Sex-Specific Differences in Cardiovascular Risk Factors and Blood Pressure Control in Hypertensive Patients

Konstantinos Tziomalos, MD, PhD; Vasilios Giampatzis, MD; Maria Baltatzi, MD, PhD; Elias Efthymiou, MD; Konstantia Psianou, MD; Natalia Papastergiou, MD; Dimitra Magkou, MD; Vagia Bougatsa, MD; Christos Savopoulos, MD, PhD; Apostolos I. Hatzitolios, MD, PhD

From the First Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece

Cardiovascular disease (CVD) and cardiovascular risk factors are frequently undertreated in women. However, it is unclear whether the prevalence of additional cardiovascular risk factors and the total cardiovascular risk differ between hypertensive men and women. There are also limited data regarding rates of blood pressure control in the two sexes outside the United States. The authors aimed to compare the cardiovascular risk profile between sexes. A total of 1810 hypertensive patients (40.4% men, age 56.5±13.5 years) attending the hypertension outpatient clinic of our department were studied. Men were more frequently smokers than women and were more heavy smokers than the latter. Serum high-density lipoprotein cholesterol levels were lower and serum triglyceride levels were higher in men. On the other hand, abdominal obesity and chronic kidney disease were more prevalent in women. The estimated cardiovascular risk was higher in men than in women but the prevalence of established CVD did not differ between the sexes. The percentage of patients with controlled hypertension and the number of antihypertensive medications were similar in men and women. In conclusion, hypertensive men have more adverse cardiovascular risk factor profile and greater estimated cardiovascular risk than women. However, the prevalence of established CVD does not differ between sexes. These findings further reinforce current guidelines that recommend that management of hypertension and of other cardiovascular risk factors should be as aggressive in women as in men in order to prevent cardiovascular events. *J Clin Hypertens (Greenwich).* 2014;16:309–312.

Cardiovascular disease (CVD) represents the leading cause of mortality in both men and women.[1] Even though the prevalence of coronary heart disease (CHD) is higher in men, the prevalence of stroke and the absolute annual number of CVD deaths are higher in women.[1] Despite these findings, both women and physicians tend to underestimate the cardiovascular risk in the female population.[2,3] Moreover, in women, the frequently atypical manifestation of CHD and the underuse of diagnostic procedures result in delayed diagnosis of CHD.[2,4] The management of CVD in women is also suboptimal, as they are often prescribed fewer drugs than men[2] and are less likely to undergo revascularization after coronary angiography.[4]

Hypertension is a major modifiable cardiovascular risk factor.[5] It was reported that elevated blood pressure (BP) contributes more to cardiovascular morbidity and mortality in women.[6,7] Hypertension often clusters with other cardiovascular risk factors; 80% to 98% of hypertensive patients have at least one additional cardiovascular risk factor.[8,9] The presence of other traditional cardiovascular risk factors in hypertensive patients is independently associated with target organ damage.[10] However, discrepant results have been reported regarding the prevalence of other traditional cardiovascular risk factors in hypertensive men and women. Some studies have reported a higher prevalence of other traditional cardiovascular risk factors in women[11] but others have reported higher rates and higher total cardiovascular risk in men.[12,13] Moreover, even though several studies compared rates of BP control in the two sexes in the United States,[11,14–16]there are limited relevant data outside of the United States.[17,18]

The aim of the present study was to evaluate whether the cardiovascular risk profile differs between treated hypertensive men and women. We also aimed to compare BP control rates between sexes.

PATIENTS AND METHODS

We studied the medical records of the last visit of all patients (n=1810; 40.4% men, age 56.5±13.5 years) who attended the hypertension outpatient clinic of our department at least once during the last decade (2002–2011).

Office BP measurements were performed according to current guidelines.[19] Patients remained seated for 5 minutes before measurements, with their arm supported at heart level. Caffeine and alcohol consumption, cigarette smoking, and exercise were discouraged on the day of examination. A calibrated mercury sphygmomanometer with an appropriately sized cuff was used. A minimum of two measurements were performed in each patient and the average was recorded. Controlled hypertension was defined according to the 2007 European Society of Hypertension/European

Address for correspondence: Konstantinos Tziomalos, MD, PhD, AHEPA University Hospital, 1 Stilponos Kyriakidi street, 546 36, Thessaloniki, Greece
E-mail: ktziomalos@yahoo.com

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Society of Cardiology guidelines as BP <140/90 mm Hg in the absence of type 2 diabetes mellitus (T2DM) or chronic kidney disease (CKD).[19] In patients with T2DM and/or CKD, controlled hypertension was defined as BP <130/80 mm Hg.[19]

In all patients, weight, height, and waist circumference were measured. Body weight was measured with an analog scale with the patients wearing light-weight clothing. Height was measured by a stadiometer with the patient barefoot. Body mass index (BMI) was calculated by dividing weight (in kg) by height squared (in meters). Waist circumference was measured at the level of the umbilicus. All BP and anthropometric measurements were performed by experienced physicians of the hypertension outpatient clinic.

Blood samples were collected in the morning after an overnight fast. Serum glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), and creatinine levels were determined. Low-density lipoprotein cholesterol (LDL-C) levels were calculated using Friedewald's formula.[20] Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) equation.[21]

Other cardiovascular risk factors, including smoking, T2DM, obesity, metabolic syndrome (MetS), and CKD were recorded. Abdominal obesity was defined as waist circumference ≥102 and 88 cm in men and women, respectively.[22] Diagnosis of MetS was based on the definition proposed by the American Heart Association/National Heart, Lung, and Blood Institute.[22] According to this definition, the diagnosis of MetS requires the presence of at least 3 of the following features: (1) abdominal obesity (waist circumference ≥102 and ≥88 cm in men and women, respectively); (2) serum TG levels ≥150 mg/dL or drug treatment for elevated TG levels; (3) serum HDL-C levels <40 and <50 mg/dL in men and women, respectively, or drug treatment for low HDL-C levels; (4) systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg or antihypertensive treatment and serum glucose levels ≥100 mg/dL; (5) serum glucose levels ≥100 mg/dL or antidiabetic treatment.[22] CKD was defined as estimated GFR <60 mL/min/1.73 m^2. Established CVD, including CHD and stroke, was also recorded based on patients' self-report. Among patients without T2DM, CHD, or stroke (n=1499), the 10-year risk for myocardial infarction and fatal CHD was estimated using the Framingham risk score.

Statistical Analysis

All data were analyzed using the statistical package SPSS (version 17.0; SPSS, Chicago, IL). Data are presented as percentages or as mean and standard deviation. Because women were older than men (58.1±11.8 vs 54.2±15.4 years, respectively; *P*<.001), comparisons of categorical variables between women and men were performed with binary logistic regression analysis adjusting for age. Accordingly, comparisons of continuous variables between women and men were performed with analysis of covariance adjusting for age. In all cases, a two-tailed *P*<.05 was considered significant.

RESULTS

Comparisons of demographic characteristics and comorbidities between men and women are shown in Table I. Both obesity (BMI ≥30 kg/m^2) and abdominal obesity were more prevalent in women (51.2% vs 36.5% in men [*P*<.001] and 79.3% vs 56.4% in men [*P*=.001], respectively). The prevalence of CKD was also higher in women than in men (22.7% vs 12.2%, respectively; *P*=.001). Among patients with CKD, 11.3% and 2.8% had a history of CHD and stroke, respectively. In contrast, men were more frequently smokers than women (29.3% vs 21.7%, respectively; *P*=.001) and were more heavy smokers than the latter (16±24 vs 10±16 package-years, respectively; *P*=.028). The prevalence of T2DM, MetS, CHD, and stroke did not differ between sexes (Table I). Among patients with T2DM, 82.3% and 83.7% did not have a history of CHD or stroke, respectively. The prevalence of T2DM without CVD (CHD or stroke) did not differ between sexes (6.3% and 6.9% in men and women, respectively). Among patients without T2DM, CHD, or stroke (n=1499), the estimated cardiovascular risk was higher in men than in women (15.3±9.4 vs 6.2±5.4, respectively; *P*<.001).

Comparisons of BP data between sexes are shown in Table II. Systolic and diastolic BP did not differ between men and women (systolic BP, 146±21 mm Hg vs

TABLE I. Demographic Characteristics and Comorbidities of the Study Population[a]

	Men (n=731)	Women (n=1079)	*P* Value (Adjusted for Age)
Age, y	54.2±15.4	58.1±11.8	NA
Smoking	29.3	21.7	.001
Package-years	16±24	10±16	.028
Type 2 diabetes mellitus	7.7	8.4	NS
Metabolic syndrome	15.5	17.0	NS
Normal weight/overweight/obese	16.0/47.5/36.5	16.2/32.6/51.2	<.001
Abdominal obesity	56.4	79.3	<.001
Chronic kidney disease	12.2	22.7	.001
Coronary heart disease	8.6	6.8	NS
Stroke	4.5	4.5	NS
Estimated cardiovascular risk[b]	15.3±9.4	6.2±5.4	<.001

Abbreviations: NA, not applicable; NS, not significant. [a]Data are presented as percentages except age, package-years, and estimated cardiovascular risk, which are presented as mean±standard deviations. [b]In 605 men (82.8% of the total male population) and 894 women (82.8% of the total female population) without coronary heart disease, stroke, or type 2 diabetes mellitus.

TABLE II. Clinical and Laboratory Characteristics of the Study Population

	Men (n=731)	Women (n=1079)	*P* Value (Adjusted for Age)
Systolic blood pressure, mm Hg	146±21	148±23	NS
Diastolic blood pressure, mm Hg	89±14	88±14	NS
Controlled hypertension, %	20.8	23.2	NS
No. of antihypertensive medications	1.1±1.2	1.3±1.2	NS
No. of visits in the hypertension clinic	1.5±0.5	1.4±0.4	NS
New diagnosis of hypertension, %	30.7	34.3	NS
Heart rate	75±10	76±11	NS
Body mass index, kg/m^2	29.3±4.8	30.7±6.1	.001
LDL cholesterol, mg/dL	150±52	148±58	NS
HDL cholesterol, mg/dL	45±11	54±14	<.001
Triglycerides, mg/dL	164±94	148±75	.014
Glucose, mg/dL	107±31	107±34	NS
Estimated GFR, mL/min/1.73 m^2	85±23	75±23	<.001

Abbreviations: GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant. [a]Data are expressed as mean±standard deviation unless otherwise indicated.

148±23 mm Hg, respectively; diastolic BP, 89±14 mm Hg vs 88±14 mm Hg, respectively). The percentage of patients with controlled hypertension was similar in men and women (20.8% and 23.2%, respectively; *P*=not significant [NS]) and did not differ between age quartiles (≤48 years, 49–58 years, 59–66 years, and ≥67 years) in either men or women (data not shown). The number of antihypertensive medications was also comparable in the two sexes (1.1±1.2 and 1.3±1.2 in men and women, respectively; *P*=NS) and progressively increased with age in both men (0.7±0.9, 1.2±1.1, 1.2±1.1, and 1.5±1.3, respectively; *P* for trend <.001) and women (0.8±0.9, 1.2±1.1, 1.5±1.2, and 1.6±1.2, respectively; *P* for trend <.001). Only 11.3% of the study population visited the hypertension clinic only once. When these patients were excluded from the analysis, BP control rates increased but again did not differ between the sexes (22.3% and 25.3% in men and women, respectively). Moreover, only 2.5% of the study population was not receiving any antihypertensive medication. The proportion of patients not receiving any antihypertensive medication did not differ between men and women (2.9% and 2.2%, respectively).

Comparisons of other clinical and laboratory characteristics between men and women are shown in Table II. Women had higher BMI than men (30.7±6.1 kg/m^2 vs 29.3±4.8 kg/m^2, respectively; *P*=.001) and also had lower estimated GFR (75±23 mL/min/1.73 m^2 vs 85±23 mL/min/1.73 m^2, respectively; *P*<.001). In contrast, serum HDL-C levels were lower in men (45±11 mg/dL vs 54±14 mg/dL in women, respectively; *P*<.001) and serum TG levels were higher (164±94 mg/dL and 148±75 mg/dL in men and women, respectively; *P*=.014). Serum LDL-C and glucose levels did not differ between sexes. The proportion of patients treated with statins was very low, did not differ between men and women (3.0% and 4.0%, respectively), and did not differ between age quartiles in either men or women (data not shown).

DISCUSSION

In the present study, the prevalence of smoking was higher and the lipid profile was more adverse in treated hypertensive men than in hypertensive women. These differences resulted in a higher estimated cardiovascular risk in men. However, the prevalence of established CVD (CHD and stroke) did not differ between sexes.

The prevalence of smoking was greater in men in our study and the number of package-years was also higher, in accordance with previous reports from European referral outpatient clinics.[12,13] In addition, serum HDL-C levels were lower and serum TG levels were higher in men. This is in agreement with other reports from Greek referral centers[12] but is in contrast with findings of studies from the general US population, in which hypertensive men had higher HDL-C levels.[11] In addition to the different settings (referral centers vs general population), sociodemographic, and lifestyle differences between the US and Greek populations might underlie this discrepancy.

The estimated cardiovascular risk was higher in men than in women in our study. To the best of our knowledge, only one study compared the estimated cardiovascular risk between hypertensive men and women and reported similar findings.[12] Despite the higher estimated risk in women, the prevalence of established CVD did not differ between sexes, in contrast with previous reports, which reported higher rates in men.[13,23] A possible explanation for this finding is that the Framingham equation underestimates the cardiovascular risk in women.[24,25] This is of particular importance, since treatment decisions in hypertensive patients should be based not only on BP levels but also on total cardiovascular risk.[19] Therefore, our findings reinforce the current recommendations that hypertension in women should be managed as aggressively as that in men.[19]

In contrast to the higher prevalence of some traditional CVD risk factors in men, CKD and abdominal obesity were more frequent in hypertensive women, in agreement with previous reports.[11–13,26,27] Both CKD and abdominal obesity are associated with increased cardiovascular risk[28–30] but neither is included in the Framingham equation. Interestingly, a recent study reported that women with newly diagnosed hypertension not only have higher rates of CKD but also are at greater risk for developing CKD.[31] These findings stress the need for close monitoring of renal function in both male and female hypertensive patients.

BP control rates did not differ between sexes in our study. Some earlier studies reported similar findings,[11,17,18] whereas others observed better BP control in hypertensive men.[15,16] In the latter studies, however, men were being treated with more antihypertensive agents than women,[15,16] whereas the number of prescribed antihypertensive agents was comparable in men and women in our study. BP control rates were lower in our study than in previous reports.[11,15–18] A likely explanation for this finding is that our department is a referral center that covers a wide geographical area in Northern Greece, whereas the latter studies assessed BP control rates in the general population.

CONCLUSIONS

Treated hypertensive men have a more adverse cardiovascular risk factor profile and greater estimated cardiovascular risk than women. However, the prevalence of established CVD does not differ between sexes. These findings further reinforce current guidelines recommending that management of hypertension and of other cardiovascular risk factors should be as aggressive in women as in men in order to prevent cardiovascular events.

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