Prolactin and Preclinical Atherosclerosis in Menopausal Women With Cardiovascular Risk Factors

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Abstract—Hyperprolactinemia has been associated with endothelial dysfunction and an adverse cardiovascular risk profile, possibly as a result of the vasoconstrictive properties of prolactin. In this cross-sectional study, we examined the hypothesis that prolactin contributes to the increased cardiovascular risk occurring in early menopause by studying apparently healthy women without hyperprolactinemia. Prolactin serum levels were measured by immunoassay in 76 women aged 54.4±4.9 years in menopause for 4.9±2.8 years, and possible correlations with traditional cardiovascular risk factors and surrogate markers of preclinical atherosclerosis, arterial stiffening, and endothelial and microcirculatory function were examined. Positive correlations between prolactin serum levels and arterial blood pressure, but no other traditional risk factors, were found. Prolactin also correlated with central aortic systolic \( r = 0.337; \, P = 0.002 \) and diastolic \( r = 0.272; \, P = 0.012 \) blood pressures and pulse wave velocity \( r = 0.264; \, P = 0.02 \), a marker of aortic stiffness, but not with endothelial or microcirculatory function or carotid intima-media thickness. By multivariate regression analysis, prolactin levels determined, independent of traditional risk factors, both blood pressures and aortic stiffness. Notably, prolactin correlated with European Society of Cardiology HeartScore \( r = 0.364; \, P = 0.002 \), a composite index that predicts 10-year cardiovascular mortality. Prolactin levels >8.0 ng/mL had 100% sensitivity to predict a high peripheral blood pressure. Prolactin may play a role in accelerated arteriosclerosis in early menopause by affecting central/peripheral blood pressure and arterial stiffness. In contrast, no correlation was observed with other risk factors or surrogate markers of atherosclerosis. Prospective studies to assess whether prolactin is an additional hormone increasing cardiovascular risk are warranted. (Hypertension. 2009;54:98-105.)

Key Words: prolactin ■ menopause ■ blood pressure ■ cardiovascular risk ■ atherosclerosis

Experimental studies performed 30 years ago had shown that prolactin exerts positive chronotropic and vasoconstrictive effects. In later years, isolated reports suggested a discrete role of prolactin in the human cardiovascular system. As shown recently, high levels of prolactin play a pathogenetic role in preeclampsia, affecting peripheral sympathetic tone, and may be a useful diagnostic marker for this syndrome. Prolactin blood levels are higher in men with essential hypertension, whereas lowering these levels may contribute to blood pressure control. No data are currently available on such a role of prolactin in postmenopausal women. On the other hand, both male and female patients with prolactinomas present a more deteriorated cardiovascular risk profile associated with elevated insulin resistance, body mass index, homocysteine, and low-grade inflammation. Consequently, these patients had endothelial dysfunction as compared with healthy matched controls, which was reversed after successful treatment of prolactinomas. Whether excess prolactin directly affects endothelial function is not known.

In early menopause, cardiovascular risk increases substantially, mainly because of the loss of the protective effects of estrogens. As several studies have shown, the decline of estrogens, as the pivotal change in these individuals, has significant adverse cardiovascular effects and is associated with accelerated atherosclerosis. In the context of the biological complexity and multipathway interactions of hormones, additional female sex–specific factors may contribute to accelerated atherosclerosis postmenopause. Because the potential role of prolactin in the cardiovascular system function in these women has not been investigated, the present study examined the hypothesis that prolactin contributes to increased cardiovascular risk after menopause. Herein, we searched for correlations between circulating prolactin levels, when not exceeding the limits considered as normal, and traditional risk factors for cardiovascular disease, as well as various surrogate markers of preclinical atherosclerosis. We specifically focused on possible associations with peripheral and central arterial blood pressures and arterial stiffness.
because of the known attributes of prolactin as a vasoconstrictor and its possible role in hypertension. Potential associations on ≥1 of these markers could reveal a prognostic role of prolactin in the management of cardiovascular risk in apparently healthy postmenopausal women.

Materials and Methods

Study Design

For the purposes of this study, women in the first decade after menopause referred for evaluation of osteopenia to the Athens University Medical School Department of Menopause were recruited within a 3-month period and consecutively enrolled in a cross-sectional design. Menopause was confirmed by history of >1 year since the last menses and follicular-stimulating hormone and estradiol measurements. Women with clinically overt or treated cardiovascular disease or those receiving exogenous hormone administration were excluded from the study. Women with prolactin levels exceeding normal values for our laboratory (>25 ng/mL) were also excluded. Subjects were asked to abstain from the use of tobacco, alcohol, and caffeine for 24 hours and from food for 12 hours before the study.

Studies were performed in all of the patients in the supine position (except for the sitting position during pulse wave analysis) in a quiet, temperature-controlled (20°C to 25°C) room. All of the biochemical and vascular measurements took place in 1 visit for every subject between 9:30 AM and 11:30 AM on the basis of previous data showing only minimal fluctuation during these hours. Blood pressure was recorded in each subject twice (1 minute apart) by oscillometry using the automated Omron 705IT device (Omron) after resting in the sitting position for 5 minutes, and the average of these measurements was used in data analysis. In each case, the vascular tests were conducted in a fixed order by the same operator who was blinded to the cardiovascular risk profiles of the participants: pulse wave analysis followed by intima-media thickness (IMT) and pulse wave velocity (PWV). Finally, endothelial and microcirculatory function were assessed.

Risk factors for cardiovascular disease were carefully recorded based on medical history, clinical examination, and the results of biochemical testing (blood glucose and lipid profile). Cardiovascular risk factors were defined as follows: arterial hypertension, as systolic arterial pressure >140 mmHg and/or diastolic arterial pressure >90 mmHg, after 2 blood pressure measurements in each of 2 consecutive office visits or treatment for hypertension; cigarette smoking, as current and recently ceased (6 months) smoking; diabetes mellitus, as fasting blood glucose levels of >126 mg/dL or reported in clinical history or treatment for diabetes mellitus; hyperlipidemia; and as history of treatment for hyperlipidemia or total blood cholesterol level >200 mg/dL or low-density lipoprotein level >160 mg/dL in patients with <2 cardiovascular risk factors or >130 mg/dL in patients with ≥2 cardiovascular risk factors. Exercise was defined as any aerobic activity (including walking) of a minimum duration of 20 minutes for ≥5 times a week.

The research protocol of the present study was approved by the local ethics committee, and all of the subjects gave informed consent.

Computation of Total Cardiovascular Risk

The European Society of Cardiology online HeartScore calculator, taking in account age, sex, systolic blood pressure, total cholesterol level, and smoking status (http://www.heartscore.org/Pages/welcome.aspx), was used for the computation of current 10-year risk adjusted for the Greek population.11

Biochemical Measurements

Serum total cholesterol, high-density lipoprotein cholesterol, and triglycerides were assessed enzymatically by an autoanalyzer (COBAS-MIRA, Roche Diagnostics Ltd). Low-density lipoprotein cholesterol was estimated as described by the Friedewald equation (low-density lipoprotein cholesterol=total cholesterol−triglycerides/5−high-density lipoprotein cholesterol). The total coefficient of variation (percentage) and the sensitivity of the kit were 4.3% and 0.5 mmol/L, respectively. Prolactin was measured with the Abbott AxSYM Prolactin kit based on Microparticle Enzyme Immunoassay technology on an AxSYM analyzer (Abbott Laboratories). The total coefficient of variation ranged from 3.4% to 6.3%.

Vascular Measurements

Endothelial Function

Endothelial function of conduit arteries was evaluated by ultrasound measures of flow-mediated, endothelium-dependent vasodilation (FMD).12 Lower FMD has been linked to worse coronary function and adverse cardiovascular outcome.13 Assessment of FMD was performed by using a 14.0-MHz multifrequency linear array probe attached to a high-resolution ultrasound machine (Vivid 7 Pro, General Electric). The brachial artery of each participant was longitudinally imaged at the antecubital fossa in a supinated position of the forearm. A continuous ECG trace was recorded for timing diastole. Subjects rested in the supine position for 10 minutes before each measurement. A pneumatic cuff was placed around the forearm and after the initial measurements at resting conditions, and the cuff was rapidly inflated to 250 mm Hg for 5 minutes. After deflation of the cuff, the increase of arterial flow (reactive hyperemia) was monitored for 90 seconds, and the diameter of the brachial artery was measured at 30, 60, and 90 seconds. FMD was calculated as the percentage maximal change of lumen diameter between baseline and reactive hyperemia. To increase the chance of compliance of the participants in the protocol, we did not perform nitrate-induced vasodilatation on the basis of previous data showing that this marker of vascular smooth muscle layer function does not correlate with prolactin, even at very high levels of this hormone, and does not change after lowering prolactin with treatment.2 All of the subjects were scanned by a single experienced investigator (coefficient of variation: 11.6%).

Carotid IMT

IMT of the carotid artery reflects the condition of the structural components of the arterial wall and is a widely used and validated surrogate marker of cardiovascular disease, with robust predictive value for adverse cardiovascular and cerebrovascular outcome.14 IMT was measured using high-resolution B-mode ultrasound imaging (14.0-MHz multifrequency linear array probe, Vivid 7 Pro, General Electric). All of the scans were digitally recorded for offline analysis. Carotid IMT was measured at 3 paired segments: in the right and left common carotid artery, the carotid bulb, and the internal carotid artery, as described previously.15 The average of the maximal IMT from all 6 of the carotid segments was defined as the mean carotid IMT from each carotid segment used separately in the analysis. In each segment, 3 measurements of the maximal IMT in the far wall were averaged. All of the scans and offline analyses were performed by a single operator blinded to the cardiovascular risk profiles of the participants (coefficient of variation for mean carotid IMT: 10.6%). Plaques were defined as a focal structure that encroaches into the arterial lumen of ≥0.5 mm or 50% of the surrounding IMT value or that demonstrates a thickness >1.5 mm.16

Arterial Stiffness

Pulse travels at a higher velocity in stiff arterial vessels. Increased PWV is an established index of aortic stiffness and an independent predictor of worse cardiovascular prognosis.17,18 PWV was calculated from measurements of pulse transit time and the distance traveled between 2 recording sites with a validated noninvasive device (Complior, Artech Medical) that allows online pulse wave recording and automatic calculation of PWV (PWV equals distance [in meters] divided by transit time [in seconds]). Two different pulse waves were obtained simultaneously at 2 sites with 2 transducers. The distance between the 2 sites was calculated by subtracting the carotid (sternal notch from the carotid)-femoral distance. PWV between the common carotid artery and the common femoral artery was assessed (coefficient of variation: 2.4% for 2 repeated measurements).
Table 1. Demographic Characteristics and Biochemical and Vascular Parameters of 76 Women Under Study

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>54.45±8.48</td>
</tr>
<tr>
<td>Years of menopause</td>
<td>4.87±2.83</td>
</tr>
<tr>
<td>Smoking, yes</td>
<td>20/76 (26.3)</td>
</tr>
<tr>
<td>Hyperlipidemia, yes</td>
<td>49/73 (67.1)</td>
</tr>
<tr>
<td>Hypertension, yes</td>
<td>10/76 (13.2)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0/76 (0.0)</td>
</tr>
<tr>
<td>Exercise, yes</td>
<td>25/71 (35.2)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.84±4.86</td>
</tr>
<tr>
<td>Biochemical parameters</td>
<td></td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>92.95±9.37</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>228.01±37.79</td>
</tr>
<tr>
<td>Low-density lipoprotein, mg/dL</td>
<td>146.05±40.02</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>93.97±39.23</td>
</tr>
<tr>
<td>Follicle-stimulating hormone, mIU/mL</td>
<td>77.3±30.0</td>
</tr>
<tr>
<td>Prolactin, median (SE), ng/mL</td>
<td>7.2±0.3</td>
</tr>
<tr>
<td>Estradiol, median (SE), pg/mL</td>
<td>22±0.72</td>
</tr>
<tr>
<td>Free estradiol index</td>
<td>0.179±0.152</td>
</tr>
<tr>
<td>Vascular parameters</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>118.33±17.06</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>75.01±9.11</td>
</tr>
<tr>
<td>Central systolic blood pressure, mm Hg</td>
<td>110.99±16.52</td>
</tr>
<tr>
<td>Central diastolic blood pressure, mm Hg</td>
<td>76.59±9.43</td>
</tr>
<tr>
<td>Augmentation index at 75 bpm, %</td>
<td>29.39±9.1</td>
</tr>
<tr>
<td>Blood pressure amplification</td>
<td>1.29±0.25</td>
</tr>
<tr>
<td>Time to the beginning of the reflected wave, ms</td>
<td>135.37±10.99</td>
</tr>
<tr>
<td>PWV, carotid-femoral, m/s</td>
<td>8.67±1.88</td>
</tr>
<tr>
<td>Mean carotid IMT, median (SE), mm</td>
<td>0.68±0.01</td>
</tr>
<tr>
<td>Common carotid IMT, median (SE), mm</td>
<td>0.6±0.01</td>
</tr>
<tr>
<td>Carotid bifurcation IMT, median (SE), mm</td>
<td>0.8±0.02</td>
</tr>
<tr>
<td>Internal carotid IMT, median (SE), mm</td>
<td>0.6±0.02</td>
</tr>
<tr>
<td>Carotid plaques, %</td>
<td>17/74 (23)</td>
</tr>
<tr>
<td>FMD, %</td>
<td>5.8±2.4</td>
</tr>
<tr>
<td>TM (N=56), s</td>
<td>35.93±28.75</td>
</tr>
<tr>
<td>TR (N=56), s</td>
<td>0.66±0.55</td>
</tr>
<tr>
<td>TH1 (N=56), s</td>
<td>2.64±3.04</td>
</tr>
<tr>
<td>TH2 (N=56), s</td>
<td>61.48±39.39</td>
</tr>
</tbody>
</table>

All of the normally distributed variables are presented as mean±SD and non-normally distributed as medians (SE). Data are mean±SD or n/N (%), unless otherwise specified. TM indicates time until the peak flow is reached after the occlusion is released; TR, time until the rest flow is reached after the occlusion is released; TH1, time from the release of occlusion until the perfusion value reaches half the value of the peak flow; TH2, time from the release of occlusion until the perfusion value decreases halfway to the rest flow from the peak flow.

Central Blood Pressure Assessment

Radial artery tonometry was used to acquire and analyze the pulse waveform of the aorta (SphygmoCor System-Atcor Medical). Central blood pressures add prognostic information over peripheral blood pressures and offer valuable information as an end point in the assessment of interventions targeting cardiovascular disease. Peripheral pressure waveforms were recorded at the radial artery using a hand-held high-fidelity tonometer (Millar, Instruments) and calibrated by using arterial pressures measured at the brachial artery. Aortic pressure waveforms were then calculated by applying generalized transfer functions, as described previously. Analysis of the derived aortic waveform allows for the calculation of indices that correspond mainly with measures of arterial and particularly aortic stiffness and the intensity of reflected waves. The following parameters were measured from the central aortic waveform: (1) augmentation index (percentage) normalized for the heart rate of 75 bpm, which is the difference between the second and the first peaks of the central aortic waveform expressed as a percentage of the aortic pulse pressure; (2) central systolic and diastolic pressures; (3) time to the beginning of the reflected wave; (4) blood pressure amplification calculated as the ratio of peripheral pulse pressure:central pulse pressure. Mean difference±SD for 2 repeated measurements for augmentation index normalized for the heart rate of 75 bpm was −0.2±4.3 and for time to the beginning of the reflected wave was −5.2±15.8.

Laser Doppler Fluximetry

Laser Doppler fluximetry is a sensitive, noninvasive method for monitoring changes in the cutaneous peripheral microcirculation. Impaired microvascular function in the skin is associated with the presence of coronary heart disease. In this study, the Periflux 5001 (Perimed) measurement system was used. Subjects were placed in a
quiet, temperature-controlled room and rested in a supine position for ≥15 minutes. The scanning probe was attached in the middle of the second phalanx on the second finger and kept constant for the whole investigation. A 10-minute record at rest was followed by a 5-minute ischemization of the limb (cuff inflation at 240 mm Hg). Postocclusive reactive hyperemia was recorded after sudden cuff deflation. The following variables of microvascular reactivity were evaluated using Perimed software: time until the peak flow is reached after the occlusion is released, time until the rest flow is reached after the occlusion is released, time from the release of occlusion until the perfusion value reaches half the value of the peak flow, and time from the release of occlusion until the perfusion value decreases halfway to the rest flow from the peak flow.

**Statistical Analysis**

Data are expressed as the mean value ± SD. The 1-sample Kolmogorov-Smirnov test was used to test parameters for normal distribution. Prolactin and estradiol measurements were log transformed to reduce skewness. Two-sample Student t test was used to compare normally distributed variables between groups. Univariate linear regression analysis was used to identify significant correlations between prolactin and demographic, hemodynamic, and biochemical parameters. Multivariate stepwise linear regression analysis was used to identify independent determinants for hemodynamic parameters. Only when prolactin was associated with a hemodynamic parameter was the corresponding multivariate analysis performed to check for an independent association. Variables with P values of <0.1 in univariate regression analysis were inserted in the multivariate models, and stepwise forward procedure was applied to determine independent predictors for dependent variables. Receiver operating characteristic curve analysis was used to assess the predictive value of prolactin for a high blood pressure (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg). The curves were constructed by plotting sensitivity against 1-specificity. A P value of 0.05 was considered to be the level of statistical significance.

**Results**

**Prolactin, Traditional Coronary Risk Factors, and Central Aortic Blood Pressure**

Of the 78 women recruited for this study, 2 were excluded, because prolactin serum levels exceeded the normal range (>25 ng/mL). Demographic characteristics are shown in Table 1. As shown in Table 2, prolactin did not correlate with traditional risk factors of coronary artery disease, eg, age, smoking, body mass index, blood lipid profile, and blood glucose. However, by univariate analysis, prolactin correlated with both systolic and diastolic peripheral blood pressures (Figure 1A and 1B), as well as with both central systolic and diastolic blood pressures (Figure 1C and 1D). By taking into account these hemodynamic parameters as dependent variables, multivariate linear regression analysis showed that prolactin levels and body mass index were independent predictors of central and peripheral blood pressures (Table 3). Prolactin levels were significantly higher in hypertensive than normotensive women (median [range]: 9.2 [5.3 to 15.5] ng/mL; P = 0.046). Associations between prolactin and blood pressure amplification (r = −0.107; P = 0.362) or heart rate (r = 0.065; P = 0.580) were not established.

**Prolactin and Vascular Structure and Function**

As shown in Table 2, prolactin serum levels did not significantly correlate with surrogate markers of cardiovascular disease, eg, endothelial function (FMD; r = −0.01; P = 0.945), reflected waves (time to the beginning of the reflected wave; r = −0.172; P = 0.14) and augmentation index [percentage] normalized for the heart rate of 75 bpm; r = 0.907; P = 0.407),
mean carotid IMT ($r = -0.124; P = 0.339$), common carotid IMT ($r = 0.072; P = 0.58$), carotid bulb IMT ($r = -0.121; P = 0.349$), and internal carotid IMT ($r = -0.104; P = 0.423$). However, a significant correlation was observed between prolactin and arterial stiffness (PWV; $r = 0.276; P = 0.02$; Figure 2). By multivariate regression analysis, prolactin determined PWV independently of other risk factors for cardiovascular disease, but this correlation was lost after adjusting for mean arterial pressure (Table 3).

Prolactin levels did not differ between individuals with and without atheromatous plaques ($7.7 \pm 2.6$ versus $7.7 \pm 2.8$ ng/mL, respectively; $P = 0.953$). Significant correlations between prolactin and parameters associated with microcirculatory function (time from the release of occlusion until the perfusion value decreases halfway to the rest flow from the peak flow; $r = -0.178; P = 0.198$), time until the peak flow is reached after the occlusion is released ($r = -0.01; P = 0.940$), time until the rest flow is reached after the occlusion is released ($r = -0.053; P = 0.702$), and time from the release of occlusion until the perfusion value reaches half the value of the peak flow ($r = -0.196; P = 0.152$) were not established (Table 2).

**Prolactin Serum Levels and Cardiovascular Risk**

As shown in Figure 3, prolactin serum levels correlated with HeartScore, a composite index that predicts 10-year cardiovascular mortality by taking into account age, sex, systolic
blood pressure, total cholesterol, and smoking status ($r=0.364; P=0.002$). Moreover, all 7 of the subjects with a high blood pressure (systolic blood pressure $\geq 140$ and/or diastolic blood pressure $\geq 90$) had prolactin levels $>8.0$ ng/mL, revealing a sensitivity of 100% and specificity of 71% by receiver operating characteristic curve analysis for this cutoff to predict a high blood pressure (Figure 4).

**Discussion**

By demonstrating associations between prolactin with risk factors of cardiovascular disease and vascular markers of early atherosclerosis, the data presented herein imply a novel role of prolactin in the cardiovascular system of apparently healthy women in early menopause. Interestingly, only parameters associated with hypertension showed significant correlations. Prolactin was associated with both peripheral and central blood pressures. Central aortic pressures are the final resultants of numerous components of the cardiovascular system, eg, stroke volume, heart rate, reflected waves, arterial stiffness, and peripheral arterial resistance. This association was independent of other determinants of blood pressure. Prolactin was also correlated with arterial stiffness, a major hemodynamic determinant of blood pressure, and might, therefore, mediate the adverse effects of prolactin. The correlation of prolactin with total cardiovascular risk further supports our hypothesis of this hormone’s adverse cardiovascular effects.

Although prolactin levels in menopause women reach those in men, at least 1 study has shown differences in circulating prolactin levels between patients with arterial hypertension and controls in a population with prolactin levels $<50$ ng/mL. Similar patterns have been observed with other hormonal systems associating hormone levels ranging within normal limits with cardiovascular marker deterioration. For example, subjects with high-normal thyroid-stimulating hormone levels have worse endothelial function as compared with controls with thyroid-stimulating hormone at lower normal levels.

In general, blood pressure increases after menopause, but the mechanisms mediating this phenomenon are not fully elucidated. Activation of the sympathetic nervous system, oxidative stress, obesity, and the renin-angiotensin system seem to be involved in this process, either in concert or independently. Because prolactin affects most of these newly introduced mechanisms after menopause, we may speculate that, although circulating levels decrease with time, variations may remain physiologically relevant and may augment mechanisms mediating hypertension. Prolactin may increase arterial stiffness through changes in vascular tone, induction of low-grade inflammation, and smooth muscle cell proliferation and may, thus, influence central and peripheral hemodynamics. Because prolactin is considered a hormone associated with stress, mental stress may be a potential mechanism linking higher levels of this hormone with high blood pressure. However, there was no correlation of prolactin with heart rate, a parameter strongly correlated with mental stress. In agreement with this, an elegant recent study dissociated prolactin from stress-induced blood pres-
sure rising. On the other hand, our results cannot exclude the possibility of high blood pressure acting as a stimulus for elevations of prolactin levels. For this reason and because the correlations presented herein do not offer proof of causality, prolactin could be a marker of arterial stiffness and hypertension and not a risk factor. Nevertheless, taken together with experimental results indicating that prolactin-mediated mechanisms alter vascular integrity, our findings may trigger further research to confirm or reject the hypothesis of a causative relationship between this hormone and hypertension.

On the other hand, structural markers of preclinical atherosclerosis, such as, IMT, or the presence of atheromatous plaques did not correlate with the levels of prolactin, implying a rather selective deteriorating effect of prolactin toward arteriosclerosis rather than toward atheromatosis. Although prolactin at very high circulating levels is associated with endothelial dysfunction of the conduit arteries, we did not find such associations in the macrovasculature or in the microvasculature, possibly because of the much lower prolactin levels in our population. Thus, prolactin may exert differential effects on the cardiovascular system depending on its blood concentrations. High-normal levels of prolactin are associated with hypertension-related parameters, whereas high or very high levels of prolactin may impair endothelial function and possibly other markers of atheromatosis.

An adverse role of prolactin in the cardiovascular system function is further suggested by its association, albeit established cross-sectionally in our population, with estimated total cardiovascular risk. HeartScore is an important tool, contributing to the management of individuals with regard to primary prevention of cardiovascular disease. The European Society of Cardiology online HeartScore calculator with country-specific settings was used, which allows a more accurate estimate of risk in the Greek population.

The main limitation of this study is its cross-sectional design with a relatively small sample size. Therefore, our results should be viewed as preliminary and warrant confirmation by more powerful cross-sectional and longitudinal studies focusing on associations of prolactin with blood pressure and arterial stiffening. In addition, the effects of prolactin on the cardiovascular system might be masked or underestimated in our population carrying multiple risk factors for cardiovascular disease, despite statistical adjustment. On the other hand, it should be noted that the high prevalence of risk factors in postmenopausal women is very often met; thus, it may be less clinically relevant to assess the net effect of prolactin in risk-factor–free women.

In conclusion, we found that prolactin levels correlated with arterial blood pressure possibly by increasing arterial stiffness and not with other traditional cardiovascular risk factors. In contrast, no association was observed between prolactin levels and atheromatosis, as assessed by multiple surrogate markers, eg, endothelial and microcirculatory function, IMT, and atheromatous plaques. Finally, individual prolactin levels in early menopause correlated positively with HeartScore, an established estimate that is widely used for the prediction of cardiovascular mortality.

**Future Perspectives**

The findings of this study suggest that prolactin may contribute to accelerated arteriosclerosis in postmenopausal women and introduce clinical implications for cardiovascular risk stratification after menopause in terms of primary prevention. These attributes may be at least partly associated with the effects of prolactin on arterial stiffening and blood pressure. Prospective studies to examine the role of prolactin as a new cardiovascular risk factor and particularly the impact on arterial stiffening and increasing blood pressure by decreasing the blood levels of this hormone are warranted.

**Disclosures**

None.

**References**


[Further references list]

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