Ambulatory Blood Pressure Monitoring in HIV-Infected Patients: Usefulness for Cardiovascular Risk Assessment

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Abstract

Background: There is a lack of consensus regarding the risk of hypertension in HIV-infected patients compared to the general population. Ambulatory blood pressure monitoring (ABPM) is the most accurate method for the hypertension diagnosis. Nevertheless, it is rarely used in HIV clinical care. **Materials and Methods:** All HIV-infected patients who underwent 24 hours ABPM were included. The agreement between office blood pressure (BP) readings and ABPM was analyzed. The rate of patients with masked hypertension (MH), isolated clinical hypertension, and nocturnal hypertension was obtained. Furthermore, it was analyzed if the differences between both methods may affect the cardiovascular risk (CVR) assessment. **Results:** A total of 116 patients were included. The κ coefficient between office BP and ABPM was 0.248. Over a quarter of the cohort was diagnosed with MH—25.8% (CI 95% 17.7%-34.0%), and 12% (CI 95%: 6.1%-16.1%) was diagnosed with ICH. Moreover, 19% of patients had hypertension exclusively during the night. The patients classified as low risk according to the CVR scores had a different diagnosis with ABPM than with office BP ($P < .001$). **Conclusions:** The agreement between office BP and ABPM was low in HIV-infected patients. Ambulatory BP monitoring is useful in HIV-infected patients as a hypertension diagnosis method, especially among patients classified as low risk.

Keywords

hypertension, HIV, cardiovascular risk, ambulatory blood pressure monitoring

Introduction

Considered as one of the most prevalent causes of morbidity and mortality in patients living with HIV,[1] cardiovascular events are more frequently observed in patients infected with HIV than in uninfected individuals.[2,3] Immune deregulation,[4] antiretroviral treatment exposure,[5] and classic cardiovascular disease (CVD) are considered risk factors for cardiovascular events.[6] Regarding the classical risk factors, an altered lipid metabolism associated or not with antiretroviral drugs and smoking habit are frequently observed in HIV-infected patients.[7-9] However, there is a lack of consensus regarding the real prevalence of hypertension in these patients compared to that of the general population.[10-13] Usually, the screening for hypertension is performed by measuring the arterial pressure in the office; however, this technique may not be sufficiently accurate. Measuring blood pressure (BP) in the office as a reliable hypertension diagnostic method may be compromised

by dependent and independent causes of the appropriate BP protocol application.[14] Consequently, the most recent recommendations suggest that ambulatory blood pressure monitoring (ABPM) is the standard hypertension diagnostic method among patients who present with varying BP measurements in addition to other diagnostic indications.[15] Ambulatory blood pressure monitoring has greater accuracy in the diagnosis of

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What Do We Already Know about This Topic?

Ambulatory blood pressure monitoring is the gold standard as a blood pressure (BP) measurement method, but research studies in HIV-infected patients are scarce.

How Does Your Research Contribute to the Field?

Findings of this study support the diagnosis of hypertension should not be based on a set of BP readings at office, due to the high rates of masked hypertension, isolated clinical hypertension, and nocturnal hypertension in HIV-infected patients.

What Are Your Research's Implications toward Theory, Practice, or Policy?

Twenty-four-hour ambulatory BP monitoring (ABPM) is the most accurate method for measuring blood pressure in HIV-infected patients, and it should be used on this population to assess cardiovascular risk.

hypertension than other diagnostic methods because it provides several measurements in real-life settings, avoiding health care influence. Therefore, ABPM has become the gold standard method for the diagnosis of hypertension because it has a better correlation with subclinical vascular lesion, cardiovascular events, and mortality than office BP measurement.[16-19] This study aimed to evaluate the agreement between ABPM and office BP measurement in the diagnosis of hypertension for HIV-infected patients in the routine clinical practice and to investigate the value of ABPM in the CVD risk assessment in these patients.

Methods

A retrospective cohort study was conducted. HIV-infected patients who were followed up in the outpatient clinics of a public university hospital, who were over 18 years old, and underwent 24-hour ABPM were recruited between 2008 and 2016. Patients under antihypertensive treatment and those with an ABPM less than 80% of the valid measurements or incomplete records were excluded. Ambulatory blood pressure monitoring was performed using Spacelabs or Microlife WatchBP 03 device, programmed to record BP measurements every 20 minutes during daytime and every 30 minutes during nighttime. Records were read using the Spacelabs Reports Administration System of ABP Version 1.03.16 and WatchBP 03 Analyzer. Placement and removal of the ABPM device and patients' training regarding ABPM device handling were conducted by a specialized nurse. Blood pressure measurement in the office was performed using the calibrated and validated

Omron M6 device in the dominant arm with the patient assuming a seating position according to the current international hypertension measurement protocol.[14]

The diagnosis of hypertension by office BP measurement was established when systolic pressure (SP) was ≥ 140 mm Hg and/or diastolic pressure (DP) was ≥ 90 mm Hg. The diagnosis of hypertension by ABPM was established according to either of the following criteria[20]: (1) Within a 24-hour period, the mean SP was ≥ 130 mm Hg and/or the mean DP was ≥ 80 mm Hg; and/or (2) during daytime, the mean SP was ≥ 135 mm Hg and/or the mean DP was ≥ 85 mm Hg; and/or (3) during nighttime, the mean SP was ≥ 120 mm Hg and/or the mean DP was ≥ 70 mm Hg.[15] High BP values both in ABPM and in office BP measurement were defined as *sustained hypertension* (SH). Normal BP values both in ABPM and in office BP measurement were defined as *normotension* (NT). High BP values in office BP measurement but normal BP values in ABPM were defined as *isolated clinical hypertension* (ICH). Normal BP values in office BP measurement but high BP values in ABPM were defined as *masked hypertension* (MH; Figure 1). *Nighttime hypertension* was diagnosed in patients who exclusively presented high BP values at the nighttime record.

Demographic and clinical data were recorded, including CVD risk assessment using the Framingham Risk Score and SCORE tables and the type of antiretroviral treatment and duration of exposure. For both cardiovascular assessment risk scales, the very high- and high-risk groups were considered as a single high-risk group.

Descriptive analysis was performed using measures of central tendency and distribution. Differences between patient groups (NT versus MH and ICH versus SH) were calculated using the χ^2 equation or Fisher exact test for qualitative variables. Moreover, T-student equation was used for quantitative variables with a normal distribution (using the Kolmogorov-Smirnov method) and nonparametric test for variables with non-normal distribution. As the objective was to describe the population and not establish causality, a univariate analysis was performed.

The agreement between both BP measurement techniques (ABPM and office BP measurement) was calculated using the Cohen κ index. McNemar test for paired data was used to estimate the usefulness of ABPM as a diagnostic test within the different CVD risk strata. P value lower than 5% was considered to be statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences version 23.0.0 International Business Machines Corporation program.

Ethical Statements

Ethical Approval and Informed Consent

The study was conducted according to the principles expressed in the Helsinki Declaration of 1983. This study was approved (Protocol number 3018*Act 05/17) by the Institutional Review Board (CEIm Hospital La Princesa), which did not consider necessary to ask for the written consent of patients. Nevertheless, patients who continued their follow-up at the Infectious Diseases
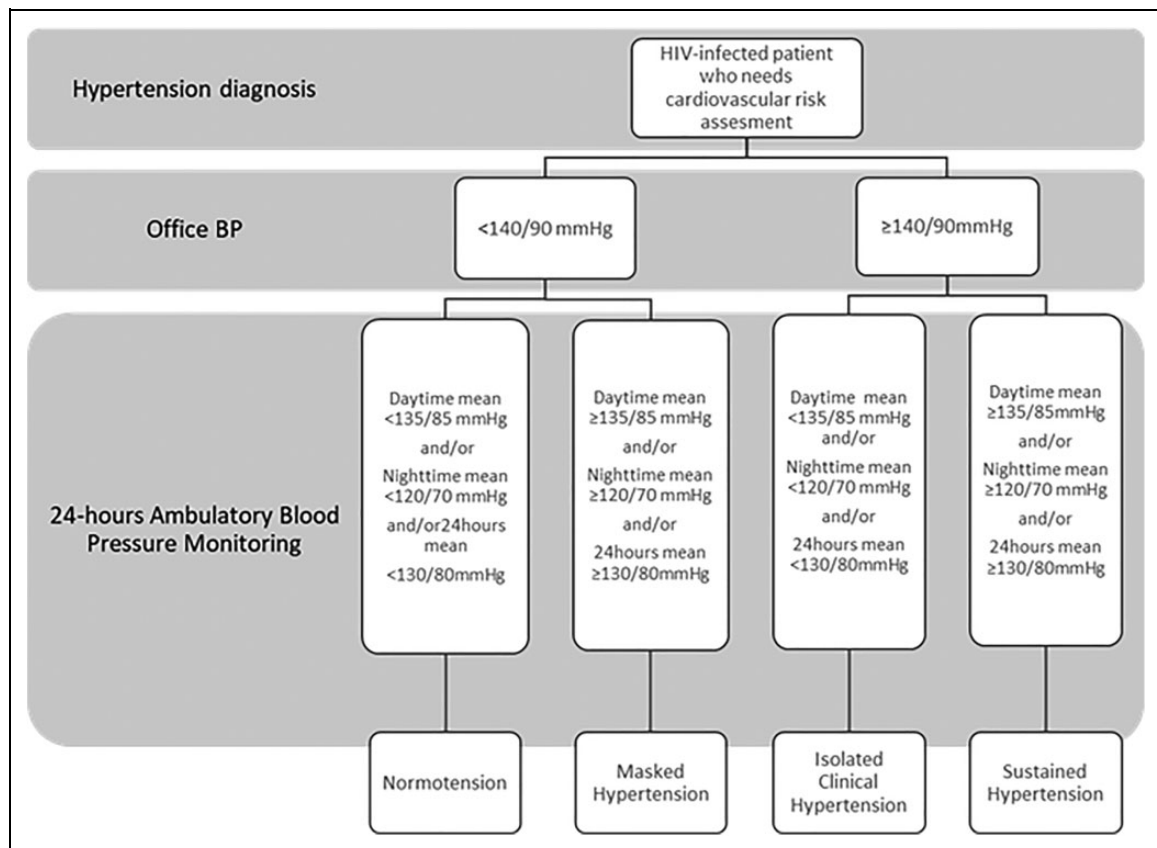
Figure 1. Blood pressure patterns based on office and out of office (24-hour ambulatory blood pressure monitoring).

Department were informed about the study, and verbal consent was obtained. The Instiutional Review Board (IRB) are governed by national regulations: those contained in Royal Decree 1090/2015 and in the Standards of Good Clinical Practice (CPMP / ICH / 135/95), in addition to Decree 39/94 of the Community of Madrid.

Results

All patients (172) registered on ABPM during the study were included. A total of 58 patients were excluded because of the following reasons: 36 patients were taking antihypertensive drugs, 17 patients had nonvalid ABPM record, and 5 patients had insufficient clinical data.

Patients were mostly males (85%), and the mean age was 49.5 years old (standard deviation [SD]: 8.6). Table 1 shows the demographic characteristics of the population.

According to the office BP measurement, 56 and 60 patients had and did not have hypertension, respectively. The mean SP and DP in the sample were 133 (SD, 16.7) and 84 (SD, 10.8) mm Hg, respectively. Among patients with hypertension, the mean SP and DP were 144.5 (SD, 13.2) and 92 (SD, 7.6) mm Hg, respectively. Among normotensive patients, the mean SP and DP were 122.4 (SD, 11.9) and 77.8 (SD, $\pm$8.7) mm Hg, respectively.

Seventy-two patients had high BP by ABPM, and 44 had normal records. The means of BP according to ABPM are shown in Table 2.

Regarding both measurements (office BP measurement and ABPM), 26.5% (95% CI, 18.1%-36.1%) had MH, 12.1% (95% CI, 6.0%-18.1%) had ICH, 36.2% (95% CI, 27.6%-45.7%) had SH, and 25.9% (95% CI, 17.2%-36.6%) had no hypertension. The ABPM measurement reclassified the hypertension status previously defined by BP office measurement. Among patients with high BP by BP office measurement, a quarter of patients had ICH, while among normotensives according to office BP measurement, half of the patients had MH (Table 3).

The baseline data and demographic characteristics comparing real BP status according to ABPM records in normotensive patients at office BP measurement (NT versus MH) and patients with hypertension at office BP measurement (SH versus ICH) are shown in Tables 1 and 2.

According to these data, the positive-predictive value of the office BP for the diagnosis of hypertension was 75% (95% CI, 62.3%-84.5%), the negative-predictive value was 50% (95% CI, 37.7%-62.3%), sensitivity was 58.3% (95% CI, 46.8%-69%), and specificity was 68.2% (95% CI, 53.4%-80%), with a positive likelihood ratio of 1.8 (95% CI, 1.1-2.9). The agreement between the 2 different techniques of BP measurement (κ index) was 0.248 (standard error, 0.09; 95% CI, 0.07-0.42).

Patients with hypertension according to ABPM were diagnosed due to a pathologic 24-hour record in 43% of cases, altered daytime record in 17% of cases, altered daytime and nighttime

Table 1. General Characteristics and Differences Between Groups Classified with ABPM.

| General characteristics | Total, N = 116 | | Normal blood pressure at office, n = 60 | | | | | High blood pressure at office, n = 56 | | | | |
| | | | NT | | MH | | | ICH | | SH | | |
			n = 30	(50%)	n = 30	(50%)	p-value	n = 14	(21%)	n = 42	(79%)	p-value
Age, years[a]	49.5	8.6	46.9	7.7	48.8	9.6	0.83	53.8	7.9	50.7	9.1	0.84
Men, %	18	16	24	80	27	90	0.47	10	71	37	88	0.20
Race												
Caucasian, n (%)	94	81	22	73	28	93	0.11	10	71	34	81	0.31
Hispanic, n (%)	10	9	3	10	1	3		3	21	3	7	
African Americans, n (%)	12	10	5	17	1	3		1	7	5	12	
CRF												
Diabetes mellitus, n (%)	17	15	4	13	3	10	0.50	6	43	4	9	0.11
Dyslipidemia, n (%)	50	43	10	33	17	57	0.06	8	57	15	36	0.14
Smokers, n (%)	47	40	14	47	11	37	0.30	8	57	14	33	0.10
Statin treatment, n (%)	35	30	7	23	13	43	0.17	7	50	8	19	0.03
Antidiabetic treatment, n (%)	11	9	3	10	2	7	0.08	4	29	2	5	0.03
Alcohol abuse, n (%)	8	7	4	13	2	7	0.34	1	7	1	2	0.44
Cocaine use, n (%)	2	2	0	0	0	0	-	1	7	1	2	0.40
Transmission risk group												
IDU, n (%)	30	26	11	37	7	23	0.40	4	29	8	19	0.26
MSM, n (%)	63	54	15	50	17	57		6	43	25	59	
HTS, n (%)	22	19	4	13	6	20		4	29	8	19	
Chronic hepatitis, n (%)	17	15	5	17	3	10	0.35	3	21	6	14	0.39
HCV coinfection, n (%)	5	4	2	7	1	3	0.50	1	7	1	2	0.44
Time since diagnosis, months	160	80	144	75	191	65	0.01	151	71	151	92	0.42
Indetectable, months[b]	99	104-374	90	56	115	102	0.17	98	48	121	228	0.46
Nadir CD4, cell/μL[b]	274	41-157	255	158	275	186	0.67	220	197	320	224	0.15
AIDS, n (%)	37	32	11	38	10	33	0.46	5	36	11	26	0.36
ART												
No ART, n (%)	9	8	1	3	2	7	0.50	1	7	5	12	0.53
Exp. to NRTI, n (%)	108	93	28	93	25	86	0.32	13	94	36	88	0.52
Exp. to NNRTI, n (%)	82	71	23	82	23	79	0.53	10	77	26	74	0.58
Exp. to PI, n (%)	73	63	19	68	21	72	0.41	12	92	21	60	0.03
Total time on ART, months	129	66	118	62	156	53	0.04	157	51	109	72	0.03
Time on NRTI, months	107	63	97	70	135	60	0.01	156	82	108	76	0.03
Time on NNRTI, months	68	54	68	66	90	41	0.20	63	46	70	57	0.81
Time on PI, months	92	60	81	62	114	70	0.42	99	57	82	63	0.69

Abbreviations: ABPM, ambulatory 1 blood pressure monitoring; ART, antiretroviral treatment; CRF, cardiovascular risk factors; Exp., Exposition; HCV, hepatitis C virus; HTS, heterosexual behavior; ICH, isolated clinical hypertension; IDU, injection drug user; MH, masked hypertension; NNRTI, non nucleosides reverse transcriptase inhibitors; NRTI, nucleot(s)ides reverse transcriptase inhibitors; NT, normotension; MSM, men who have sex with men; PI, protease inhibitors; SH, sustained hypertension.
[a]All data are expressed as Mean and SD.
[b]Expressed as Median and IQR.

BP mean but a normal 24-hour mean in 10% of cases, and exclusively altered nighttime record in 30% of cases. According to these data, 19% of the total samples had nocturnal hypertension.

The lack of agreement between ABPM and BP office measurement (white coat hypertension or ICH) was not consistent among patients classified by categories according to CVD risk scores. Patients classified as low risk according to Framingham Risk Score and SCORE showed a significant difference between office BP measurement and ABPM (*P* < .001; Figures 2 and 3).

Discussion

The evaluation of CVD risk has become increasingly important in the comprehensive care of HIV-infected patients. However, strategies for an accurate BP assessment have not been properly established, resulting in a negative impact on its clinical management.[21]

Several techniques are used to diagnose subclinical target organ damage, but most of them are arduous, expensive, and frequently invasive.[22-24] Some cardiovascular risk assessment tools, such as Framingham Risk Score and SCORE, and specific scales for the HIV-infected population[25-28] have also been used, but none of them has proven to be effective in predicting the onset of cardiovascular events.[29] These scores include classical CVD risk factors, family history of premature CVD, smoking, hypertension, diabetes, or dyslipidemia.[30-31] The diagnosis of some of these factors, such as diabetes or dyslipidemia, could be easier than the diagnosis of hypertension. The

Table 2. Baseline Situation at the Time of the Ambulatory Blood Pressure Monitoring (Current ART, Immune Status, and Blood Pressure at Office).[a]

| | | Normal blood pressure at office, n = 60 | | | | | High blood pressure at office, n = 56 | | | | |
| | | NT | | MH | | | ICH | | SH | | |
Baseline situation	Total, N = 116	n = 30	(50%)	n = 30	(50%)	p-value	n = 14	(21%)	n = 42	(79%)	p-value
ART											
NRTI+NNTRI, n (%)	60	52	19	66	17	59	1.0	5	38	19	51	1.0
NRTI+PI, n (%)	31	27	6	21	8	28	0.77	4	31	13	35	0.04
NRTI+IIN, n (%)	1	1	0	0	0	0	NA	0	0	1	3	NA
Immune status											
CD 4 cell/μL[b]	687	499-881	742	314	708	268	0.68	721	392	701	319	0.86
CD4/CD8 ratio[b]	0.65	0.48-0.93	0.84	0.47	0.73	0.43	0.51	0.73	0.3	0.67	0.38	0.54
Pressure at office											
SP, mm Hg	132	17	118	12	126	10	0.01	141	9	145	14	0.26
DP, mm Hg	84	11	74	9	82	7	0.01	87	8	93	7	0.03
High-normal, n (%)	26	22	6	20	20	67	0.01	0	0	0	0	NA
Grade 1 hypertension, n (%)	41	35	0	0	0	0	NA	12	86	29	69	0.01

Abbreviations: ART, antiretroviral treatment; DP, diastolic pressure; Exp., Exposition; ICH, isolated clinical hypertension; IQR, interquartile range; MH, masked hypertension; NA, Not applicable; NNRTI, non-nucleosides reverse transcriptase inhibitors; NRTI, nucleot(s)ides reverse transcriptase inhibitors; NT, normotension; PI, protease inhibitors; SH, sustained hypertension; SP, systolic pressure.
[a] All data are expressed as Mean and SD.
[b] Expressed as Median and IQR.

Table 3. Four-Fold Table that Represents Patients Classified at Office with High Blood Pressure and Normal Blood Pressure versus Patients Classified with High and Normal Blood Pressure with Ambulatory Blood Pressure Monitoring.

| | ABPM | | | | | |
| | Normal | | High | | Total | |
Blood pressure at office	n	%	n	%	n	%
Normal	30 (NT)	50	30 (MH)	50	60	52
High	14 (ICH)	25	42 (SH)	75	56	48
Total	44	41	72	59	116	100

Abbreviations: ABPM, ambulatory blood pressure monitoring; ICH, isolated clinical hypertension; MH, masked hypertension; NT, normotension, SH, sustained hypertension.
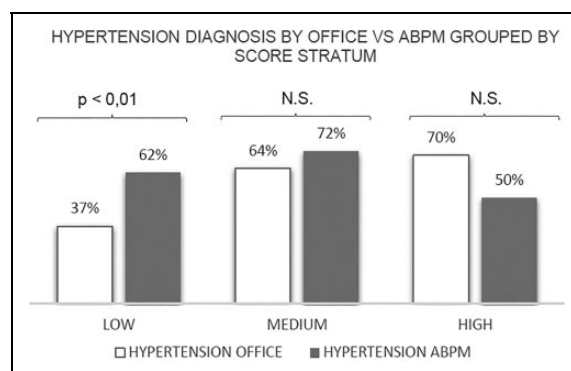
Figure 3. Hypertension diagnosis by office versus ABPM grouped by SCORE stratum. ABPM indicates ambulatory blood pressure monitoring; N.S., no statistically significant difference were found.
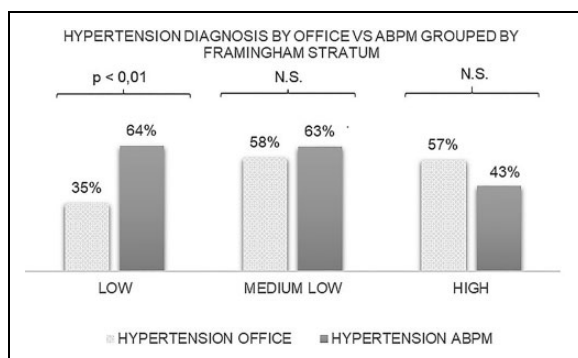
Figure 2. Hypertension diagnosis by office versus ABPM grouped by Framingham stratum. ABPM indicates ambulatory blood pressure monitoring; N.S., no statistically significant difference were found.

diagnosis of hypertension is difficult to establish because of the potential errors associated with the techniques of BP measurement on the clinic.

Despite the importance of CVD risk in HIV-infected population, knowledge about ABPM is scarce. Small series of patients with preexisting high BP had been previously published.[32,33] Other studies have described circadian pattern and have proven the higher prevalence of "non-dipper" pattern among these patients.[34] The meta-analysis published by Kent and colleagues compare 7 studies with ABPM use in HIV-infected patients;[35] nevertheless, data about the agreement rate between office BP measurement and ABPM had not been published yet.

The study presented here shows that ABPM is useful as a hypertension diagnostic method in HIV-infected patients,

particularly among those patients classified as low risk according to Framingham risk score or SCORE scales.

The data analysis shows a poor agreement between both diagnostic techniques evaluated, the office BP measurement and ABPM. Previous investigations in non-HIV-infected population showed a greater "κ index" (better agreement) compared to the cohort in this study.[17,36] In non-HIV-infected population, disagreement is mainly due to patients with ICH (diagnosis of hypertension by office BP measurement with a normal ABPM),[15,17,37,38] while the lack of concordance observed in this HIV-infected patient cohort is due to the high prevalence of MH. Some studies with HIV-infected patients conducted in South Africa also found a high proportion of MH, and other study conducted in United States shows a prevalence higher among African Americans than among whites.[39-41] Furthermore, high prevalence of MH had already been described in African Americans in large cohorts of non-HIV-infected population.[42] Additionally, the ICH proportion in patients previously diagnosed with hypertension is similar to that of our cohort, according to other authors.[32,43]

We found a statistical association between the exposure to nucleot(s)ides reverse transcriptase inhibitors and MH diagnosis. Other authors have described the association between altered daytime ABPM recordings and HIV duration.[34] The increased risk for hypertension in patients exposed to protease inhibitors has also been published.[44]

The present study evaluates the potential impact of ABPM on CVD risk assessment. According to our results, achieving a more accurate diagnosis of hypertension by ABPM could have an impact on patients with low risk on the Framingham Risk Score and SCORE scales.

This finding has significant clinical value since including hypertension assessed using ABPM in the algorithm would change the global CVD risk assessment, particularly in HIV-infected patients who could change from low to moderate risk. This could be one of the multiple reasons for the failure of cardiovascular risk estimation methods in HIV-infected patients.

A high proportion of patients with MH were diagnosed because they had nocturnal hypertension, which is exclusively diagnosed by ABPM. Nocturnal hypertension has been previously described in HIV-infected patients, especially among African Americans,[41] and it is considered that it has similar causal mechanisms with nondipper pattern. Nondipper pattern was found more frequently in HIV-infected than in non-HIV patients in previous case–control studies.[45,46] In general populations, non-dipper pattern has been associated with psychological and social factors, such as depression and social isolation, or sleeping disorders such as obstructive sleep apnea syndrome or insomnia. Interestingly, these factors are particularly common in HIV-infected population.[47]

Nocturnal hypertension is a separate entity to nondipper pattern, despite both having similar pathophysiological factors; moreover, nocturnal hypertension has direct impact on cardiovascular morbidity and mortality.[48,49] Nocturnal hypertension can be recognized by ABPM but neither by office BP measurement nor by home BP monitoring. In this study, a higher proportion of nighttime hypertension is observed more than that in the previously reported study in the general population, which could be a hidden cause of the increased CVD risk in HIV-infected patients.

This study has the following limitations. First, this study does not establish the real prevalence of MH or ICH because ABPM was not performed in a systematic way; nonetheless, the sample was not different from the total HIV-infected patients in our hospital. Second, the protocol included patients with 2 in-office readings at a single visit but was not repeated at 2 separate visits, which could affect the data. Third, this study is composed of a small sample size; hence, studies consisting of large sample sizes are required in the future.

Some of the patients who were asked to undergo the ABPM refused to do so, probably due to the fact that the technique was uncomfortable. Excluding patients undergoing antihypertensive treatment could be considered a limitation of the study; however, in our opinion, patients who were diagnosed and treated with hypertension are not suitable in this study because the hypertensive drug regimen might interfere with the ABPM records. Hence, these patients should be studied separately.

Conclusions

The agreement between office BP measurement and ABPM is very weak in HIV-infected patients. The discrepancy was associated with the high proportion of MH in our sample. According to these data, office BP measurement is not effective for the diagnosis of hypertension in HIV-infected patients. One of every 5 patients who underwent ABPM was diagnosed with isolated nocturnal hypertension. The routine use of ABPM would have a particular clinical relevance among HIV-infected patients with low risk in Framingham Risk Score or SCORE scales, in who an accurate diagnosis of hypertension would modify the initial estimate of CVD risk.

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References

1. Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-

2006: collaborative analysis of 13 HIV cohort studies. *Clin Infect Dis*. 2010;50(10):1387–1396. doi:10.1086/652283

2. Freiberg MS, Chang CCH, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med*. 2013;173(8):614–622. doi:10.1001/jamainternmed.2013.3728

3. Drozd DR, Kitahata MM, Althoff KN, et al. Increased risk of myocardial infarction in HIV-infected individuals in North America compared with the general population. *J Acquir Immune Defic Syndr*. 2017;75(5):568–576. doi:10.1097/QAI.0000000000001450

4. Stein JH, Hsue PY. Inflammation, immune activation, and CVD risk in individuals with HIV infection. *JAMA*. 2012;308(4):405–406. doi:10.1001/jama.2012.8488

5. Friis-Møller N, Sabin CA, Weber R, et al. Combination antiretroviral therapy and the risk of myocardial infarction. *N Engl J Med*. 2003;349(21):1993–2003. doi:10.1056/NEJMoa030218

6. Aberg JA.Cardiovascular complications in HIV management: past, present, and future. *J Acquir Immune Defic Syndr*. 2009;50(1):54–64. doi:10.1097/QAI.0b013e31818ceaa4

7. Masiá M, Pérez-Cachafeiro S, Leyes M, et al. Cardiovascular risk in human immunodeficiency virus-infected patients in Spain. CoRIS cohort, 2011 [in Spanish]. *Enferm Infecc Microbiol Clin*. 2012;30(9):517–527. doi:10.1016/j.eimc.2012.02.014

8. Lang S, Mary-Krause M, Cotte L, et al. Increased risk of myocardial infarction in HIV-infected patients in France, relative to the general population. *AIDS*. 2010;24(8):1228–1230. doi:10.1097/QAD.0b013e328339192f

9. Rasmussen LD, Helleberg M, May MT, et al. Myocardial infarction among Danish HIV-infected individuals: population-attributable fractions associated with smoking. *Clin Infect Dis*. 2015;60(9):1415–1423. doi:10.1093/cid/civ013

10. Gelpi M, Afzal S, Lundgren J, et al. Higher risk of abdominal obesity, elevated LDL cholesterol and hypertriglyceridemia, but not of hypertension, in people living with HIV: results from the Copenhagen Comorbidity in HIV Infection (COCOMO) Study. *Clin Infect Dis*. 2018;67(4):579–586. doi:10.1093/cid/ciy146

11. Antonello VS, Antonello ICF, Grossmann TK, Tovo CV, Pupo BBD, Winckler L de Q. Hypertension—an emerging cardiovascular risk factor in HIV infection. *J Am Soc Hypertens*. 2015;9(5):403–407. doi:10.1016/j.jash.2015.03.008

12. van Zoest RA, Wit FW, Kooij KW, et al. Higher prevalence of hypertension in HIV-1-infected patients on combination antiretroviral therapy is associated with changes in body composition and prior stavudine exposure. *Clin Infect Dis*. 2016;63(2):205–213. doi:10.1093/cid/ciw285

13. Peck RN, Shedafa R, Kalluvya S, et al. Hypertension, kidney disease, HIV and antiretroviral therapy among Tanzanian adults: a cross-sectional study. *BMC Med*. 2014;12:125. doi:10.1186/s12916-014-0125-2

14. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206–1252. doi:10.1161/01.HYP.0000107251.49515.c2

15. Parati G, Stergiou G, O'Brien E, et al. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *J Hypertens*. 2014;32(7):1359–1366. doi:10.1097/HJH.0000000000000221

16. Asayama K, Thijs L, Li Y, et al. Setting thresholds to varying blood pressure monitoring intervals differentially affects risk estimates associated with white-coat and masked hypertension in the population. *Hypertension*. 2014;64(5):935–942. doi:10.1161/HYPERTENSIONAHA.114.03614

17. Ohkubo T, Kikuya M, Metoki H, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama Study. *J Am Coll Cardiol*. 2005;46(3):508–515. doi:10.1016/j.jacc.2005.03.070

18. Tientcheu D, Ayers C, Das SR, et al. Target organ complications and cardiovascular events associated with masked hypertension and white-coat hypertension: analysis from the Dallas Heart Study. *J Am Coll Cardiol*. 2015;66(20):2159–2169. doi:10.1016/j.jacc.2015.09.007

19. Banegas JR, Ruilope LM, Williams B. Ambulatory blood pressure and mortality. *N Engl J Med*. 2018;379(13):1287–1288. doi:10.1056/NEJMc1809851

20. O'Brien E, Parati G, Stergiou G. Ambulatory blood pressure measurement: what is the international consensus? *Hypertension*. 2013;62(6):988–994. doi:10.1161/HYPERTENSIONAHA.113.02148

21. Sherer R, Solomon S, Schechter M, Nachega JB, Rockstroh J, Zuniga JM. HIV provider-patient communication regarding cardiovascular risk: results from the AIDS treatment for life international survey. *J Int Assoc Provid AIDS Care*. 2014;13(4):342–345.

22. Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. *JAMA*. 2012;308(4):379–386. doi:10.1001/jama.2012.6698

23. Metkus TS, Brown T, Budoff M, et al. HIV infection is associated with an increased prevalence of coronary noncalcified plaque among participants with a coronary artery calcium score of zero: multicenter AIDS Cohort Study (MACS). *HIV Med*. 2015;16(10):635–639. doi:10.1111/hiv.12262

24. Hsue PY, Lo JC, Franklin A, et al. Progression of atherosclerosis as assessed by carotid intima-media thickness in patients with HIV infection. *Circulation*. 2004;109(13):1603–1608. doi:10.1161/01.CIR.0000124480.32233.8A

25. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2007;25(6):1105–1187. doi:10.1097/HJH.0b013e3281fc975a

26. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *Circulation*. 2014;129(25 suppl 2): S1–45. doi:10.1161/01.cir.0000437738.63853.7a

27. Law MG, Moller NF, El Sadr WM, et al. The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D Study.

HIV Med. 2006;7(4):218–230. doi:10.1111/j.1468-1293.2006 .00362.x

28. Friis-Møller N, Ryom L, Smith C, et al. An updated prediction model of the global risk of cardiovascular disease in HIV-positive persons: the data-collection on adverse effects of anti-HIV drugs (D: A: D) study. *Eur J Prev Cardiol*. 2016;23(2):214–223. doi:10 .1177/2047487315579291

29. Triant VA, Perez J, Regan S, et al. Cardiovascular risk prediction functions underestimate risk in HIV infection. *Circulation*. 2018; 137(21):2203–2214. doi:10.1161/CIRCULATIONAHA.117. 028975

30. *ASCVD Risk Estimator*. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk and the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. Accessed April 3, 2019. http://tools.acc.org/ASCVD-Risk-Estimator/.

31. Rigshospitalet, University of Copenhagen. CHIP.DK > Tools & Standards > Clinical risk scores. Accessed April 3, 2017. http:// www.cphiv.dk/Tools

32. Baekken M, Os I, Sandvik L, Oektedalen O. Hypertension in an urban HIV-positive population compared with the general population: influence of combination antiretroviral therapy. *J Hypertens*. 2008;26(11):2126–2133. doi:10.1097/HJH.0b013e3 2830ef5fb

33. De Socio GV, Ricci E, Maggi P, et al. Prevalence, awareness, treatment, and control rate of hypertension in HIV-infected patients: the HIV-HY study. *Am J Hypertens*. 2014;27(2): 222–228. doi:10.1093/ajh/hpt182

34. Manner IW, Baekken M, Oektedalen O, Sandvik L, Os I. Effect of HIV duration on ambulatory blood pressure in HIV-infected individuals with high office blood pressure. *Blood Press*. 2010;19(3): 188–195. doi:10.3109/08037051.2010.483055

35. Kent ST, Bromfield SG, Burkholder GA, et al. Ambulatory blood pressure monitoring in individuals with HIV: A systematic review and meta-analysis. *PLoS ONE*. 2016;11(2):e0148920. doi:10. 1371/journal.pone.0148920.

36. Schwartz JE, Burg MM, Shimbo D, et al. Clinic blood pressure underestimates ambulatory blood pressure in an untreated employer-based us population: results from the masked hypertension study. *Circulation*. 2016;134(23):1794–1807. doi:10.1161/ CIRCULATIONAHA.116.023404

37. Mancia G, Facchetti R, Bombelli M, Grassi G, Sega R. Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. *Hypertension*. 2006;47(5):846–853. doi:10.1161/01.HYP.0000215363 .69793.bb

38. Gorostidi M, Vinyoles E, Banegas JR, de la Sierra A. Prevalence of white-coat and masked hypertension in national and

international registries. *Hypertens Res*. 2015;38(1):1–7. doi:10. 1038/hr.2014.149

39. Schutte AE, Ware LJ, Rennie KL, et al. 6A.08: High frequency of masked hypertension and associated arterial stiffness in Africans. *J Hypertens*. 2015;33(suppl 1):e75. doi:10.1097/01.hjh.0000 467554.83144.df

40. Ware LJ, Rennie KL, Gafane LF, et al. Masked hypertension in low-income South African adults. *J Clin Hypertens (Greenwich)*. 2016;18(5):396–404. doi:10.1111/jch.12768

41. Kent ST, Schwartz JE, Shimbo D, et al. Race and sex differences in ambulatory blood pressure measures among HIV+ adults. *J Am Soc Hypertens*. 2017;11(7):420–427.e3. doi:10.1016/j.jash.2017 .05.002

42. Diaz KM, Veerabhadrappa P, Brown MD, Whited MC, Dubbert PM, Hickson DA. Prevalence, determinants, and clinical significance of masked hypertension in a population-based sample of African Americans: the Jackson Heart Study. *Am J Hypertens*. 2015;28(7):900–908. doi:10.1093/ajh/hpu241

43. Bernardino JI, Mora M, Zamora FX, et al. Hypertension and isolated office hypertension in HIV-infected patients determined by ambulatory blood pressure monitoring: prevalence and risk factors. *J Acquir Immune Defic Syndr*. 2011;58(1):54–59. doi:10 .1097/QAI.0b013e3182267406

44. Chow DC, Souza SA, Chen R, Richmond-Crum SM, Grandinetti A, Shikuma C. Elevated blood pressure in HIV-infected individuals receiving highly active antiretroviral therapy. *HIV Clin Trials*. 2003;4(6):411–416. doi:10.1310/5E7Q-PGWB-16UE -J48U

45. Baekken M, Os I, Stenehjem A, Sandvik L, Oektedalen O. Association between HIV infection and attenuated diurnal blood pressure rhythm in untreated hypertensive individuals. *HIV Med*. 2009;10(1):44–52. doi:10.1111/j.1468-1293.2008.00655.x

46. Manner IW, Grevbo BW, Witczak BN, et al. Immune markers, diurnal blood pressure profile and cardiac function in virologically suppressed HIV-infected patients. *Blood Press*. 2017;26(6): 332–340. doi:10.1080/08037051.2017.1346459

47. Kent ST, Burkholder GA, Tajeu GS, Overton ET, Muntner P. Mechanisms influencing circadian blood pressure patterns among individuals with HIV. *Curr Hypertens Rep*. 2015;17(11):88. doi: 10.1007/s11906-015-0598 -1

48. Boggia J, Li Y, Thijs L, et al. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. *Lancet*. 2007; 370(9594):1219–1229. doi:10.1016/S0140-6736(07)61538-4

49. Fan HQ, Li Y, Thijs L, et al. Prognostic value of isolated nocturnal hypertension on ambulatory measurement in 8711 individuals from 10 populations. *J Hypertens*. 2010;28(10):2036–2045. doi: 10.1097/HJH.0b013e32833b49fe