INTRODUCTION

Hypertension is currently considered the worldwide leading cause of death, and its prevalence is increasing.\(^1\) Considering the routine use of out-of-office blood pressure (BP) measurement methods both for diagnosis and management of hypertension, such as ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM), subjects can be classified into one of four categories. In patients treated for hypertension, these categories are sustained controlled hypertension, when both office and out-of-office measurements are normal; sustained uncontrolled hypertension, when both are abnormal; white coat uncontrolled hypertension, when BP is elevated in the office but normal when measured out-of-office; and masked uncontrolled hypertension (MUCH), when BP is normal in the office but elevated when measured by ABPM or HBPM.\(^2,3\) This last category has aroused special interest, given that the risk for hypertension-mediated organ damage and fatal and nonfatal cardiovascular events in these individuals is high, similar to or even higher than in sustained hypertension.\(^4,5\) The prevalence of this entity is high, between 10% and 40%\(^.\)\(^7,8\) However, very few studies have evaluated its reproducibility. In fact, many of them have actually determined the persistence of MUCH in a long period of time (6 months)

Reproducibility of masked uncontrolled hypertension detected through home blood pressure monitoring

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Abstract
Masked uncontrolled hypertension (MUCH) is an entity described in treated hypertensive subjects, where office blood pressure (BP) is well controlled and out-of-office BP is elevated. It has been related to a higher cardiovascular risk. However, the reproducibility of MUCH has been scarcely studied. In this study, we aimed to determine the reproducibility of MUCH detected through home blood pressure monitoring (HBPM). Two sets of measurements were performed in hypertensive adults under stable treatment with a 1-week interval. Each set of measurements included three office BP readings and a 4-day HBPM with duplicate readings in the morning, afternoon, and evening (the same validated oscillometric device was employed in both settings). We determined the percentage of agreement regarding the presence of MUCH in the two sets of measurements and quantified such agreement through the Cohen’s kappa coefficient (κ), its 95% confidence interval, and P value. We included 105 patients (median age 58.6 [IQR 45.6-67.2] years old, 53.4% men). MUCH prevalence on at least one occasion was 22.3% (95% CI: 15.2-31.5). The reproducibility of MUCH was scant: κ = 0.19 (95% CI: 0.0002-0.38), P = 0.02, due to the poor reproducibility of the office BP component of MUCH in comparison with the home BP component: κ = 0.21 (95% CI: 0.03-0.39), P = 0.01 vs κ = 0.48 (95% CI 0.29-0.67), P < 0.001, respectively. In conclusion, the reproducibility of MUCH detected through HBPM is minimal, mainly due to the poor reproducibility of office BP measurements. An HBPM-based strategy for the management of patients with MUCH may be more adequate in terms of cardiovascular morbidity and mortality.

1  |  INTRODUCTION

Hypertension is currently considered the worldwide leading cause of death, and its prevalence is increasing.\(^1\) Considering the routine use of out-of-office blood pressure (BP) measurement methods both for diagnosis and management of hypertension, such as ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM), subjects can be classified into one of four categories. In patients treated for hypertension, these categories are sustained controlled hypertension, when both office and out-of-office measurements are normal; sustained uncontrolled hypertension, when both are abnormal; white coat uncontrolled hypertension, when BP is elevated in the office but normal when measured out-of-office; and masked uncontrolled hypertension (MUCH), when BP is normal in the office but elevated when measured by ABPM or HBPM.\(^2,3\) This last category has aroused special interest, given that the risk for hypertension-mediated organ damage and fatal and nonfatal cardiovascular events in these individuals is high, similar to or even higher than in sustained hypertension.\(^4,5\) The prevalence of this entity is high, between 10% and 40%.\(^7,8\) However, very few studies have evaluated its reproducibility. In fact, many of them have actually determined the persistence of MUCH in a long period of time (6 months.
to 5 years) and not its reproducibility. Most of the studies that have indeed assessed the reproducibility of the phenomenon were conducted in untreated subjects and using ABPM as the out-of-office measurement method. In treated hypertensives, there is a gap in the knowledge regarding the reproducibility of MUCH determined through HBPM, which is the recommended method for the assessment of BP control status in this population, given its greater availability and tolerability by patients in comparison with ABPM. Therefore, the purpose of our study was to determine the reproducibility of MUCH in hypertensive patients under treatment, using HBPM as the out-of-office measurement method.

2 | METHODS

2.1 | Design, setting and study population

This was an observational study with prospective enrollment, conducted in the Hypertension Section of Hospital Italiano de Buenos Aires. Patients were selected during a routine clinic visit. We included patients 18-79 years old with an established diagnosis of hypertension, who were under stable antihypertensive treatment (for at least 4 weeks), had an office BP level between 130 and 159 mm Hg for systolic BP and/or between 80 and 99 mm Hg for diastolic BP, and were asked to perform an HBPM by their treating physician in order to assess their hypertension control status. Exclusion criteria were office BP level >159 and/or 99 mm Hg, the presence of atrial fibrillation or other arrhythmias where the oscillometric method of measurement is less accurate, vital crisis (such as loss of a relative or work instability) which could alter BP and require treatment adjustments, and active oncologic or terminal disease.

The protocol was approved by the Ethics Committee for Research Protocols of Hospital Italiano de Buenos Aires, and participants gave their written informed consent. Once the selection criteria were checked and informed consent was signed, we proceeded to perform BP measurements.

2.2 | Blood pressure measurements

We performed two sets of measurements, with a 1-week interval. In each set of measurements, we registered office BP and home BP (Figure S1).

2.3 | Office blood pressure

Office BP was measured three times by the study investigators, with 1-minute intervals, in the nondominant arm, with the subjects in sitting position and after five minutes of resting. For that purpose, we used a validated oscillometric device Omron 7200 (Omron) and an appropriate cuff according to the patients’ arm circumference.

The average of the three readings was used for analysis.

Office BP readings were repeated after 1 week, at the same time of the day, in the same conditions, and using the same device.

2.4 | Home blood pressure monitoring

Immediately after office BP measurements, patients performed a 4-day HBPM protocol, with duplicate sitting BP readings (one minute apart) in the nondominant arm, during fixed hours in the morning (8-12 AM), afternoon (14-18 PM), and evening (20-24 PM). Morning BP readings were registered before antihypertensive drug intake. We used the same oscillometric device employed for office BP measurements. According to the current recommendations, average of all readings discarding first day measurements was used for analysis.

To avoid misreporting, only the measurements stored in the memory were used in the study (not self-reported measurements).

Patients with fewer than 16 home BP readings were excluded from the analysis.

Home BP readings were repeated after 1 week, in the same conditions and using the same device.

2.5 | Definition of main variables

According to the accepted cutoff values to define elevated BP level (≥140 and/or 90 mm Hg for office BP and ≥135 and/or 85 mm Hg for home BP), subjects were classified into one of four categories, in each set of BP measurements: (a) those with normal office BP and normal HBPM (sustained controlled hypertension), (b) those with high office BP and high HBPM (sustained uncontrolled hypertension), (c) those with high office BP but normal HBPM (white coat uncontrolled hypertension), and (d) those with normal BP at the office but elevated HBPM (MUCH).

2.6 | Other variables evaluated

At the first visit, patients were interviewed and electronic clinical records were reviewed in order to gather information regarding demographic data, cardiovascular risk factors, established cardiovascular disease and the type and dose of antihypertensive drugs. Weight and height were also recorded at that first visit.

Active smokers were defined as those subjects who had consumed at least 100 cigarettes during their lifetime and, at the moment of the study visit, smoked every day or most days; past smokers were defined as those subjects who had consumed at least 100 cigarettes during their lifetime but were not currently smoking at the time they were interrogated; and non smokers were defined as those that never smoked more than 100 cigarettes.

Alcohol consumption was assessed using the criteria developed by Trudel et al: mild (<1 glass per week), moderate (1-5 glasses per week), and heavy (>5 glasses per week).

The presence of diabetes was considered when fasting plasma glucose was ≥ 26 mg/dL on at least two occasions or the patient reported the use of antidiabetic drugs, whereas the presence of dyslipidemia was defined according to the ATP III criteria or the use of lipid-lowering drugs.

In relation to the history of cardiovascular disease, coronary heart disease was defined as a history of myocardial infarction,
unstable angina, chronic stable angina, or coronary bypass surgery; cerebrovascular disease was defined as a history of stroke or transient ischemic attack.

Finally, body mass index was calculated as weight (kg)/(height [m])².

2.7 | Statistical considerations

2.7.1 | Sampling and sample size calculation

We performed a systematic sampling, with a random starting point on the date the first patient was included and sampling interval = 1.

Sample size calculation was based on the null hypothesis of the absence of agreement (κ = 0), with a power of 80% and an alpha error of 5%. We used the nomogram proposed by Hong et al for the sample size estimation for a dichotomic measurement. This approach avoids the so-called "kappa paradox" by which small differences in the percentage of agreement may determine substantial changes in terms of the κ coefficient. We estimated a MUCH prevalence of 20%, according to the previous reports. In order to be able to introduce the data in the nomogram, we used its counterpart: an 80% prevalence of the absence of MUCH. Under the null hypothesis of no agreement, the presence of MUCH in the two sets of measurements (or the absence of MUCH) represents independent events. Therefore, the expected frequency of a patient having MUCH (or the absence of MUCH) on the two occasions is 0.8 × 0.8 = 0.64. We considered a 0.11 difference between the null hypothesis (0.64) and a clinically relevant agreement of 0.75. This last figure was obtained from previous studies, where the agreement between the two sets of measurements regarding the presence of MUCH was between 0.68 and 0.82.

Introducing these data into the nomogram, it was necessary to include 100 subjects in the study. We anticipated a 5% lost to follow-up. As a consequence, we decided to include 105 individuals.

2.8 | Statistical analysis

Results are reported as the relative and absolute frequency for categorical variables, and mean ± standard deviation or median and interquartile range for continuous variables, according to the data distribution.

We estimated the prevalence of the four phenotypes (sustained controlled hypertension, sustained uncontrolled hypertension, white coat uncontrolled hypertension, and MUCH) in each time of measurement (morning, afternoon, and evening). Among those who were diagnosed with MUCH in the first determination, four subjects (33.3%) persisted with the same phenotype in the second determination. Figure 1 depicts the migration to other phenotypes for the rest of the patients. Most of them migrated to sustained controlled hypertension in the second set of measurements.

The reproducibility of MUCH, determined through the κ coefficient, was scant: κ = 0.19 (95% CI: 0.0002–0.38), P = 0.02, which indicates minimal agreement according to the Landis and Koch criteria.

When we analyzed the two components of MUCH (office controlled hypertension and home uncontrolled hypertension) separately and evaluated the reproducibility for each component, we found that reproducibility in the diagnosis was much better for HBPM than for office BP: κ = 0.48 (95% CI: 0.29–0.67), P < 0.001 vs κ = 0.21 (95% CI: 0.03–0.39), P = 0.01, respectively. This finding shows that it is the scant reproducibility of office BP control which explains the limited reproducibility found for MUCH.

On the other hand, when we evaluated the reproducibility of MUCH in each time of measurement (morning, afternoon, and evening), we found that reproducibility was better for morning and evening MUCH (fair agreement) than for afternoon MUCH (minimal agreement) (Table 4).

4 | DISCUSSION

In the present study, we found that the reproducibility of MUCH assessed through HBPM is minimal, which is mainly due to the poor reproducibility of the office BP component of MUCH.

The same analysis was repeated considering MUCH in the different times of home BP measurement: morning, afternoon, and evening. Therefore, we defined morning, afternoon, and evening MUCH office BP was normal and morning, afternoon, or evening home BP was elevated, respectively, and independently of the overall home BP average taking into account the three times of measurement altogether.

3 | RESULTS

We included 105 patients in the study. Two of these subjects had less than 16 measurements in one of the two HBPMs, and, therefore, 103 patients were finally included in the analysis.

Median age was 58.6 (IQR 45.6–67.2) years old, and 53.4% (n = 55) were men. Baseline characteristics of the study population are depicted in Table 1. BP profiles at the office and at home are depicted in Table 2, for both sets of measurements.

The global prevalence of MUCH (on at least one occasion) was 22.3% (95% CI: 15.2–31.5). Table 3 shows the prevalence of sustained controlled hypertension, sustained uncontrolled hypertension, white coat uncontrolled hypertension, and MUCH in each set of measurements.

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On the other hand, when we evaluated the reproducibility of MUCH in each time of measurement (morning, afternoon, and evening), we found that reproducibility was better for morning and evening MUCH (fair agreement) than for afternoon MUCH (minimal agreement) (Table 4).
The prevalence of MUCH on at least one occasion found in our investigation—22.3%—was in the range of values reported in previous studies, but somewhat lower than that reported in studies that specifically included hypertensives under treatment. We believe this could be explained by the fact that a more strict standardization of measurements and the use of the same oscillometric device for office and home BP measurements in our study may have contributed to minimize bias associated with other measurement methodologies, such as the auscultatory method, that was employed in former studies. The inadequate deflation rate and terminal digit preference inherent to this technique would underestimate office BP, increasing the chances to diagnose MUCH.

The reproducibility of MUCH found in our research is lower than previously reported. We believe this could be mainly due to two reasons: First, studies that assessed reproducibility of MUCH were based mostly on ABPM, which would be superior to HBPM. This fact was evaluated in the study conducted by Viera et al., where 420 untreated subjects with high-normal office BP underwent both ABPM and HBPM to establish the reproducibility of MUCH, finding a κ coefficient of 0.40 in the case of ABPM and 0.30 in the case of HBPM. Second, most published studies evaluated the reproducibility of the phenomenon in untreated subjects (masked hypertension) rather than in treated ones (MUCH). This reproducibility would be better in the first group, as is shown in the study conducted by Ben Dov et al. In that study, treated and untreated subjects were analyzed separately in terms of MUCH reproducibility, finding a κ coefficient of 0.26 and 0.64 in medicated and non-medicated participants, respectively. In another study, Verberk et al. found that the persistence of MUCH in treated patients detected through ABPM was only 50% in the second set of measurements (the authors did not report the κ coefficient).

Of note, studies including treated hypertensive patients evaluate the persistence of MUCH in a longer period of time (1-1.5 years) than the 2 weeks assessed in our study. Changes in lifestyle and in antihypertensive medication could partially explain the poor reproducibility found there. However, these issues do not apply to our findings since

### Table 1: Baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, IQR</td>
<td>58.6 (45.6-67.2)</td>
</tr>
<tr>
<td>Male sex, % (n)</td>
<td>53 (55)</td>
</tr>
<tr>
<td>Diabetes, % (n)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Smoking habits, % (n)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>49 (50)</td>
</tr>
<tr>
<td>Current</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Past</td>
<td>42 (43)</td>
</tr>
<tr>
<td>Alcohol consumption, % (n)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>59 (61)</td>
</tr>
<tr>
<td>Moderate</td>
<td>24 (25)</td>
</tr>
<tr>
<td>Heavy</td>
<td>17 (17)</td>
</tr>
<tr>
<td>BMI, kg/m², SD</td>
<td>29.9 (5.2)</td>
</tr>
<tr>
<td>Dyslipidemia, % (n)</td>
<td>56 (58)</td>
</tr>
<tr>
<td>History of coronary heart disease, % (n)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>History of cerebrovascular disease, % (n)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Time since hypertension diagnosis, years, IQR</td>
<td>9 (6-16)</td>
</tr>
<tr>
<td>Number of antihypertensive drugs, SD</td>
<td>2.3 (1.2)</td>
</tr>
<tr>
<td>Diuretics, % (n)</td>
<td>33 (34)</td>
</tr>
<tr>
<td>ACEI, % (n)</td>
<td>52 (54)</td>
</tr>
<tr>
<td>ARB, % (n)</td>
<td>33 (34)</td>
</tr>
<tr>
<td>BB, % (n)</td>
<td>41 (42)</td>
</tr>
<tr>
<td>CCB, % (n)</td>
<td>62 (64)</td>
</tr>
<tr>
<td>Other, % (n)</td>
<td>7 (7)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BB, beta blockers; BMI, body mass index; CCB, calcium channel blockers; IQR, interquartile range; SD, standard deviation.

### Table 2: Blood pressure profiles at the office and at home

<table>
<thead>
<tr>
<th>bp measurement</th>
<th>1st set of measurements</th>
<th>2nd set of measurements</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg, SD)</td>
<td>136.6 (9.2)</td>
<td>130 (10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mm Hg, SD)</td>
<td>82.1 (7.4)</td>
<td>79.3 (8.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HR (bpm, SD)</td>
<td>72.9 (11.9)</td>
<td>72 (12.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Number of measurements (SD)</td>
<td>23.3 (1.5)</td>
<td>23.1 (1.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Total SBP (4 d) [mm Hg, SD]</td>
<td>127.8 (9.9)</td>
<td>127.2 (9.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Total DBP (4 d) [mm Hg, SD]</td>
<td>76 (7.9)</td>
<td>75.4 (7.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>HR (4 d) [bpm, SD]</td>
<td>70 (9.6)</td>
<td>69.1 (9.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>SBP discarding first day measurements (mm Hg, SD)</td>
<td>127.3 (9.8)</td>
<td>127.3 (9.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Total SBP (4 d) [mm Hg, SD]</td>
<td>75.7 (8.1)</td>
<td>75.4 (7.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Morning SBP (mm Hg, SD)</td>
<td>126.6 (12.2)</td>
<td>127 (10.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Morning DBP (mm Hg, SD)</td>
<td>76.2 (8.6)</td>
<td>76.4 (8.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Afternoon SBP (mm Hg, SD)</td>
<td>126.1 (9.8)</td>
<td>126.3 (10.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Afternoon DBP (mm Hg, SD)</td>
<td>74.6 (8.7)</td>
<td>73.9 (8.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Evening SBP (mm Hg, SD)</td>
<td>128.5 (11.7)</td>
<td>128.6 (10.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Evening DBP (mm Hg, SD)</td>
<td>76.2 (8.7)</td>
<td>75.7 (8.4)</td>
<td>ns</td>
</tr>
</tbody>
</table>

**Abbreviations:** BP, blood pressure; bpm, beats per minute; DBP, diastolic blood pressure; HBPM, home blood pressure monitoring; HR, heart rate; ns, nonsignificant; SBP, systolic blood pressure; SD, standard deviation.

*Paired t test
our evaluation was in the field of short-term reproducibility and antihypertensive medication was unchanged. We consider that, in our case, the main explanation for the scant reproducibility of MUCH is due to the office BP component. The diagnosis of MUCH is based on a normal office BP (office BP component) and an elevated out-of-office BP (in this case, HBPM component). According to our results, the office BP component would be poorly reproducible, with a much better reproducibility for the HBPM component. This could be due in part to the so-called “regression to the mean,” a statistical phenomenon in which extreme values found in a subject tend to be closer to the mean when measurements are repeated. This phenomenon seems to have more weight on office than on home BP, given that BP determinations have an inherent measurement error which decreases as the number of measurements increases, and office BP readings generally are (and were in this study) less numerous than home BP readings (3 vs 24 on each set of measurements). Another explanation for the scant reproducibility of office BP is the adaptation to BP measurement with decrease of the white coat effect at the second measurement. The higher home BP reproducibility as compared to office BP gives support to some expert recommendations of using office BP only as a screening tool, which must always be confirmed with out-of-office measurements (ABPM or HBPM) and also to some guidelines that suggest the use of an out-of-office BP measurement method to guide the treatment of MUCH. Remarkably, no randomized clinical trial has currently demonstrated the superiority of this management strategy in terms of hypertension-mediated organ damage and/or cardiovascular events.

In contrast to investigations that evaluated the persistence of MUCH in a longer period of time, most patients that did not persist with MUCH in the second set of measurements in our study migrated to the “sustained controlled hypertension” phenotype, whereas in the aforementioned studies, the main pattern of migration was to the “sustained uncontrolled hypertension” phenotype. This could be due to the different follow-up periods, more prolonged in other studies and therefore evaluating more the persistence of the phenomenon than its reproducibility. Besides, we believe that the “Hawthorne effect” (subjects modifying their behavior in response to their awareness of being observed) could have led to an improvement in the adherence to pharmacological therapy and, therefore, to a better BP control.

An interesting finding of our study is that the reproducibility of MUCH is different depending on the time of the day when measurements are performed, being higher in the morning and evening, as compared to the afternoon. In the same line, Kawabe et al studied the reproducibility of MH (through HBPM) in 503 untreated subjects in the morning and in the evening. The authors found that this was better in the morning, and speculate that the lower reproducibility in the evening may be due to cultural Japanese aspects, such as nighttime bathing and drinking habits, which decrease BP, leading to a lower prevalence of MH in that moment of the day and thus affecting its reproducibility. In our case, we believe that antihypertensive drug

### TABLE 3: Prevalence of sustained controlled hypertension, sustained uncontrolled hypertension, white coat uncontrolled hypertension, and masked uncontrolled hypertension in each set of measurements

<table>
<thead>
<tr>
<th></th>
<th>1st set of measurements</th>
<th>2nd set of measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCH, % (95% CI)</td>
<td>53.4 (43.6-62.9)</td>
<td>67 (57.2-75.4)</td>
</tr>
<tr>
<td>SUH, % (95% CI)</td>
<td>15.5 (9.7-24)</td>
<td>3.9 (1.4-10)</td>
</tr>
<tr>
<td>WUCH, % (95% CI)</td>
<td>19.4 (12.8-28.4)</td>
<td>14.6 (8.9-22.9)</td>
</tr>
<tr>
<td>MUCH, % (95% CI)</td>
<td>11.7 (6.7-19.6)</td>
<td>14.6 (8.9-22.9)</td>
</tr>
</tbody>
</table>

Abbreviations: MUCH, masked uncontrolled hypertension; SCH, sustained controlled hypertension; SUH, sustained uncontrolled hypertension; WUCH, white coat uncontrolled hypertension; 95% CI, 95% confidence interval.

### TABLE 4: Reproducibility of masked uncontrolled hypertension in each time of measurement (morning, afternoon, and evening)

<table>
<thead>
<tr>
<th></th>
<th>$\kappa$ coefficient (95% CI)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUCH (taking into account the three periods of measurements)</td>
<td>0.19 (0.0002-0.38)</td>
<td>0.02</td>
</tr>
<tr>
<td>MUCH in the morning</td>
<td>0.30 (0.11-0.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MUCH in the afternoon</td>
<td>0.20 (0.009-0.40)</td>
<td>0.02</td>
</tr>
<tr>
<td>MUCH in the evening</td>
<td>0.32 (0.13-0.51)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: MUCH, masked uncontrolled hypertension; 95% CI, 95% confidence interval.
consumption is the main factor influencing the lower reproducibility of MUCH during the afternoon: As it occurs in the rest of the world, most of our patients take their medication during the morning. As a consequence, morning and evening BP readings would be farther from medication than afternoon measurements, more closely resembling measurements performed in untreated subjects in whom the reproducibility of the phenomenon is better, as previously stated.

Finally, our results must be interpreted in the context of the study limitations: First, the time subjects took their antihypertensive medication was not controlled, which may have increased the variability in BP measurements. Second, adherence to pharmacologic treatment was not formally assessed, and different grades of adherence among patients could have led to a lower reproducibility of MUCH. Third, changes in physical activity during the study along with changes in dietary sodium intake and/or licorice consumption were not evaluated. These issues could have modified the prevalence of MUCH. Fourth, the prevalence of obstructive sleep apnea and insomnia was not assessed in our study. These entities could have influenced home BP values. Fifth, the low prevalence of a history of cardiovascular disease and diabetes in our study population limits the extrapolation of the results to hypertensive patients with a higher risk. On the other hand, our study has also some strengths: First, measurements were performed with the same validated oscillometric device both at the office and at home, avoiding some sources of systematic error, such as the observer bias. Second, home BP data used for analysis were extracted directly from the equipment’s memory, precluding the misreporting of BP readings which has been found to reach 35% in some studies where patients used a logbook, and third, investigators did not change antihypertensive drug prescriptions during the study, avoiding an extra source of BP variability.

In conclusion, the reproducibility of MUCH detected through HBPM is minimal, mainly due to the poor reproducibility of office BP measurements. An HBPM-based strategy for the management of patients with MUCH may be more adequate in terms of cardiovascular morbidity and mortality.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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