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Androgen Levels in Older Men Who Have or Who Are at Risk of Acquiring HIV Infection

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Abstract

Objective—To determine the prevalence of, risk factors for, and clinical manifestations of low androgen levels in older men who have or who are at risk of acquiring human immunodeficiency virus (HIV) infection, we performed a cross-sectional analysis of an observational cohort of men aged ≥49 years old.

Methods—A standardized interview (regarding demographic characteristics, behaviors, and medical history) was performed, and body mass index, HIV serologic data, $CD4^+$ cell count, the presence of hepatitis C virus (HCV) markers, and serum testosterone and human sex-binding hormone levels were determined. Factors associated with androgen levels were assessed using logistic regression models.

Results—Among 502 men (age, 49−81 years) who were not taking androgens, 54% had total testosterone levels of <300 ng/dL. Low androgen levels were associated with injection drug use, HCV infection, high body mass index, and use of psychotropic medications ($P < .05$); black race was associated with higher androgen levels. Only among men who reported having sex with men was low testosterone level associated with HIV infection (adjusted odds ratio [OR_{adj}] for total testosterone level of <300 ng/dL, 5.1; 95% confidence interval [CI], 1.2−22.4), but among all HIV-seropositive men, HIV load of >10,000 copies/mL was associated with a testosterone level of <200 ng/dL (OR_{adj}, 2.1; 95% CI, 1.1−4.3; $P = .03$). On univariate analysis, low androgen levels were associated with decreased interest in sex, depressive symptoms, loss of concentration/memory, difficulty sleeping, osteopenia, and poorer subjective health ($P < .05$).

Conclusions—Most older men at risk for HIV infection have low androgen levels. Injection drug use, high body mass index, HCV infection, and use of psychotropic medications are associated with low androgen levels, and low androgen levels are associated with symptoms of hypogonadism.

Early in the HIV/AIDS epidemic, it was recognized that hypogonadism was common in men with AIDS [1]. Low testosterone levels in men with HIV infection have been correlated with advanced immunodeficiency and with severe clinical manifestations, such as wasting [2,3].

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The prevalence of androgen deficiency in men increases with age [4], with total testosterone levels decreasing by 1%−2% annually starting in the fourth decade of life [5]. The use of HAART has led to dramatic decreases in mortality [6–8], increasing the numbers of persons with HIV infection who live to old age. Because androgen levels decrease with aging and occur commonly in persons with HIV infection, it is important to determine the prevalence of and factors associated with low androgen levels in older men with HIV infection. However, the majority of studies of androgen levels in men with HIV infection have included predominantly men in their fourth and fifth decades of life. Here, we report the prevalence of and risk factors for low androgen levels in a cohort of older men who have or who are at risk of acquiring HIV infection.

METHODS

The cohort of HIV at-risk aging men's prospective study (CHAMPS) is a study of selected medical outcomes in older men with or at risk for HIV infection enrolled from the community in the Bronx, New York. Men within 1 year of their 50th birthday or older were eligible if they had HIV infection or if they were at risk of acquiring it through injection drug use, unprotected sex with men, ≥5 sexual partners within the prior 5 years, exchanging of sex for money or drugs, or unprotected sex with a woman who had HIV infection, had injected drugs, or had unprotected sex with a bisexual man or an injection drug user. Men were excluded if they were unable to participate in a detailed standardized interview and unable to provide a blood specimen.

Men who provided written, informed consent underwent standardized interviews. Phlebotomy was performed to determine HIV antibody test results, HIV-1 load, lymphocyte subsets, antibody to hepatitis C virus (HCV), and HCV RNA level using methods described elsewhere [9]. Follow-up interviews and phlebotomy were scheduled at 6-month intervals.

Interview data

The interview elicited information about sociodemographic characteristics, personal and family medical history, use of antiretrovirals and other medication, and sex and drug-use behaviors. Depression was assessed using the Center for Epidemiologic Studies Depression Scale. Final scores range from 0 to 60, and a score of ≥16 indicates depressive symptoms. Erectile dysfunction was defined as difficulty in getting or maintaining an erection.

Bone mineral density

Bone mineral density of the lumbar spine (L2–L4) and hip (femoral neck) was measured by dual x-ray absorptiometry using a Prodigy densitometer (Lunar). Control data used by this machine are derived from the National Health and Nutrition Study. Osteopenia and osteoporosis were defined according to World Health Organization criteria (i.e., osteopenia was defined as a T score less than −1.0 and greater than or equal to −2.5 SDs from the average peak bone mass in young adults, and osteoporosis was defined as a T score less than −2.50 SDs). Because of the low prevalence of osteoporosis, osteopenia and osteoporosis were considered to be present if the criteria were met at either the hip or the spine.

Sex hormones

Assays were performed on stored serum samples from the second study visit and included total testosterone, sex hormone–binding globulin (SHBG), and luteinizing hormone. Luteinizing hormone levels were measured in duplicate using time-resolved immunofluorometric assays (DELFIA; Pharmacia), as described elsewhere [10,11]. Coefficients of variation were calculated from within- and between-assay quality-control duplicates at 3 levels for luteinizing hormone and SHBG levels and at 2 levels for total testosterone level. Respective intra- and

interassay coefficients of variation were 2.5% and 6.0% for luteinizing hormone level, 4.3% and 8.6% for SHBG level, and 9.0% and 10.6% for total testosterone level. The sensitivity of the testosterone assay was 0.04 ng/mL. For each specimen, a free androgen index was calculated using the formula, FAI = total testosterone/SHBG×100.

Statistical analysis

Initial analyses of free androgen index and total testosterone levels were performed using χ^2 test or Fisher's exact test for categorical variables and the Wilcoxon rank sum test or Kruskall-Wallis test for continuous variables. Logistic regression models were used to assess factors associated with low free androgen indices and total testosterone levels. A recent consensus conference noted that 300 ng/dL is the lower limit of the normal range for testosterone levels in healthy young men, and total testosterone levels of <200 ng/dL clearly indicate hypogonadism [12]. For this study, we defined low free androgen index as <14.8, low total testosterone level as <300 ng/dL, and very low total testosterone level as <200 ng/dL. Analyses were performed excluding men who reported currently taking androgens and were then repeated including these men, assuming that these men would have had low levels in the absence of androgen replacement.

Ethics approval

This study was approved by the Institutional Review Board for Protection of Human Subjects of Montefiore Medical Center (Bronx, NY).

RESULTS

Of the 556 men studied, 54 (9.7%) reported currently taking androgens. Current androgen use was significantly more common among HIV-seropositive men (OR, 10.3; 95% CI, 3.7−29.0) and men who reported having had sex with men within the previous 5 years (OR, 6.4; 95% CI, 3.5−11.5), with no significant difference by race, age, smoking, or illicit drug use.

Selected characteristics of the 502 men who were not currently taking androgens are shown in table 1. HIV-seropositive men were significantly more likely to be nonwhite, to have had sex with men, and to have used sildenafil recently; they were significantly less likely to have used drugs recently and to be overweight or obese. Among HIV-seropositive men, $CD4^+$ lymphocyte counts were ≥500 cell/mm^3 in 26%, 200−499 cells/mm^3 in 49%, and <200 cells/mm^3 in 25%. Nearly two-thirds of subjects reported that they were currently taking HAART, and 44% were taking protease inhibitors; the viral load was undetectable in 36% of HIV-seropositive men.

Total testosterone levels were ≥300 ng/dL in 229 men (45.6%), 200−299 ng/dL in 111 (22.1%), and <200 ng/dL in 162 (32.3%). The majority of specimens (290 [58%] of 502) had been obtained in the morning, with the remainder obtained in the afternoon. Univariate associations of demographic, behavioral, and medical variables with free androgen index and total testosterone level are shown in table 2. Injection drug use within the past 5 years, smoking cigarettes, not having sex with men within 5 years, current use of psychotropic medications, being seropositive for antibody to HCV, and having detectable HCV RNA were significantly associated with lower free androgen indices and lower total testosterone levels. Seropositivity for antibody to HCV was associated with low androgen levels, even when we excluded men with detectable HCV RNA or the 55 men who had ever received IFN treatment (data not shown). Only testosterone levels differed significantly by race and ethnic background and by body mass index; testosterone levels were significantly lower in overweight and obese men. Very low testosterone levels were significantly less prevalent among HIV-seropositive men than among HIV-seronegative men. Among the 275 HIV-seropositive men only, univariate

results were similar. Injection drug use, smoking, having sex with men, and body mass index remained significantly associated with androgen levels, but race no longer was, likely as a result of the reduced sample size (data not shown). Low and very low testosterone levels were significantly more common among men with HIV-1 loads of >10,000 copies/mL (table 2). Inclusion of the 54 men (50 HIV-seropositive men and 4 HIV-seronegative men) who reported currently taking androgens, with the assumption that their unmodified androgen levels would have been low in the absence of exogenous androgen therapy, had only minor effects on the factors associated with androgen levels.

Mean luteinizing hormone levels (± SD) among men with low testosterone levels, compared with those without low testosterone levels, were 3.6±3.5 U/L and 5.9±4.0 U/L ($P < .001$), respectively, for HIV-seronegative men, and they were 7.0±7.4 U/L and 7.5±3.9 U/L ($P < .001$), respectively, for HIV-seropositive men. Mean luteinizing hormone levels (± SD) among men with very low testosterone levels, compared with those without very low testosterone levels, were 3.4±3.8 U/L and 5.4±3.8 U/L ($P < .001$), respectively, for HIV-seronegative men, and they were 5.3±5.1 U/L and 8.0±6.2 U/L ($P < .001$), respectively, for HIV-seropositive men. Thirty-nine men (8%) had luteinizing hormone levels of <1.0 U/L, of whom 18 (46%) had testosterone levels of <200 ng/ dL. The 89 men (18%) who had any history of receipt of androgens (median duration, 6 months; range, <1 to 120 months) did not have lower luteinizing hormone levels than those who had never received androgens. Of the 89 men who had a history of androgen use, only 23 (26%) had taken androgens recently (i.e., since the most recent study visit); of these, estimated median lifetime duration of use was 3 months (range, <1 to 72 months), and luteinizing hormone levels were not lower, compared with men who had not taken androgens recently. Among men with low or very low testosterone levels, there was no association between luteinizing hormone levels and history of injection drug use for either HIV-seropositive or HIV-seronegative men.

Factors found by multivariate analysis to be associated with low androgen levels are shown in table 3. Injection drug use, being overweight or obese, seropositivity for HCV, current receipt of psychotropic medications (i.e., barbiturates, sleeping pills, antidepressants, or tranquilizers), and having had blood drawn in the afternoon were associated with ≥1 of the following findings: low free androgen index, low testosterone level, or very low testosterone level. Replacing detectable seropositivity for HCV with detectable HCV RNA levels in the model had little effect on the findings (data not shown). Only among men who reported having had sex with men was HIV infection significantly associated with low testosterone levels. However, among all seropositive men, an HIV load of >10,000 copies/ mL was associated with a testosterone level of <200 ng/dL (adjusted OR [OR_{adj}], 2.1; 95% CI, 1.1−4.3; $P = .03$). Black race was inversely associated with low testosterone levels.

The univariate associations with androgen levels of selected symptoms possibly attributable to hypogonadism and of measured bone density are shown in table 4. Reported decreased interest in sex, depressive symptoms, poorer overall health, and osteopenia noted by dual x-ray absorptiometry scan were significantly associated with each of the androgen measurements. Perceived loss of concentration or memory and difficulty sleeping were significantly associated with low testosterone levels, but not with free androgen index. Reported erectile dysfunction was not associated with androgen levels, and current use of sildenafil was significantly associated only with very low testosterone levels; men who currently used sildenafil had a significantly lower prevalence of very low testosterone than men who did not. Men who reported having erectile dysfunction did have a greater number or frequency of depressive symptoms than those without erectile dysfunction (median Center for Epidemiologic Studies Depression Scale for HIV-seronegative men, 21 [range, 14−58] vs. 15 [range, 8−55]; median for HIV-seropositive men, 17 [range, 11−45] vs. 12.5 [range, 7−40]; $P < .001$ for both).

DISCUSSION

The prevalence of low total testosterone levels in healthy men increases with aging, reportedly reaching levels of <325 mg/dL in ~20% of men aged 160 years and in ~50% of those aged 180 years [13]. Decreased serum testosterone levels occur in up to 60% of men with HIV infection, depending on stage of disease, weight loss, and receipt of antiretroviral therapy [1, 3,14,15]. Therefore, the finding of total testosterone levels <300 ng/mL in both HIV-seropositive and HIV-seronegative men in this study is consistent with the findings of prior reports. We observed an association between low testosterone level and HIV infection only in men who reported having had sex with men. However, among all HIV-seropositive men, very low testosterone level was associated with a high viral load. We did not find any significant association between low androgen level and stage of HIV disease (as measured by $CD4^+$ cell count), receipt of antiretroviral therapy, or low body mass index.

A history of injection drug use was associated with low free androgen index. Low testosterone levels have been reported in opiate addicts [16], and long-term administration of opiates to rats during sexual maturation leads to decreased testosterone levels, with more transient effects in adult animals [17,18]. Opiates may act by suppressing the hypothalamo-pituitary-gonadal axis [16]. The fact that luteinizing hormone levels were significantly lower among men with low testosterone levels than among those without low testosterone levels in both HIV-seropositive and HIV-seronegative subjects, and the fact that levels appeared to be unrelated to lifetime or recent androgen use, suggest that at least some of the low androgen levels seen were due to hypogonadotropic hypogonadism in both groups. Additional investigation into pituitary function in such men seems warranted.

In this study, HCV infection had the strongest association with low androgen levels. Although severe liver disease may be associated with low androgen levels [19,20], we are aware of only limited data suggesting an association between low levels and HCV infection per se. In an Italian study, the authors noted that plasma levels of total and free testosterone were “generally lower” in 207 patients with hepatitis C than in 2010 Italian men previously evaluated for erectile dysfunction, but data on the latter group were not shown, and it is not clear whether the difference was significant [21]. In contrast, among 50 male blood donors with antibody to HCV in a Polish study, there were no characteristic changes in testosterone levels noted [22]. Further study of the possible effect of HCV infection on androgen levels seems to be warranted.

Altered mood has been associated with low testosterone levels [23], and use of psychotropic medications may lead to sexual dysfunction, including testosterone deficiency resulting from hyperprolactinemia [24]. We found that current receipt of psychotropic medications was associated with low androgen levels on multivariate analysis, and lower levels were found in men reporting depressive symptoms. However, in this cross-sectional study, we were not able to determine causality.

Being overweight and being obese were associated with lower testosterone levels in this study. Obesity, particularly central obesity, has been associated previously with low total testosterone levels [25]. Serum total testosterone levels decrease with increasing body mass because of declining SHBG levels [26]. It seems likely that the small proportion of underweight men in this study (only 5.6% of HIV-seropositive men and 2.2% of HIV-seronegative men) did not provide the power to assess any possible association of low androgen levels with wasting. This may also explain the limited association with HIV infection found.

Higher testosterone levels in African American men than in white men have been reported previously [27–29], but participants were generally younger than the sample of older men studied here, sample sizes were often small, and not all studies found a difference by race

[25,30]. Signs and symptoms of androgen deficiency are nonspecific, so screening tests for hypogonadism using clinical findings have limitations with regard to both sensitivity and specificity [5,31,32], whereas assays of testosterone levels are objective measurements. There has been consensus that both clinical signs and symptoms, as well as measured low testosterone levels, should be used to define androgen deficiency [12]. The associations of low androgen levels with decreased libido, depressive symptoms, and decreased bone mineral density found in this study are consistent with clinical findings reported in men with hypogonadism [33–35].

Hypogonadism in men with AIDS-related wasting has been associated with depression, independent of weight, virologic status, or other disease factors [36]. It is interesting that we did not observe an association of lower androgen levels with erectile dysfunction or sildenafil use. This is consistent with a recent report that, among men receiving methadone maintenance, although erectile dysfunction was associated with older age, there was no association with plasma testosterone levels [37]. Erectile dysfunction was significantly associated with a greater number or frequency of depressive symptoms. Although, in a cross-sectional analysis, it is not possible to determine causality, this suggests that most erectile dysfunction may have occurred on a psychological basis, rather than as a result of low androgen levels.

Several study limitations should be noted. Reliable information about the reason for androgen use among men who reported using androgens was not available. Therefore, we repeated analyses including these men while assuming that they would have had low levels if they were not taking androgens; this did not have an important impact on study findings. There is a diurnal variation in testosterone levels, especially in young men [38,39]. We were unable to obtain all specimens at the same time of day; the time at which they were drawn depended primarily on participant availability, so that systematic bias seems unlikely. Lower androgen levels were associated with having blood drawn in the afternoon, but our multivariate analysis adjusted for time of phlebotomy, and restricting analyses to only those men whose levels were obtained in the morning did not have any important effect on findings (data not shown). We measured total testosterone and sex hormone binding globulin concentration to calculate free androgen index, and the calculation of free androgen index assumes normal serum albumin levels. Our findings must be interpreted with caution for patients with decreased albumin levels (e.g., nephrotic syndrome and liver cirrhosis). Neither albumin level nor other determinants of liver function were measured in this study; thus, we have no information on the severity of liver disease in patients with HCV infection. Our information on use of psychotropic medications included such medications in aggregate; therefore, we do not have data on individual medications used. Finally, we measured total—rather than free— testosterone levels. However, it is not clear that free testosterone level is superior to total testosterone level for defining androgen deficiency, so that total testosterone level may be more useful in determining when hormone replacement therapy is appropriate [39,40].

In summary, this study of older men who had or who were at risk of acquiring HIV infection found that a majority of both HIV-seropositive men and HIV-seronegative men had low serum androgen levels. Risk factors for low androgen levels included injection drug use, being overweight or obese, HCV infection, receipt of psychotropic medications, and undergoing phlebotomy in the afternoon rather than the morning, whereas black race was associated with a decreased risk. Among HIV-seropositive men, low androgen levels were significantly associated with evidence of HIV activity, as measured by viral load, but not with the stage of HIV disease, as measured by $CD4^+$ lymphocyte count. Both low free androgen index and low androgen levels were associated with several clinical findings suggestive of hypogonadism. These findings suggest that older men with or at risk for HIV infection should be assessed for androgen deficiency, with consideration of replacement therapy for those with clinical evidence of hypogonadism.

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Table 1

Selected characteristics of 502 men not currently taking androgens by HIV status

Characteristic	HIV-seronegative men (*n* = 227)	HIV-seropositive men (*n* = 275)	*P*
Age, median years (range)	55 (50−81)	54 (49−74)	**.03**
Age in years			
49−54	113 (49.8)	152 (55.3)	
55−59	66 (29.1)	74 (26.9)	
60−64	28 (12.3)	39 (14.2)	
>64	20 (8.8)	10 (3.6)	.08
Race			
White	43 (18.9)	29 (10.5)	
Black	110 (48.5)	172 (62.5)	
Hispanic	56 (24.7)	60 (21.8)	
Other	18 (7.9)	14 (5.1)	**.006**
Sex with men within prior 5 years	15 (6.7)	57 (20.7)	**<.001**
Injection drug use within prior 5 years	23 (10.2)	28 (10.3)	.91
Drug use since last study visit	90 (40.0)	79 (29.0)	**.008**
Cigarettes since last study visit	164 (72.0)	181 (65.8)	.07
Sexually active within prior 6 months	162 (71.4)	173 (62.9)	.03
ED in past 2 weeks	68 (31.1)	85 (32.4)	.41
Androgen use since last visit	8 (3.6)	15 (5.6)	.21
Sildenafil use			
Since last visit	26 (11.6)	65 (23.7)	**<.001**
Current use	17 (7.6)	51 (18.7)	**<.001**
Current use of psychotropic drugs[a]	69 (29.9)	110 (34.1)	.34
BMI[b]			
Median value	27.3 (16.7−50.0)	25.0 (17.0−44.8)	**<.001**
≤19	4 (1.9)	15 (5.7)	
>19 and ≤25	66 (30.8)	116 (44.4)	
>25 and <30	83 (38.8)	93 (35.6)	
≥30	61 (28.5)	37 (14.2)	**<.001**
$CD4^+$ lymphocyte count, cells/mm^3			
≥500	...	71 (25.8)	
200−499	...	135 (49.1)	
<200	...	69 (25.1)	
HIV-1 load, copies/mL			
≤75	...	100 (36.4)	
76−1000	...	52 (18.9)	
1001−10,000	...	39 (14.2)	
10,001−100,000	...	68 (24.7)	
>100,000	...	16 (5.8)	
HAART use			
Within prior 6 months		191 (70.5)	
Current	...	172 (63.5)	
PI use			
Within prior 6 months	...	137 (50.6)	
Current	...	118 (43.5)	

NOTE. Data are no. (%) of subjects, unless otherwise indicated. Boldface *P* values are statistically significant. Denominators occasionally may add up to less than 502 because of refusal to provide information or because values were missing or indeterminate. BMI, body mass index; ED, erectile dysfunction; PI, protease inhibitor.

[a] Psychotropic medications included barbiturates, sleeping pills, antidepressants or tranquilizers

[b] Patients with a BMI of ≤19 were considered to be underweight, those with a BMI of >19 to ≤25 were considered to have a normal weight, those with a BMI of >25 to <30 were considered to be overweight, and those with a BMI of ≥30 were considered to be obese.

Table 2

Associations of free androgen index (FAI) and total testosterone (TT) level with demographic, behavioral, and medical characteristics in 502 men who were not currently taking androgens.

	FAI				TT level					
	Mean value		Value of <14.8		Mean level		Level <300 ng/dL		Level <200 ng/dL	
Characteristic	Mean ± SD	*P*	Proportion (%) of subjects[a]	*P*	Mean ng/dL ± SD	*P*	Proportion (%) of subjects[a]	*P*	Proportion (%) of subjects[a]	*P*
Age in years										
49−54	15.6 ± 14.3		164/265 (61.9)		295 ± 183		151/265 (57.0)		88/265 (33.2)	
55−59	17.3 ± 18.1		84/140 (60.0)		324 ± 269		74/140 (52.9)		45/140 (32.1)	
60−64	15.5 ± 11.0		40/67 (59.7)		322 ± 199		32/67 (47.8)		21/167 (31.3)	
>64	21.7 ± 22.7	.46	15/30 (50.0)	.65	381 ± 477	.64	16/30 (53.3)	.56	8/30 (26.7)	.90
Race										
White	18.7 ± 20.6		45/72 (62.5)		306 ± 339		46/72 (63.9)		29/72 (40.3)	
Black	16.4 ± 14.2		163/282 (57.8)		327 ± 207		135/282 (47.9)		70/282 (24.8)	
Hispanic	15.6 ± 16.5		76/116 (65.5)		284 ± 254		75/116 (64.7)		54/116 (46.6)	
Other	14.7 ± 12.9	.61	19/32 (59.4)	.53	286 ± 135	**.005**	17/32 (53.1)	**.006**	9/32 (28.1)	**<.001**
Injection drug use in past 5 years										
No	17.3 ± 16.2		256/448 (57.1)		320 ± 244		238/448 (53.1)		137/448 (30.6)	
Yes	8.7 ± 8.5	**<.001**	45/51 (88.2)	**<.001**	236 ± 176	**.002**	34/51 (66.7)	.09	25/51 (49.0)	**.01**
Drug use since last study visit										
No	16.5 ± 15.4		198/329 (60.2)		322 ± 261		176/329 (53.5)		104/329 (31.6)	
Yes	16.4 ± 16.5	.33	102/169 (60.4)	.95	292 ± 188	.33	95/169 (56.2)	.63	57/169 (33.7)	.71
Cigarette use since last visit										
No	21.5 ± 19.2		76/157 (48.4)		349 ± 299		78/157 (49.7)		41/157 (26.1)	
Yes	14.1 ± 13.3	**<.001**	227/345 (65.8)	**<.001**	295 ± 203	**.03**	195/345 (56.5)	.18	121/345 (35.1)	.06
Sex with men within past 5 years										
No	15.3 ± 15.1		274/426 (64.3)		298 ± 213		237/426 (55.6)		150/426 (35.7)	
Yes	23.2 ± 18.1	**<.001**	26/72 (36.1)	**<.001**	402 ± 341	**<.001**	33/72 (45.8)	.16	9/72 (12.5)	**<.001**
BMI[b]										
≤ 19	14.6 ± 13.2		14/22 (63.6)		479 ± 446		10/22 (45.5)		7/22 (31.8)	
> 19 and ≤25	14.6 ± 14.2		123/187 (65.8)		350 ± 276		79/187 (42.2)		45/187 (24.1)	
>25	17.7 ± 16.8	.41	165/290 (54.6)	.15	273 ± 173	**<.001**	184/290 (63.4)	**<.001**	110/290 (37.9)	**.007**
Androgen use since last visit										
No	16.5 ± 15.8		282/468 (60.3)		316 ± 243		249/468 (53.2)		147/468 (31.4)	
Yes	15.8 ± 15.5	.60	15/23 (65.2)	.80	265 ± 148	.37	16/23 (69.6)	.19	9/23 (39.1)	.58
Present use of psychotropic medications[c]										
No	17.7 ± 16.8		199/356 (55.9)		336 ± 259		176/356 (49.4)		99/356 (27.8)	
Yes	13.3 ± 12.5	**.002**	103/144 (71.5)	**<.001**	250 ± 163	**<.001**	97/144 (67.4)	**<.001**	63/144 (43.8)	**<.001**
Present use of lipid-lowering drugs										
No	15.7 ± 15.0		282/457 (61.7)		306 ± 216		249/457 (54.5)		148/457 (32.4)	
Yes	23.5 ± 20.8	**.005**	21/44 (47.7)	.10	367 ± 404	**.39**	24/44 (54.5)	.88	14/44 (31.8)	.93
Present use of antihypertensive medication										
No	16.8 ± 16.3		200/337 (59.3)		320 ± 260		180/337 (53.4)		102/337 (30.3)	
Yes	15.7 ± 14.7	.43	101/162 (62.3)	.29	295 ± 185	.37	92/162 (56.8)	.27	59/162 (36.4)	.20
Antibody to hepatitis C virus										
No	29.2 ± 19.6		29/133 (21.8)		404 ± 294		43/133 (32.3)		10/133 (7.5)	
Yes	11.1 ± 9.6	**<.001**	271/355 (76.3)	**<.001**	275 ± 206	**<.001**	223/355 (62.8)	**<.001**	149/355 (42.0)	**<.001**

Characteristic	FAI				TT level					
	Mean value		Value of <14.8		Mean level		Level <300 ng/dL		Level <200 ng/dL	
	Mean ± SD	*P*	Proportion (%) of subjects[a]	*P*	Mean ng/dL ± SD	*P*	Proportion (%) of subjects[a]	*P*	Proportion (%) of subjects[a]	*P*
Detectable HCV RNA[d]										
No	15.2 ± 8.2		38/64 (59.4)		264 ± 184		39/64 (60.9)		31/64 (48.4)	
Yes	9.8 ± 8.2	**<.001**	216/266 (81.2)	**<.001**	275 ± 214	.66	169/266 (63.5)	.81	111/266 (41.7)	.41
HIV seropositive										
No	18.5 ± 17.8		128/227 (56.4)		302 ± 211		126/227 (55.5)		86/227 (37.9)	
Yes	14.7 ± 13.6	.10	175/275 (63.6)	.12	320 ± 259	.24	147/275 (53.5)	.71	76/275 (27.6)	**.02**
HIV-1 load, copies/mL[e]										
≤10,000	15.1 ± 12.9		116/191 (60.7)		330 ± 240		94/191 (49.2)		43/191 (22.5)	
>10,000	13.9 ± 15.1	.10	59/84 (70.2)	.17	296 ± 297	**.004**	53/84 (63.1)	**.046**	33/84 (39.3)	**.007**
Taking HAART										
No	14.7 ± 12.6		62/99 (62.6)		293 ± 209		58/99 (58.6)		30/99 (30.3)	
Yes	14.7 ± 14.3	.90	112/172 (65.1)	.78	336 ± 285	.17	86/172 (50.0)	.22	45/172 (26.2)	.55
Time of phlebotomy										
Morning	17.3 ± 16.3		168/290 (57.9)		318 ± 213		153/290 (52.8)		85/290 (29.3)	
Afternoon	15.3 ± 14.9	.13	135/212 (63.7)	.23	303 ± 269	.06	120/212 (56.6)	.45	77/212 (36.3)	.12

NOTE. Boldface *P* values are statistically significant. Denominators occasionally may add up to less than 502 because of refusal to provide information or because values were missing or indeterminate. BMI, body mass index; HCV, hepatitis C virus.

[a] No. of men with FAI or TT level/no. of men with characteristic (%).

[b] Patients with a BMI of ≤19 were considered to be underweight, those with a BMI of >19 to ≤25 were considered to have a normal weight, those with a BMI of >25 to <30 were considered to be overweight, and those with a BMI of ≥30 were considered to be obese.

[c] Psychotropic medications included barbiturates, sleeping pills, antidepressants, and tranquilizers

[d] Among men seropositive for antibody to HCV.

[e] Among HIV-seropositive men.

Table 3

Factors associated with low androgen levels on multivariate analysis.

Characteristic	Free androgen index of <14.8		Total testosterone level, ng/dL			
			<300 ng/dL		<200 ng/dL	
	OR_{adj} (95% CI)	*P*	OR_{adj} (95% CI)	*P*	OR_{adj} (95% CI)	*P*
Race[a]						
Black	NR	NR	0.43 (0.23−0.82)	**.01**	0.42 (0.22−0.79)	<**.001**
Hispanic	NR	NR	0.86 (0.42−1.8)	.68	1.2 (0.60−2.4)	.61
Other	NR	NR	0.72 (0.27−1.9)	.52	0.57 (0.21−1.6)	.28
Injection drug use within past 5 years	4.2 (1.5−11.6)	**.006**	NR	NR	NR	NR
Sex with men within past 5 years	NR	NR	...[b]	...	NR	NR
Body mass index[c]						
>25	NR	NR	2.7 (1.8−4.1)	<**.001**	2.1 (1.3−3.4)	**.001**
≤19	NR	NR	1.1 (0.40− 2.8)	.91	1.9 (0.63− 5.5)	.26
Hepatitis C virus seropositive	10.4 (6.3−17.2)	<**.001**	4.3 (2.6−7.0)	<**.001**	9.3 (4.6−18.9)	<**.001**
Receipt of psychotropic medication	2.0 (1.2−3.2)	**.005**	NR	NR	NR	NR
HIV seropositivity	NR	NR	...[b]	...	NR	NR
Phlebotomy performed in the morning	0.59 (0.38−0.94)	**.03**	NR	NR	0.64 (0.41−0.998)	**.049**
Any history of androgen use	1.2 (0.41−3.3)	.76	1.9 (0.70−5.4)	.19	1.03 (0.38−2.8)	.95

NOTE. Separate models were run for low free androgen index and for each of the 2 low testosterone levels categories. Boldface *P* values are statistically significant. NR, variable not retained in the final model; OR_{adj}, adjusted OR.

[a] Reference was white race.

[b] There was a significant interaction between HIV infection status and report of having had sex with men. Only among men who reported having had sex with men within the past 5 years was there a significant association between low total testosterone level (<300 ng/dL) and HIV seropositivity (OR_{adj}, 5.1; 95% CI, 1.2−22.4).

[c] Reference value, >19 to ≤25.

Table 4

Associations of symptoms and measured bone loss with free androgen index (FAI) and total testosterone (TT) level in 502 men who were currently not taking androgens.

Characteristic	FAI				TT level					
	Mean value		Value of <14.8		Mean level		Level <300 ng/dL		Level <200 ng/dL	
	Mean ± SD	*P*	Proportion (%) of subjects[a]	*P*	Mean ng/dL ± SD	*P*	Proportion (%) of subjects[a]	*P*	Proportion (%) of subjects[a]	*P*
Decreased interest in sex										
No	17.6 ± 16.1		181/324 (55.9)		326 ± 215		163/324 (50.3)		92/324 (28.4)	
Yes	14.8 ± 15.5	**.02**	103/154 (66.9)	**.03**	289 ± 283	**.002**	94/154 (61.0)	**.04**	60/154 (39.0)	**.03**
Erectile dysfunction										
No	16.3 ± 15.7		198/328 (60.4)		307 ± 207		179/328 (54.6)		100/328 (30.5)	
Yes	17.0 ± 16.5	.92	91/153 (59.5)	.93	322 ± 295	.82	81/153 (52.9)	.81	55/153 (35.9)	.28
Felt “depressed”										
No	15.7 ± 14.2		165/275 (60.0)		324 ± 252		134/275 (52.4)		82/275 (29.8)	
Yes	17.2 ± 17.6	.93	132/217 (60.8)	.93	295 ± 222	.08	124/217 (57.1)	.33	77/217 (35.5)	.22
Depressive symptoms[b]										
No	17.3 ± 14.9		141/259 (54.4)		334 ± 233		130/259 (50.2)		70/259 (27.0)	
Yes	15.5 ± 16.6	**.01**	162/243 (66.7)	**.007**	288 ± 242	**.002**	143/243 (58.8)	.06	92/243 (37.9)	**.01**
Loss of concentration/ memory										
No	16.6 ± 14.5		168/291 (57.5)		329 ± 232		149/291 (51.2)		85/291 (29.2)	
Yes	16.1 ± 17.7	.07	130/200 (65.0)	.13	283 ± 243	**.005**	117/200 (58.5)	.13	75/200 (37.5)	.07
Difficulty sleeping										
No	16.5 ± 14.1		130/222 (58.6)		331 ± 211		109/222 (49.1)		57/222 (25.7)	
Yes	16.2 ± 16.8	.11	172/278 (61.9)	.51	295 ± 255	**.002**	163/278 (58.6)	**.04**	104/278 (37.4)	**.007**
Subjective overall health										
Excellent	16.8 ± 9.1		9/22 (40.9)		348 ± 137		9/22 (40.9)		3/22 (13.6)	
Good	18.3 ± 16.7		116/204 (56.9)		349 ± 280		98/204 (48.0)		49/204 (24.0)	
Fair	15.3 ± 15.9		137/214 (64.0)		288 ± 211		126/214 (58.9)		81/214 (37.9)	
Poor	13.4 ± 13.2	**.003**	35/52 (67.3)	.08	246 ± 184	<**.001**	36/52 (69.2)	**.01**	26/52 (50.0)	<**.001**
Current sildenafil use										
No	16.3 ± 15.8		261/429 (60.8)		311 ± 249		236/429 (55.0)		147/429 (34.3)	
Yes	17.8 ± 15.7	.58	38/68 (55.9)	.52	319 ± 165	.18	33/68 (48.5)	.39	14/68 (20.6)	**.04**
Osteopenia										
No	19.8 ± 17.4		97/186 (52.2)		334 ± 181		84/186 (45.2)		45/186 (24.2)	
Yes	14.5 ± 13.9	**.001**	123/195 (63.1)	**.04**	294 ± 232	**.003**	115/195 (59.0)	**.009**	68/195 (34.9)	**.03**
Osteoporosis										
No	17.1 ± 15.1		190/332 (57.2)		313 ± 187		172/332 (51.8)		94/332 (28.3)	
Yes	17.0 ± 20.5	.24	30/49 (61.2)	.36	315 ± 325	.24	27/49 (55.1)	.78	19/49 (38.8)	.18

NOTE. Data are no. of men with FAI or TT level/no. of men with characteristic (%), unless otherwise indicated. Denominators occasionally may add up to less than 502 because of refusal to provide information or because values were missing or indeterminate. Boldface *P* values are statistically significant.

[a] No. of men with FAI or TT level/no. of men with characteristic (%).

[b] Center for Epidemiologic Studies Depression Scale of ≥ 16.