Prevalence, Awareness, Treatment, and Control Rate of Hypertension in HIV-Infected Patients: The HIV-HY Study

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BACKGROUND
We aimed to assess the prevalence of hypertension in an unselected human immunodeficiency virus (HIV)–infected population and to identify factors associated with hypertension prevalence, treatment, and control.

METHODS
We used a multicenter, cross-sectional, nationwide study that sampled 1,182 unselected, consecutive, HIV-infected patients. Office blood pressure was accurately measured with standard procedures.

RESULTS
Patients were 71% men and 92% white, with a median age of 47 years (range = 18–78); 6% were antiretroviral treatment naive. The overall prevalence of hypertension was 29.3%; high-normal pressure accounted for an additional 12.3%. Among hypertensive subjects, 64.9% were aware of their hypertensive condition, 52.9% were treated, and 33.0% were controlled (blood pressure < 140/90 mm Hg). Blood pressure–lowering medications were used in monotherapy in 54.3% of the subjects. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers were the most frequently used drugs (76.1%; monotherapy = 39.1%, combination treatment = 37.0%). In multivariable regression models, hypertension was independently predicted by traditional risk factors, including age ≥50 years, male sex, family history of cardiovascular disease, body mass index ≥25 kg/m², previous cardiovascular events, diabetes, central obesity, and metabolic syndrome, as well as by duration of HIV infection, duration of antiretroviral therapy, and nadir CD4+ T-cell count <200/μl. The choice of protease inhibitors vs. nonnucleoside reverse transcriptase inhibitors as a third antiretroviral drug was irrelevant.

CONCLUSIONS
Hypertension affects nearly 30% of HIV adult outpatients in Italy. More than one-third of the hypertensive subjects are unaware of their condition, and more than two-thirds are uncontrolled. A higher level of attention to the diagnosis and treatment of hypertension is mandatory in this setting.

Keywords: antiretroviral therapy; arteriosclerosis; blood pressure; cardiovascular disease; Framingham risk score; human immunodeficiency virus (HIV); hypertension.

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Atherosclerotic cardiovascular disease (CVD), a leading cause of morbidity and mortality in the general population, is an increasing concern for human immunodeficiency virus (HIV)–infected patients. HIV-infected individuals are exposed to accelerated vascular aging, 1 and this issue has become even more relevant since antiretroviral therapy has impressively extended the life span of HIV-infected individuals. 2,3 Hypertension is a treatable major established risk factor for CVD and a common condition in HIV infection, with a prevalence ranging 13%–36%. 4,7 New-onset hypertension occurred with an incidence of 29.8 per 1,000 person-years in a recent report from Norway. 8 The suggestion that antiretroviral therapy and/or HIV infection may be associated with higher blood pressure (BP) has been repeatedly raised, 9–11 although conclusive evidence is yet missing. 12 More important, recent data suggest that both elevated and borderline high BP are associated with a substantially greater relative risk of acute myocardial infarction in HIV-positive compared with HIV-negative subjects. 12 Thus, identifying and appropriately managing
hypertension is a clinically relevant issue in HIV-infected patients.

In this study, we aimed to assess the prevalence of hypertension in an unselected sample of HIV-infected patients enrolled at several Italian sites and to identify its correlates. For the first time, to our knowledge, in this specific setting, we also investigated rates of hypertension awareness, drug treatment, and control.

**METHODS**

**Characteristics of the sample and study design**

The study was conducted from May 2010 through May 2011 by the Coordinamento Italiano per lo Studio di Allergia e Infezione da HIV (CISAI, Italian Coordination Group for the Study of Allergies and HIV Infection). Over this period, 1,272 adult HIV patients attending scheduled or unscheduled outpatient visits at hospital sites involved in the CISAI group were eligible. We excluded from the study pregnant women (n = 7) and patients with current or recent infectious diseases (n = 83). The remaining 1,182 patients underwent the following standardized procedures and were included in the study.

As reported in Table 1, the database was complete for nearly 95% of the study cohort. Sex, age, body weight, height, targeted anthropometric measures, smoking habits, BP, waist circumference, history of diabetes, lipodystrophy, metabolic syndrome, chronic hepatitis, and HIV stage according to the Centers for Disease Control classification were all recorded using a standard data collection form. Laboratory tests included absolute CD4+ T-lymphocyte count and fasting total and high-density lipoprotein cholesterol, triglycerides, and blood glucose. Duration of HIV infection was

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal BP (n = 689)</th>
<th>High-normal BP (n = 145)</th>
<th>Hypertension (n = 348)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>44.9 ± 9</td>
<td>47.6 ± 9</td>
<td>50.8 ± 9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Men, %</td>
<td>66.5</td>
<td>73.8</td>
<td>79.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index, kg/m² (n = 1,176)</td>
<td>23.4 ± 4</td>
<td>24.8 ± 4</td>
<td>25.8 ± 4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current cigarette smoking, % (n = 1,181)</td>
<td>50.7</td>
<td>44.8</td>
<td>41.4</td>
<td>0.007</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>114.6 ± 8.4</td>
<td>130.5 ± 5.6</td>
<td>137.4 ± 14.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>73.6 ± 6.4</td>
<td>81.7 ± 4.4</td>
<td>87.9 ± 9.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>41.0 ± 7.4</td>
<td>48.9 ± 8.0</td>
<td>49.5 ± 11.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate, bpm (n = 1,122)</td>
<td>73.1 ± 8.8</td>
<td>75.1 ± 9.2</td>
<td>75.6 ± 10.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl (n = 1,179)</td>
<td>195 ± 44</td>
<td>203 ± 51</td>
<td>199 ± 41</td>
<td>0.07</td>
</tr>
<tr>
<td>Triglycerides, mg/dl (n = 1,177)</td>
<td>122 (85–179)</td>
<td>152 (100–208)</td>
<td>152(108–212)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glucose, mg/dl (n = 1,173)</td>
<td>87 (79–95)</td>
<td>90 (83–99)</td>
<td>93 (83–104)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glomerular filtration rate, ml/min/1.73 m² (n = 1,171)</td>
<td>98 ± 23</td>
<td>96 ± 24</td>
<td>92 ± 27</td>
<td>0.002</td>
</tr>
<tr>
<td>Metabolic syndrome, % (n = 1,101)</td>
<td>74 (11.5%)</td>
<td>74 (53.6%)</td>
<td>199 (61.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time since HIV diagnosis, y</td>
<td>11.0 (5.0–18.0)</td>
<td>10.0 (5.0–16.0)</td>
<td>12.0(7.0–19.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Current antiretroviral treatment, %</td>
<td>92.5</td>
<td>93.8</td>
<td>96.5</td>
<td>0.01</td>
</tr>
<tr>
<td>CDC stage C, %</td>
<td>27.0</td>
<td>31.0</td>
<td>30.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Detectable HIV RNA, %</td>
<td>21.6</td>
<td>18.8</td>
<td>16.2</td>
<td>0.04</td>
</tr>
<tr>
<td>CD4+ cell count/ml (n = 1,171)</td>
<td>570 (403–755)</td>
<td>577 (410–799)</td>
<td>560(423–780)</td>
<td>0.80</td>
</tr>
<tr>
<td>Nadir CD4+ cell count/ml (n = 1,171)</td>
<td>208 (74–313)</td>
<td>229 (117–323)</td>
<td>174 (77–282)</td>
<td>0.05</td>
</tr>
<tr>
<td>Lipodystrophy, %</td>
<td>33.1</td>
<td>31.9</td>
<td>43.2</td>
<td>0.004</td>
</tr>
<tr>
<td>Chronic hepatitis, %</td>
<td>29.6</td>
<td>19.3</td>
<td>30.8</td>
<td>0.79</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>4.1</td>
<td>8.3</td>
<td>15.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10-year Framingham Risk, % (n = 1,132)</td>
<td>5.3 (2.8–9.4)</td>
<td>9.4 (4.7–18.4)</td>
<td>15.6(9.4–25.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous cardiovascular events, %</td>
<td>2.2</td>
<td>2.1</td>
<td>9.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, median (interquartile range), or %. Mantel–Haenszel χ² test, Wilcoxon test, and analysis of variance assessed the associations between groups (normal, high-normal, high BP) and categorical variables, nonnormally distributed continuous variables, and normally distributed continuous variables, respectively.

Abbreviations: BP, blood pressure; CDC, Centers for Disease Control and Prevention.
estimated as the interval between the first serological positive test for HIV and enrollment. Lipodystrophy was defined by the physician, as described previously. Metabolic syndrome was diagnosed according to Alberti et al. The diagnosis of hypertension and diabetes was based on standard international criteria.

Patients receiving antidiabetic or BP-lowering medications were classified as having diabetes and hypertension, respectively. Office BP was measured by a physician in the outpatient clinic with a mercury sphygmomanometer, with the study subject seated for ≥10 minutes before measurement. Measurement procedures were standardized among enrolling centers before starting enrollment. The average of 3 consecutive measurements was repeated on at least 2 different visit days 3–4 months apart. Patients were classified as having normal BP (≤129/84 mm Hg), high-normal BP (130–139/85–89 mm Hg), and hypertension (≥140/90 mm Hg).

Antihypertensive drug classes included angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, calcium-channel blockers, diuretics, β-blockers, and other antihypertensive agents. Treatment rates were calculated as the number of hypertensive patients receiving antihypertensive medication(s) divided by the number of all hypertensive individuals. Rates of hypertension control were calculated as the number of treated hypertensive individuals with BP <140/90 mm Hg divided by the number of all hypertensive individuals, whether or not on treatment. Hypertension control on treatment was defined as the ratio of treated hypertensive individuals with BP <140/90 mm Hg divided by the number of hypertensive individuals treated.

Pulse pressure was calculated as the difference of systolic BP (SBP) minus diastolic BP (DBP). Mean arterial pressure was calculated as (2 × DBP + SBP)/3. The risk of major cardiovascular events over the next 10 years and the estimated vascular age were assessed in all patients and control subjects according the Framingham Risk Score.

Informed consent was not required by the ethics committee because confidentiality was guaranteed and no interventions were performed beyond ordinary good and standard clinical practices (repeated standardized BP measurements).

**Statistical analysis**

Data analysis was conducted with SAS for Windows version 9.1 (SAS Institute Inc, Cary, NC). In the crude analysis, we used the Mantel–Haenszel χ² test to assess the association between groups (normal, high-normal BP, hypertensive patients) and categorical variables. Means were compared using the analysis of variance. Odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were used to indicate the association between hypertension and patients’ characteristics. To evaluate the clinical variables potentially associated with hypertension as compared with normal/high-normal BP, we included age, sex, family history of CVD, previous cardiovascular events, body mass index, and diabetes in the regression equations as potential confounders in the multivariable analysis. The authors had full access to the data and take responsibility for their integrity. All authors have read and agreed to the manuscript as written.

**RESULTS**

**Hypertension prevalence and awareness**

A total of 1,182 eligible HIV-infected patients (mean age = 47 years; range = 18–78 years; 71% men; 92% white; 6% antiretroviral treatment naive) were included and evaluated. The overall prevalence of hypertension was 29.3%; 12.3% of the patients had high-normal BP, and 58.3% had normal BP. Among hypertensive individuals, 64.9% were aware of their hypertensive status (19.1% of the whole population), and 55.1% (10.3% of the whole population) were newly diagnosed during the investigation (Figure 1).

**Hypertension characteristics and control rate**

Average SBP/DBP was 119.9 ± 15.1/76.6 ± 9.8 mm Hg in women and 124.6 ± 14.3/79.6 ± 9.7 mm Hg in men. Figure 2a shows SBP and pulse pressure as increasing progressively with age, whereas DBP reaches a plateau in the sixth decade and decreases thereafter. Because the inclusion of treated individuals may lead to underestimation of BP, we also performed the above analysis after adding 10/5 mm Hg to the SBP/DBP of the individuals on BP-lowering medications and after excluding treated hypertensive subjects. In both cases, the trend of BP components across the different age groups was identical to the one reported above (data not shown). As shown in Figure 2b, a robust linear relation was found between age group and hypertension prevalence (χ² for trend = 44.4; P < 0.0001, after adjustment for sex, family history of CVD, previous major cardiovascular events, and diabetes). Selected characteristics of the study population according to hypertension status are reported in Table 1. As expected, hypertensive and normotensive subjects differed in several characteristics; notably, several parameters among individuals with high-normal BP were somewhat intermediate between the normotensive and hypertensive...
Table 2. Variables associated with hypertension

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude</th>
<th>Adjusted*</th>
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<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td>Age ≥50 years</td>
<td>2.39 (1.85–3.09)</td>
<td>1.94 (1.46–2.56)</td>
</tr>
<tr>
<td>Men vs. women</td>
<td>1.85 (1.37–2.49)</td>
<td>1.63 (1.18–2.26)</td>
</tr>
<tr>
<td>Body mass index ≥25 kg/m²</td>
<td>2.67 (2.06–3.45)</td>
<td>2.52 (1.91–3.33)</td>
</tr>
<tr>
<td>Family history of CV disease</td>
<td>1.74 (1.33–2.28)</td>
<td>1.58 (1.18–2.12)</td>
</tr>
<tr>
<td>Previous CV events</td>
<td>4.59 (2.54–8.30)</td>
<td>3.14 (1.65–5.99)</td>
</tr>
<tr>
<td>Central obesity</td>
<td>1.56 (1.14–2.10)</td>
<td>1.42 (1.03–1.97)</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>6.90 (5.18–9.19)</td>
<td>5.67 (4.16–7.73)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.65 (2.37–5.61)</td>
<td>2.66 (1.65–4.27)</td>
</tr>
<tr>
<td>Time since HIV diagnosis, years (by quartile)</td>
<td>1.17 (1.04–1.31)</td>
<td>1.22 (1.08–1.36)</td>
</tr>
<tr>
<td>Anti-retroviral treatment duration (by quartile)</td>
<td>1.22 (1.10–1.36)</td>
<td>1.22 (1.08–1.36)</td>
</tr>
<tr>
<td>Nadir CD4+ cell count/μL (reference: CD4+ ≥350)</td>
<td>1.65 (1.41–2.37)</td>
<td>1.60 (1.05–2.41)</td>
</tr>
<tr>
<td>200–349</td>
<td>1.26 (0.85–1.87)</td>
<td>1.31 (0.86–2.00)</td>
</tr>
<tr>
<td>Current PI use (reference: no current PI use)</td>
<td>0.93 (0.73–1.20)</td>
<td>0.91 (0.69–1.18)</td>
</tr>
<tr>
<td>Past PI use (reference: no past PI use)</td>
<td>0.73 (0.41–1.29)</td>
<td>0.67 (0.36–1.23)</td>
</tr>
<tr>
<td>Current NNRTI use (reference: no current NNRTI use)</td>
<td>1.32 (1.02–1.70)</td>
<td>1.25 (0.95–1.64)</td>
</tr>
<tr>
<td>Past NNRTI use (reference: no past NNRTI use)</td>
<td>0.57 (0.25–1.31)</td>
<td>0.74 (0.31–1.75)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CV, cardiovascular; HIV, human immunodeficiency virus; NNRTI, nonnucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor.

*For age, sex, body mass index, family history of CV disease, previous CV events, and diabetes.

Hypertension and HIV-related factors

In multivariable analyses, to compare cases of hypertension and control subjects, patients with normal and high-normal BP were combined in the final models. Age, sex, family history of CVD, previous cardiovascular events, diabetes, and body mass index were used as adjustment terms in the regression equation, and other factors were included one at a time. In multivariable regression models (Table 2), hypertension was independently predicted by age ≥50 years, male sex, family history of CVD, previous cardiovascular events, and diabetes. After adjusting for the above variables, overweight or obesity (body mass index ≥25 kg/m²), central obesity (after excluding body mass index from the model), metabolic syndrome, duration of HIV infection, and duration of antiretroviral treatment were all independently related to the presence of hypertension. A nadir CD4+ T-cell count <200/μL was significantly associated with hypertension (vs. nadir CD4+ ≥350 cells/μL). Current stable treatment with protease inhibitors or nonnucleoside reverse transcriptase inhibitors was not related to hypertension.

BP-lowering drugs

BP-lowering medications were used in monotherapy in 54.3% of the subjects. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers were the most frequently used drugs (76.1%), whether used in monotherapy (39.1%) or in combination treatment (37.0%). Calcium-channel blockers

Figure 2. Blood pressure and age. (a) Blood pressure components by age class in 1,182 human immunodeficiency virus (HIV) patients. DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure. (b) Hypertension prevalence by age group. x² for linear trend = 44.4; P < 0.0001, after adjustment for sex, family history of cardiovascular disease, previous cardiovascular events, and diabetes. Abbreviations: F, female; M, male.
were used in 16.8%, diuretics in 28.3%, β-blockers in 28.8%, and other BP-lowering agents in 7.1% (Figure 3).

DISCUSSION

The HIV and Hypertension (HIV-HY) study analyzed a large, unselected sample of Italian HIV-infected patients, mostly on combined antiretroviral treatment, observed in routine outpatient clinical care to assess the prevalence and characteristics of hypertensive patients in this population. We found that 29.3% of the subjects were hypertensive and an additional 12.3% had high-normal BP. Among hypertensive subjects, about 35% had not been previously diagnosed, suggesting that BP measurement should receive additional attention in HIV clinical settings. Uncontrolled BP has a well-known major impact on the risk for cardiovascular morbidity and mortality, carrying a heavy socioeconomic burden. The prevalence of hypertension in the HIV-HY study (29.3%) was comparable with that of other studies that involved HIV-infected patients of similar age (13%–36%).

Although this study was not designed to compare the prevalence of hypertension in HIV-infected and -uninfected persons, age-specific prevalence of hypertension as reported in an Italian general population was not dissimilar from that reported in this study. Other Italian population studies with similar age and sex distribution also showed a prevalence of hypertension ranging 29%–36%.

Our study analyzed in addition simple hemodynamic characteristics of BP in HIV patients. BP measurement provides a systolic and a diastolic value, representing the extremes of pressure fluctuation during the cardiac cycle. Two main components generate such values: mean arterial pressure, a steady component reflecting the resistance of the microvascular network and overall circulatory pressure load, and pulse pressure, reflecting large-artery stiffness and wave reflections. Aging of arteries is gauged by changes in both systolic and pulse arterial pressure, specifically by the increase of pulse pressure. This results in a sharp increase in pulse pressure with aging in both sexes, particularly in patients aged ≥50 years. The behavior of different BP components in our study was very much similar to that observed previously in the general population, with a progressive rise in SBP with increasing age. DBP, conversely, reached a plateau at approximately 60 years and declined thereafter. Chronic HIV infection may impair and negatively influence the elasticity of the arterial tree, and the age-related increase in pulse pressure may be considered a simple, although somehow indirect, measure of arterial stiffness. These aspects, however, deserve additional and specific investigations in the HIV population.

Among hypertensive patients, relatively low rates of awareness (64.9%), treatment (52.9%), and control (33.0%) were observed. Only approximately one-third of the hypertensive patients achieved the recommended BP values, with the others lagging in the abnormal range. Our data are in line with the results of other studies in the hypertensive general population, showing high proportions of patients with inadequate BP control. In particular, we report a rate of hypertension awareness of 64.9%, which is comparable with the values of 56%–70% obtained in three Italian population studies. The proportion of hypertensive patients with controlled BP (33.0% in our study) should be interpreted against the background of the corresponding values reported in population-based studies, which range 22%–30%.

Moreover, because our population regularly accessed medical settings where BP measurement might be routine, one could expect even lower rates of hypertension awareness and treatment in other clinical settings. The rate of hypertension control in HIV patients was even lower (22%) in a recent Norwegian study carried out by Manner et al. The potential consequences of a low rate of hypertension control may be even more relevant in HIV patients than in the general population. Indeed, HIV-infected subjects represent a population at particularly high cardiovascular risk due to the high prevalence of comorbidities and of major cardiovascular risk factors and the specific additional role of HIV-related factors such as antiretroviral treatment and low CD4+ cell count.

Interestingly, in our study a more advanced HIV-related disease was more frequent among hypertensive subjects (Table 1), and a low nadir CD4+ cell count and the duration of antiretroviral treatment were both independent correlates of hypertension. These data are in line with previous studies showing that a low CD4+ cell count is associated with both prevalent and incident hypertension, as well as with endothelial dysfunction and arterial stiffness.

On the other hand, in an unselected Italian population, we found no differences in the proportion of hypertensive patients among recipients of antiretroviral drug regimens based on either protease inhibitors or nonnucleoside reverse transcriptase inhibitors, in line with the findings from the D:A:D study.

The management of HIV infection is actually complicated by polypharmacy, which may increase the rate of potential drug-drug interactions with antiretroviral therapy and facilitate drug toxicity and low treatment compliance. As regards antihypertensive treatment, we found that in our population angiotensin-converting enzyme inhibitors and angiotensin receptor blockers were the most commonly used drugs, both in monotherapy and in combination treatment, in agreement with recommendations in the European AIDS Clinical Society guidelines, which
warn about the potentially significant interactions of protease inhibitors and nonnucleoside reverse transcriptase inhibitors with calcium-channel blockers and β-blockers.43

The main strengths of our study were the inclusion of an unselected multicenter sample of Italian HIV-infected patients assisted at current sites of ordinary care, which likely represents the general assisted population at the same sites, and the universal adoption of a validated and standardized procedure for BP measurements for all observed patients. The most relevant limitations in this work include the cross-sectional observational design of the study and the absence of a parallel control group of uninfected individuals.

In conclusion, this multicenter, nationwide, cross-sectional study gives an account of the impact of hypertension and associated features in an unselected sample of the HIV-infected population. Clinical management of hypertension was inadequate in many HIV patients, as more than one-third of the hypertensive patients were undiagnosed and approximately two-thirds were uncontrolled. This finding may have important implications because uncontrolled BP levels may increase the risk and impact of CVD in this population. A higher level of attention to hypertension and its treatment is warranted in the setting of HIV infection.

AUTHORS CONTRIBUTIONS

Study concept and design: GVDS. Statistical expertise: ER. Drafting of the manuscript: GVDS, ER, GS. Analysis, interpretation of data and critical revision of the manuscript for important intellectual content: all the authors.

APPENDIX

The HIV-HY group comprises the following members.

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Recruitment sites and investigators: Giuseppe Vittorio De Socio, Enisia Cecchini, Alessandra Mercuri, Andrea Tosti (Perugia); Paolo Maggi, Chiara Bellacosa, Francesca Lenoci (Bari); Giancarlo Orofino, Marta Guastavigna (Torino); Giustino Parruti, Elena Mazzotta (Pescara); Laura Carenzi, Giuliano Rizzardini (Milano); Benedetto Maurizio Celesia, Maria Gussio, Giuseppe Nunnari (Catania); Maria Stella Mura, Giordano Maddeddu, Paola Bagella (Sassari); Giovanni Penco, Giancarlo Antonucci (Genova); Tiziana Quirino, Barbara Mennaghi (Castelvetrano); Marco Franzetti, Stefano Rusconi (Milano); Canio Martinelli (Firenze); Antonio Di Biagio, Anna Calzi (Genova); Leonardo Calza (Bologna); Ilaria Caramma, Chiara Molteni, Paolo Bonfanti (Lecco).

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; 120:1640–1645.


