<0.05$; PAI-1 antigen: 27±18 ng/mL vs 15±8 ng/mL, $p<0.01$).

Furthermore, a significant correlation between ELT and PAI-1 antigen levels was observed in all the groups studied: CAD patients (r=0.442, $p<0.001$) and control groups (r=0.646, $p<0.001$).

In relation to coagulation inhibitors, protein C and protein S levels were slightly higher in post-menopausal women than in the premenopausal groups (Table 1).

Other biochemical parameters in women with CAD

We also studied several parameters, such as triglycerides, glucose, cholesterol, Lp(a) and estrogen levels, in the women included in our clinical groups. Detailed results are shown in Table 1. Briefly, we found a significant increase in BMI and glucose levels in the post-menopausal women with CAD as compared to the levels in healthy post-menopausal women.

The levels of Lp(a) were higher in the CAD premenopausal group (18±16 mg/dL) than in the healthy premenopausal group (11±8 mg/dL). However, Lp(a) levels were not higher in post-menopausal women with CAD (18±16 mg/dL) than in healthy post-menopausal women (27±23 mg/dL). An inverse correlation between the Lp(a) levels and apo(a) isoform size (r=0.33; $p<0.05$) was found. As expected, differences between the estradiol levels of premenopausal and post-menopausal women were evident ($p<0.001$).

Influence of HRT

The influence of HRT on the parameters studied is shown in Table 2. There was an increase in fibrinolytic activity evidenced by a shortening in ELT, due to a decrease in PAI-1 levels, during transdermal HRT (Table 2). No significant modifications in triglycerides or glucose levels were observed during HRT, but total cholesterol and LDL-cholesterol levels were lower after 12 months of HRT (Table 2). HRT induced a significant increase in estradiol levels and a significant decrease in Lp(a) levels (Table 2). The rest of the parameters did not show statistically significant differences. With respect to the influence of progestogen, no significant differences between the group treated with transdermal estrogen and the group treated with transdermal estrogen+progestogen were observed for any of the parameters studied (data not shown).

In order to assess whether the decrease in Lp(a) after HRT shown in Table 2 was influenced by the basal Lp(a) values we studied the correlation between these parameters. There was a significant inverse correlation between the baseline (pretreatment) levels of Lp(a) and

the variation in Lp(a) after 3-4 months (r=-0.543, $p<0.001$) or 12 months (r=-0.790, $p<0.001$) of HRT [the variation in Lp(a) during HRT was expressed as the difference between the Lp(a) levels after 3-4 or 12 months and the baseline levels]. The decrease in Lp(a) was greater in the women with baseline Lp(a) levels above 30 mg/dL. No statistical correlation was found between the baseline levels of Lp(a) and the variation in Lp(a) after 12 months in the group of women not receiving HRT.

Changes in the different parameters studied were compared in two groups of post-menopausal CAD women after 12 months with or without HRT (Figure 1). PAI-1 antigen and Lp(a) levels decreased significantly and t-PA antigen and estradiol levels increased significantly in the group of women under HRT in comparison with the patients not given HRT.

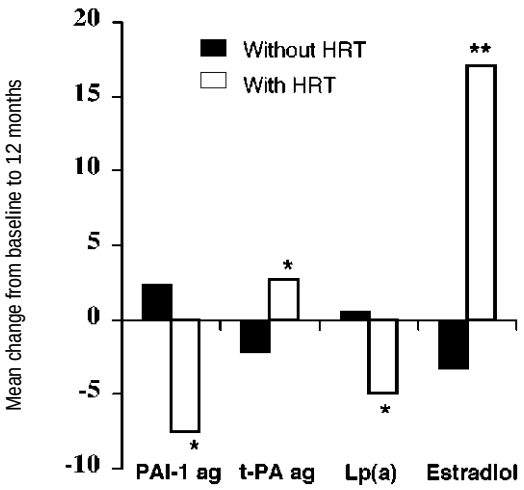

Figure 1. Mean change in plasminogen activator type 1 (PAI-1) antigen (ag) (ng/mL), tissue type plasminogen activator (t-PA)ag (ng/mL), estradiol (pg/mL) and lipoprotein(a) [Lp(a)] (mg/dL) levels in two groups of post-menopausal women with coronary artery disease 12 months after beginning the study [(with or without hormone replacement therapy (HRT)]. This change was expressed as the difference between the 12-month levels and the baseline levels. *$p<0.05$, **$p<0.001$ (with HRT vs without HRT).

Discussion

The present study shows that transdermal HRT has a favorable effect on the fibrinolytic system and on Lp(a) levels in post-menopausal women with CAD. To our knowledge this increase in fibrinolytic activity after HRT in CAD women has not been shown previously. In relation to the fibrinolytic system in CAD women, as in previous studies[14-16,17,41] the results of the present study show that in CAD there is a decrease in fibrinolytic activity due to an increase in PAI-1 levels, and that post-menopausal women with CAD have the highest PAI-1 levels. Moreover, Lp(a) levels were found to be higher in our group of premenopausal women with CAD than in healthy premenopausal women. These data support previous reports showing that high Lp(a) levels may contribute to early development of CAD.[25] Futhermore, Lp(a) levels increase in healthy post-menopausal women, as previously reported by our group and other authors.[20-22] However, Lp(a) levels were not higher in post-menopausal women with CAD than in healthy post-menopausal women. This could indicate that in our group of post-menopausal women with CAD other risk factors contributed to the disease.

Similar results on the parameters studied, except for glucose levels, were obtained when the 14 patients with DM were excluded from the group of post-menopausal women with CAD. Therefore, the hemostatic alterations observed in our group of post-menopausal women with CAD were not modified by the presence of DM.

Observational clinical studies have repeatedly demonstrated favorable associations between post-menopausal HRT and cardiovascular morbidity, mortality, and risk factors.[4,6,9,10] This protective effect may be due to several mechanisms such as an increase in the synthesis of vasodilator agents, a beneficial change of plasma lipids, and favorable changes in the fibrinolytic system.[4-6,12,13,42-44]

However, the beneficial effect of HRT on the secondary prevention of CAD in post-menopausal women with coronary disease is under discussion. While some observational studies show a decrease in CAD risk in users of estrogen replacement therapy,[28-30] the HERS report indicated that HRT with oral estrogen and progestogen did not reduce CAD events in women with established coronary heart disease, but even increased CAD risk in the first year.[31] The same study[31] did, however, indicate a favorable pattern of CAD events after several years of therapy. Our observation of the favorable effect of HRT on fibrinolysis variables and Lp(a) is in apparent contradiction with the HERS study. However, this discrepancy may reflect differences between the study populations and treatments. For instance, the HERS study evaluated the effect of oral estrogen[31] while our study evaluated that of transdermal estrogen. On the other hand, the present study as well as most of the observational studies[28-30] involved post-menopausal women with CAD who were relatively younger than those in the HERS study.[31]

Some studies have reported a beneficial effect of HRT on plasma lipids in hypercholesterolemic post-menopausal women with CAD.[32] In the present study we, too, observed a reduction in total cholesterol, LDL-cholesterol and Lp(a) levels in CAD patients after HRT. Moreover, the decrease in Lp(a) was larger in the women with higher basal Lp(a) levels. Similar results have previously been published by our group[20,22] and others,[21,45] but they were obtained from healthy post-menopausal women under HRT. Our results are in agreement with those reported by the HERS study in a recent article[46] that concludes that HRT has more favorable effects in CAD post-menopausal women with high initial Lp(a) levels. However, the HERS study evaluated oral estrogen

and our study evaluated transdermal estrogen.

In relation to the fibrinolytic system, the present study indicates that HRT in post-menopausal women with CAD improved fibrinolytic activity, fundamentally by decreasing PAI-1 levels. This favorable effect on the fibrinolytic system has also been reported in healthy post-menopausal women[10,12,13,19,20,22,42-44] and in post-menopausal women with diabetes mellitus[47] or dyslipidemia,[48] but in these studies only oral estrogens were examined and therefore in healthy post-menopausal women were due to this type of treatment.[10] However, in our study the decrease in PAI-1 levels was due to transdermal estrogens. In this context we suggest that the elevated baseline PAI-1 levels present in the post-menopausal women with CAD make it possible to detect the influence of the transdermal HRT more clearly than in healthy post-menopausal women with lower baseline PAI-1 levels.

There have been reports of an increased risk of venous thrombosis in women receiving HRT with oral estrogens.[31] Although our results show a decrease in PC levels in women under HRT with transdermal estrogens, the fact that PC levels are increased in the post-menopausal state (Table 1), means that the levels in our study remained within the normal range. However, the risk of venous thrombosis due to HRT could be increased in women with stabilized acquired or congenital thrombotic risk.

The influence of the addition of progestogen on cardiovascular disease and the lipid profile has also been studied. In the present study, no significant differences in the parameters studied were observed between the group treated with transdermal estrogen and the group treated with transdermal estrogen+progestogen, although the number of subjects included in our study may not have been large enough to detect significant differences.

In conclusion, data from this study indicate that the use of HRT (transdermal estrogen with or without progestogen) increases fibrinolytic activity and lowers Lp(a) levels and that these changes may have a favorable impact on the risk of new cardiovascular events. However the effects of other HRT regimens on hemostasis in post-menopausal women with CAD need to be studied.

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Disclosures

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Potential implications for clinical practice

Hormone replacement therapy may contribute to reduce the risk of coronary artery disease in post-menopausal women.

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