Sexual Activity and Plasma Testosterone Levels in Hypertensive Males

Roberto Fogari, Annalisa Zoppi, Paola Preti, Andrea Rinaldi, Gianluigi Marasi, Alessandro Vanasia, and Amedeo Mugellini

The aim of this study was to compare sexual activity and plasma testosterone levels of hypertensive men with those of healthy normotensive controls. We investigated 110 newly diagnosed, never treated hypertensive (blood pressure [BP] ≥140/95 mm Hg) men and 110 healthy normotensive (diastolic BP <90 mm Hg) men. All of them were aged 40 to 49 years, married, without any previous sexual dysfunction, nondiabetic, nonobese (body mass index <28 kg/m²), nonsmoking, and not taking any drug. All subjects were evaluated in the morning after an overnight fast. Clinical evaluation included BP, body weight, and height measurements, determination of testosterone, and an interview about sexual activity, assessed as number of sexual intercourse episodes per month. Hypertensive men presented a 25% reduction in sexual activity as compared to normotensive men (5.9 ± 2.6 vs 7.9 ± 2.5 sexual intercourse episodes per month, respectively, P < .01) and a 12% reduction in testosterone levels (510.6 ± 151.9 ng/dL vs 578.6 ± 146.8 ng/dL, P < .01). In both normotensive and hypertensive men Pearson’s correlation analysis showed a significant positive correlation between testosterone levels and sexual activity and a significant negative correlation between testosterone and age and between testosterone and BP values. Multiple regression analysis confirmed a significant inverse relationship between testosterone and age in normotensive men, whereas only a nonsignificant trend was found in the hypertensive ones. In addition, a significant inverse correlation between testosterone and BP levels was confirmed in hypertensive men limited to systolic BP, whereas a nonsignificant trend was observed in the normotensive controls. In conclusion, these findings suggest a relationship between essential hypertension and impaired testosterone levels in men. The elucidation of the nature of such a relationship and its physiologic and clinical significance needs further investigation.

Key Words: Sexual activity, testosterone, hypertension.

The high prevalence of sexual dysfunction in hypertensive men is well established.¹,² Such a dysfunction, including problems related to libido, erection, and ejaculation, often is first reported by patients while receiving antihypertensive treatment, which has lead to a widespread belief by patients and physicians that sexual dysfunction is caused by a specific hypotensive agent.³,⁴ However, it has been observed that the incidence of sexual dysfunction is considerably higher in untreated hypertensive men than among normotensives,⁵,⁶ therefore, it remains unclear from the available literature whether this problem is related to hypertension itself or to its therapy, or both. The incidence of sexual problems in the hypertensive patients before treatment has been inadequately investigated. Studies of sexual dysfunction in hypertensive men have usually suffered from lack of specificity as the data have often been collected as part of an overall evaluation of hypertension or its drug therapy, or both. Besides, the studies on this topic are difficult to compare because of differing methodologies, lack of standardized measures, evaluation of sexual activity unrelated with age, body weight, and marital status, which may all represent confounding factors. Sexual dysfunction seen in hypertensive men is probably the result of alterations in a number of the processes (neural, vascular, and hormonal) involved in normal sexual function.²,⁷,⁸

With regard to the role of hormonal factors, contrasting results have been reported about the relationship between endogenous sex hormones in men and blood pressure (BP), with some studies showing reduced androgen levels in subjects with essential hypertension as compared to normotensive ones⁹–¹² and other studies showing no significant difference.¹³,¹⁴ Again the disparity among the various reports might be due to the different characteristics of the examined populations and to the lack of data control for age, body composition (adiposity), marital status, smoking habits, drug intake, and history of previous sexual dysfunction.


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With this background, the aim of this study was to compare sexual activity and plasma testosterone levels of untreated hypertensive men, homogeneous for age, body mass index (BMI), marital status, and lack of previous sexual dysfunction symptoms with those of healthy normotensive controls. We specifically focused on one aspect of sexual function (ie, sexual desire), which can be quantified in terms of sexual intercourse frequency, which is considered a good index of sexual activity.

Methods

We studied 110 consecutive patients with uncomplicated essential hypertension (systolic BP \(\geq 140\) mm Hg and diastolic BP \(\geq 95\) mm Hg) and 110 healthy subjects with normal BP (diastolic BP <90 mm Hg) and without family history of hypertension. The study population was recruited in the context of a program of community control of hypertension at the work site that screened about 15,000 workers. Subjects who were found to be hypertensive at the screening visit were sent to the Hypertension Center of our clinic; those whose BP values were confirmed to exceed 140/95 mm Hg at two following measurements and fulfilled the inclusion/exclusion criteria entered the study (110 of the 255 screened subjects in the age group of interest, between 40 and 49 years). The inclusion criteria were the following: men between the ages of 40 and 49 years, married, with newly diagnosed, never treated essential hypertension (systolic BP >140 mm Hg and diastolic BP >90 mm Hg) and without family history of hypertension. The study population was recruited in the context of a program of community control of hypertension at the work site that screened about 15,000 workers. Subjects who were found to be hypertensive at the screening visit were sent to the Hypertension Center of our clinic; those whose BP values were confirmed to exceed 140/95 mm Hg at two following measurements and fulfilled the inclusion/exclusion criteria entered the study (110 of the 255 screened subjects in the age group of interest, between 40 and 49 years). The inclusion criteria were the following: men between the ages of 40 and 49 years, married, with newly diagnosed, never treated essential hypertension, and BMI <28 kg/m². Patients with diabetes mellitus, smoking habits, history of alcohol abuse (intake of more than 30 mL of ethanol per day), previous sexual dysfunction, and conditions requiring any medication were excluded from the study as were those whose wives were pregnant or had recently delivered a baby. A random-matching computer program was used to select one control from the normotensive subject of the same working community who met the matching criteria for each hypertensive subject (±1 year for age, ±0.5 kg/m² for BMI) and fulfilled the inclusion/exclusion criteria.

The protocol for this study was approved by the local Ethical Committee and informed consent was obtained from each patient before entry into the study.

All subjects were evaluated in the morning, between 8:30 AM and 9:30 AM, after an overnight fast. The clinical evaluation included BP, body weight, and height measurements, venous blood samples drawing for the determination of plasma total testosterone, and an interview about sexual activity.

Blood pressure was measured after 15 and 25 min of rest in the sitting position using a digital BP device (Omron HEM-737 Intellience [Omron Corp., Tokyo, Japan]) validated against intra-arterial BP measurements. Body weight to the nearest 0.1 kg and height to the nearest centimeter were measured with the subjects barefoot and in light clothing and BMI was calculated as weight (kilograms)/height (meters squared). Circumferences of the waist and hip regions were measured at the levels of the umbilicus and iliac crest, respectively, giving the waist-hip ratio. To limit the influence of fluctuations of plasma testosterone levels due to its episodical secretion, blood samples for testosterone evaluation were always drawn at the same time of the day, between 8:30 AM and 9:30 AM. Plasma obtained by venipuncture from fasting subjects was frozen at −70°C and stored in tightly sealed containers. Testosterone assay was performed in the same research laboratory using a radioimmunoassay method (Diagnostic Products Corporation, Los Angeles, CA) after extraction with diethylether. The maximum storage time before measurement was 4 days.

All participants were given a questionnaire with instructions for self completion. The questions dealing with sexual function (Have you noted a decrease of interest in sex? Did you have problems in gaining an erection? How many times did you have sexual intercourse in the past 2 weeks?) were part of a series of questions on various aspects of quality of life. After assurance of confidentiality, questionnaires coded by identification numbers were completed by the respondent in a private area and responses were returned in a sealed envelope. Sexual activity was assessed as mean number of sexual intercourse episodes per month. Subjects who responded yes to the first two questions dealing with sexual function were excluded from the study, as our objective was to examine subjects unaware of sexual dysfunction and regarding themselves as sexually normal. Including patients with sexual dysfunction symptoms, such as decreased libido or erectile dysfunction, would have not allow to detect the specific impact of hypertension per se on sexual activity. In fact, there would be the risk on one hand to include subjects with sexual dysfunction due to causes other than hypertension and, on the other hand, to amplify the finding of reduced sexual activity due to psychologic effects (fear of failure).

Results

The main demographic and clinic characteristics of the study population are shown in Table 1. The two groups were well matched for age, BMI, and waist/hip ratio.

Sexual activity, assessed as number of sexual intercourse episodes per month, was significantly lower in hypertensive men than in normotensive ones (5.9 ± 2.6 vs 7.9 ± 2.5 sexual intercourse episodes per month, respectively, −25%, \(P < .01\)) (Fig. 1).

Plasma testosterone levels were lower in hypertensive men (510.6 ± 151.9 ng/dL) than in normotensive ones.
(578.6 ± 146.8 ng/dL), the difference (−12%) being statistically significant ($P < .01$) (Fig. 1).

In both normotensive and hypertensive men, Pearson’s correlation analysis showed a significant positive correlation between testosterone levels and sexual activity ($r = 0.65$ in normotensives and $r = 0.71$ in hypertensives, both $P < .0001$), whereas in both groups a significant negative correlation was found between testosterone levels and age ($r = −0.57$ in normotensives and $r = −0.50$ in hypertensives, both $P < .0001$) and between testosterone and BP values (for systolic BP: $r = −0.35$ in normotensive and $−0.55$ in hypertensive, both $P < .0001$; for diastolic BP: $r = −0.32$ in normotensives, $P = .0006$ and $−0.50$ in hypertensives, $P < .0001$).

The results of multiple regression analysis having testosterone as dependent variable are reported in Table 2. There was a significant inverse correlation between plasma testosterone and age in normotensive men and a nonsignificant trend in the hypertensive ones. In addition, a significant inverse relationship between testosterone and BP levels was confirmed in hypertensive men limited to systolic BP, whereas a nonsignificant trend was found in normotensive men.

## Discussion

The results of this study are worthwhile of some methodologic comments. The study population was recruited taking into account age, BMI, marital status, a previous sexual dysfunction symptoms to examine a homogeneous sample and eliminate some important bias in the evaluation of sexual activity and plasma testosterone values.

Levels of sexual activity have been shown to decline with increasing age$^{17,18}$ and a decrease in mean serum testosterone levels with age has been described, although with a wide variation.$^{19,20}$ Therefore, to limit the confounding effects of age, we examined a middle-aged, sexually active population in a restricted age range.

<table>
<thead>
<tr>
<th></th>
<th>Normotensives</th>
<th>Hypertensives</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>44.7 ± 2.1</td>
<td>44.9 ± 2.2</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>24.8 ± 1.1</td>
<td>25.2 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.94 ± 0.09</td>
<td>0.95 ± 0.08</td>
<td>NS</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>72.0 ± 5.1</td>
<td>75.0 ± 4.8</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>123.1 ± 9.3</td>
<td>163.1 ± 13.4</td>
<td>&lt;.001</td>
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<tr>
<td>DBP (mm Hg)</td>
<td>79.1 ± 5.2</td>
<td>100.3 ± 8.5</td>
<td>&lt;.001</td>
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<tr>
<td>Blood glucose (mg/dL)</td>
<td>87.2 ± 6.9</td>
<td>87.6 ± 7.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant; BMI = body mass index; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

FIG. 1. Plasma testosterone and sexual intercourse frequency in normotensive and hypertensive men. Individual values and mean values ± SD.
A significant negative correlation between body fat (in particular central adiposity) and plasma testosterone levels has been observed and obesity could possibly contribute to reduced sexual activity.\textsuperscript{21–23} In this study obese subjects were excluded and BMI (an indicator of adipose tissue mass) and waist to hip ratio (an index of central adiposity) of the hypertensive men were not different from those in the control group, therefore we can exclude an influence of body weight on the observed differences between the two groups.

Finally, enrolling subjects never treated for hypertension, not taking any other drug, and without history of diabetes, smoking habits, alcohol abuse, and previous sexual dysfunction allowed us to assess the level of sexual activity and sex hormones more likely related to hypertension itself and not to other factors.

The results of this study showed that in untreated hypertensive men sexual activity, assessed as number of sexual intercourse episodes per month, was 25% lower than in normotensive controls.

This finding confirms previous observations of increased sexual dysfunction in hypertensive subjects independently from antihypertensive drug therapy\textsuperscript{5,6} and suggests that hypertension per se regardless of drugs may affect sexual function.

Consistent with previous observations,\textsuperscript{9–12} plasma testosterone levels were significantly lower in untreated hypertensive men than in normotensive controls, although a marked overlap in the testosterone values of the two groups was found.

The finding that hypertension is associated with lower levels of plasma testosterone as compared to normotensive controls suggests three hypotheses: 1) serum testosterone influences BP regulation; 2) elevated BP can negatively affect steroidogenesis or clearance, and 3) there are genes involved in the regulation of BP that also affect steroidogenesis.

Men with a family history of hypertension have been shown to have lower than normal serum testosterone levels,\textsuperscript{24} which suggests a possible genetic link between hypertension and serum testosterone levels. The genetic hypothesis is also supported by data obtained from Natriuretic Peptide Receptor A gene-deficient and gene-duplicated mutant mouse models demonstrating that NPR 1 gene deficiency in male mice is characterized by both high BP and low circulating testosterone levels.\textsuperscript{25}

However, the precise mechanism underlying the relationship between hypertension and low testosterone levels remain an enigma.

A significant inverse relationship between testosterone levels and BP was shown by Pearson’s correlation analysis, but such a negative correlation was confirmed by multiple regression analysis only in the hypertensive men and limited to systolic BP values. The inverse correlation between testosterone levels and systolic BP suggests that testosterone reduction in hypertensive men could contribute to increased arterial stiffness. An interaction between androgens and the vessel wall has been hypothesized because 1) steroid receptors have been found in the cardiovascular system, 2) testosterone induces direct relaxing effect on the vasculature in both normotensive and hypertensive rats\textsuperscript{26,27}, 3) testosterone infused into coronary arteries in men with coronary artery disease causes vasodilation\textsuperscript{28}, and 4) androgen withdrawal in men is associated with decreased central arterial compliance.\textsuperscript{29}

In conclusion, the results of this study, which refer to a highly selected population of middle-aged, sexually active, newly diagnosed and never treated hypertensive men and therefore have limited generalizability, demonstrated a relationship between essential hypertension and impaired plasma testosterone levels. This may be partly responsible for the reduced sexual activity observed in hypertensive men. The elucidation of the nature of this relationship and its physiologic and clinical significance might help us to better understand mechanisms of BP control and thus merits further investigation.

### Table 2. Results of multiple regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t value</td>
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</tr>
<tr>
<td>Intercept</td>
<td>10.13</td>
<td>&lt;.0001</td>
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<td>Age (y)</td>
<td>-6.18</td>
<td>&lt;.0001</td>
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<tr>
<td>SBP</td>
<td>1.94</td>
<td>0.055</td>
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<tr>
<td>DBP</td>
<td>-1.09</td>
<td>0.277</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

Dependent variable was testosterone (ng/dL).

### References


