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ORIGINAL ARTICLE

Prevalence of masked uncontrolled hypertension according to the number of office blood pressure measurements

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KEYWORDS
Masked hypertension;
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Abstract
Introduction and objectives: The reported prevalence of masked uncontrolled hypertension (MUCH) varies because many studies are not comparable as they use different measurement methodologies. To evaluate the influence of the number of office blood pressure readings on the prevalence of MUCH we conducted a cross-sectional, multicenter study in treated hypertensive patients.
Patients and methods: We carried out an observational, cross-sectional, multicenter study in 33 Spanish hospital-based hypertension units, involving 35 investigators and 12 Autonomous Communities. Six blood pressure readings and a 24-h ambulatory blood pressure monitoring were performed in treated hypertensive patients. The means of the first 3 readings (P_{123}), the 2nd, 3rd and 4th readings (P_{234}), the 3rd, 4th and 5th readings (P_{345}) and the last 3 readings (P_{456}) were compared with mean 24-h blood pressure. MUCH was defined as office blood pressure <140/90 mmHg and 24-h blood pressure ≥130/80 mmHg, considering the first 3 readings ($MUCH_{123}$), the 2nd, 3rd and 4th readings ($MUCH_{234}$), the 3rd, 4th and 5th readings ($MUCH_{345}$) and the last 3 readings ($MUCH_{456}$).
Results: We included 498 hypertensive patients. Mean (standard deviation) office blood pressure measurements were: (P_{123}) 141(18)/82(11); (P_{234}) 139(17)/81(11); (P_{345}) 138(17)/81(11) and (P_{456}) 137(16)/80(10) mmHg. Mean 24-h blood pressure was 127(13.8)/75(9.5) mmHg. The correlation coefficients between ambulatory and office systolic/diastolic blood pressure were

Abbreviations: ABPM, 24-h ambulatory blood pressure monitoring; BP, blood pressure; HBPM, self-measured blood pressure monitoring; LVH, left ventricular hypertrophy; MUCH, masked uncontrolled hypertension.

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(P_{123}):0.48/0.50; (P_{234}):0.50/0.52; (P_{345}):0.50/0.54; and (P_{456}):0.50/0.55 ($p < 0.001$, all). The prevalences of $MUCH_{123}$, $MUCH_{234}$, $MUCH_{345}$ and $MUCH_{456}$ were 14.5%, 18.9%, 19.5% and 21.1%, respectively.
Conclusions: The prevalence of MUCH diagnosis depends on the serial office blood pressure readings, being much higher for the last three blood pressure readings. Discarding the first and second office blood pressure measures seems to be the most accurate method for diagnosing MUCH.

PALABRAS CLAVE
Hipertensión enmascarada;
Hipertensión arterial no controlada;
Medición de la presión arterial en consulta

Prevalencia de hipertensión arterial enmascarada no controlada de acuerdo con el número de medidas de la tensión arterial en consulta

Resumen
Introducción y objetivos: Los datos sobre prevalencia de hipertensión arterial enmascarada no controlada (HTAE) son muy variables, ya que los registros obtenidos en diferentes estudios no son comparables al emplear diferentes métodos de medición. Se llevó a cabo un estudio transversal y multicéntrico en pacientes hipertensos tratados para evaluar la influencia de la cantidad de lecturas de la presión arterial en consulta sobre la prevalencia de la HTAE.
Pacientes y métodos: Se realizó un estudio observacional, transversal y multicéntrico en 33 unidades de hipertensión en hospitales españoles, con la participación de 35 investigadores y 12 comunidades autónomas. Se realizaron 6 lecturas de la presión arterial y un control de la presión arterial ambulatoria de 24 h en pacientes hipertensos tratados. Se compararon las medias de las 3 primeras lecturas (P_{123}), de las lecturas 2, 3 y 4 (P_{234}), de las lecturas 3, 4 y 5 (P_{345}) y de las 3 últimas lecturas (P_{456}) con la media de la presión arterial a las 24 h. Teniendo en cuenta las 3 primeras lecturas ($HTAE_{123}$), las lecturas segunda, tercera y cuarta ($HTAE_{234}$), tercera, cuarta y quinta ($HTAE_{345}$) y las últimas 3 lecturas ($HTAE_{456}$); definimos la HTAE como una presión arterial en consulta <140/90 mm Hg y una presión arterial de 24 h $\geq$ 130/80 mm Hg.
Resultados: Se incluyeron 498 pacientes hipertensos. La media de las mediciones (desviación estándar) de presión arterial en consulta fueron: (P_{123}) 141 (18)/82 (11); (P_{234}) 139 (17)/81 (11); (P_{345}) 138 (17)/81 (11) y (P_{456}) 137 (16)/80 (10) mm Hg. La presión arterial media a las 24 h fue de 127 (13.8)/75 (9.5) mm Hg. Los coeficientes de correlación entre presión sistólica/presión diastólica ambulatoria y en consulta fueron (P_{123}): 0.48/0.50; (P_{234}): 0.50/0.52; (P_{345}): 0.50/0.54; y (P_{456}): 0.50/0.55 ($p < 0.001$ de todos). Las prevalencias de $HTAE_{123}$, $HTAE_{234}$, $HTAE_{345}$ y $HTAE_{456}$ fueron 14.5%, 18.9%, 19.5% y 21.1%, respectivamente.
Conclusiones: La prevalencia de diagnóstico de HTAE depende de las series de lecturas de la presión arterial en consulta, siendo esta mucho más alta en las 3 últimas lecturas. Si descartamos la primera y segunda lecturas, la medida de la presión arterial en consulta parece ser el método más preciso para el diagnóstico de la HTAE.

Introduction

Masked uncontrolled hypertension (MUCH) is defined as hypertensive patients receiving antihypertensive treatment with controlled office blood pressure (BP) but high ambulatory BP.[1–3] These are hypertensive patients in whom ignorance of poor ambulatory BP control results in a high probability that optimal BP control is delayed for too long.

The diagnosis of MUCH requires a record of 24-h ambulatory BP monitoring (ABPM), although it may be detected using self-measured BP monitoring (HBPM). The reported prevalence of MUCH varies, although many studies are not comparable as they include differing samples of hypertensive patients or use different methodologies. A prevalence of 13.1% of all treated hypertensive patients has been reported in Spanish hypertensive units.[4] A Japanese study using self-measured blood pressure found a prevalence of 19%.[5] When only hypertensive patients with good office BP control are evaluated, more than a third may have MUCH as measured by ABPM,[6–8] although our experience suggests the prevalence may be as high as 50%.[9] Banegas et al. found a prevalence of MUCH of 31.1%, significantly higher in males, patients with borderline clinic BP, and patients at high cardiovascular risk.[10] However, other studies have found a prevalence of only 13.4% in this group of patients.[11]

This variability between studies may be explained, in part, by the different definitions of good ambulatory BP control, according to the selection of mean 24-h or mean

daytime blood pressure to define MUCH. Moreover, the methodology for measuring office BP may also explain the differences in the reported prevalence of MUCH. Therefore, the aim of this study was to determine whether the prevalence of MUCH varied according to the number of office BP readings, and to describe which pattern of office BP readings was most closely associated with subclinical organ damage.

Methods

We carried out an observational, cross-sectional, multicenter study in 33 Spanish hospital-based hypertension units, involving 35 investigators. By means of convenience sampling, hypertensive patients aged >18 years attended by the units between January and June 2012 who had been receiving stable antihypertensive medication for the previous three months and who gave written informed consent to participate were included. Night shift workers, patients with arrhythmias (atrial fibrillation or baseline heart rate > 100 beats per minute) or arm circumference > 40 cm were excluded. All subjects included underwent a history and physical examination and 6 office BP readings at baseline. The readings were made one minute apart with a validated automatic sphygmomanometer in a sitting position after five minutes of rest. A large cuff was used when necessary.

Also at baseline, each patient underwent 24-h ABPM (SpaceLabs 90207/90217, Richmond, Washington, USA) on a working day, with readings scheduled every 20 min through the 24-h period. Periods of activity and sleep were adjusted to those reported by the patients. An obese cuff was used when indicated. ABPM recordings of <24 h, with <70% of valid readings, or with periods of >1 h without a reading were rejected. Blood samples for blood and urine analysis, and an electrocardiogram were carried out. The design and carrying out of the study were approved by the Research Ethics Committee of the Catalan Foundation of Hospitals.

The variables analyzed included gender, age, body mass index, waist circumference, heart rate, office and ambulatory BP, a diagnosis of diabetes mellitus (defined as patients with ≥2 episodes of fasting glycaemia ≥126 mg/dl, according to American Diabetes Association criteria[12]), hypercholesterolemia (total cholesterol >190 mg/dl, or LDL cholesterol >115 mg/dl, or HDL cholesterol <40 mg/dl in males or <46 mg/dl in women, or use of lipid lowering drugs[13]), active smoking (defined as regular daily consumption of any type of tobacco), family history of premature cardiovascular disease (<55 years in men, <65 years in women), alcohol consumption >30 g/day, antihypertensive therapy and associated cardiovascular disease: stroke, coronary disease, chronic kidney disease [defined by estimated glomerular filtration rate according to Levey's simplified formula, MDRD <60 ml/min],[14] microalbuminuria (albumin-to-creatinine ratio >30 mg/g in males or >22 mg/g in females), peripheral artery disease and heart failure. Electrocardiographic left ventricular hypertrophy (LVH) was defined using the Cornell index (males: RaVL + SV3 > 2.8 mV; females: RaVL + SV3 > 2.0 mV) or the Sokolow-Lyon index (SV1 + RV5 o V6 > 3.5 mV) or by RaVL voltage > 6 mV.

MUCH was defined as office BP <140 mmHg (systolic) and <90 mmHg (diastolic) and mean 24-h ABPM ≥130 or ≥80 mmHg, respectively. Four successive mean office BP values were selected: the means of the 1st, 2nd and 3rd readings (P_{123}), the 2nd, 3rd and 4th readings (P_{234}), the 3rd, 4th and 5th readings (P_{345}), and the 4th, 5th and 6th readings (P_{456}), which provided four possible measurements of MUCH ($MUCH_{123}$, $MUCH_{234}$, $MUCH_{345}$, $MUCH_{456}$).

Descriptive statistics are presented as means (standard deviation, SD) or as numbers (percentage). Assuming a prevalence of MUCH of 23%,[15] with a 95% confidence interval (CI) of ≤0.08 (8%), a total of 426 subjects were estimated to be necessary for analysis of the main objective. All results were expressed with 95% CI. Pearson's coefficient was used to evaluate the correlation between ambulatory blood pressure and the 4 definitions of masked uncontrolled hypertension. Statistical significance was set at $p < 0.05$ (two-tailed). The analyses were performed using Stata/SE version 11.1 for Windows (StataCorp, LP).

Results

A total of 503 hypertensive patients were recruited, of whom 498 were finally included. Five patients were excluded due to noncompliance with selection criteria (1 case), lack of information on ABPM (2 cases), length of ABPM < 22 h (1 case), or only 66% of valid ABPM readings (1 case).

The baseline characteristics of the sample are shown in Table 1. The mean values of systolic and diastolic BP were progressively lower in each successive office BP reading (Fig. 1).

Mean (SD) office BP measurements were: (P_{123}) 141 (18)/82 (11); (P_{234}) 139 (17)/81 (11); (P_{345}) 138 (17)/81 (11) and (P_{456}) 137 (16)/80 (10) mmHg. Based on office readings, BP control (<140/<90 mmHg) was (P_{123}) 43.98%, (P_{234}) 51.2%, (P_{345}) 53.01% and (P_{456}) 55.22%. Control was observed in 200 patients using the first office BP reading (P_1), 187 of them had also controlled the successive second reading (P_1 and P_2), 93.5 [90.1–96.9] %, and 181 subjects had good control of first, second and third successive readings (P_1 and P_2 and P_3), representing a 90.5 [86.4–94.6]% of those 200 patients.

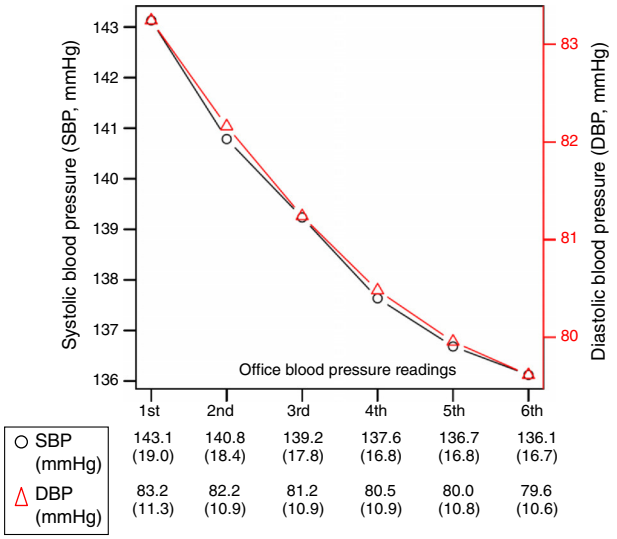

Figure 1 Mean (standard deviation) of the 6 office blood pressure readings.

Table 1 Sociodemographic and clinical characteristics of subjects. Values are numbers (percentage) unless otherwise indicated ($n = 498$).

Women	206 (41.37)
Age, years; *mean (SD)*	60 (13.0)
Family history of premature cardiovascular disease	78 (15.6)
BMI (kg/m^2); *mean (SD)*	29.1 (4.4)
Waist circumference (cm); *mean (SD)*	99.1 (12.3)
Smoking	61 (12.2)
Alcohol consumption > 30 g/day	13 (2.6)
Type 2 diabetes	130 (26.1)
Hypercholesterolemia	320 (64.2)
Electrocardiographic left ventricular hypertrophy	21 (4.6)
Chronic kidney disease	75 (18.3)
Associated cardiovascular disease	146 (29.3)
Office BP (mmHg); mean of all readings (SD)	
Systolic	139 (16.9)
Diastolic	81 (10.4)
24-h BP (mmHg); mean (SD)	
Systolic	127 (13.8)
Diastolic	75 (9.5)
Daytime BP (mmHg); mean (SD)	
Systolic	131 (14.3)
Diastolic	78 (10.2)
Night-time BP (mmHg); mean (SD)	
Systolic	120 (15.7)
Diastolic	69 (9.8)
Office heart rate *(beats per minute); mean (SD)*	74 (11.3)
Night-time HR *(beats per minute); mean (SD)*	67 (9.8)

SD: standard deviation; BMI: body mass index; BP: blood pressure

The prevalence of MUCH on the whole sample according to the various groups of office BP readings is shown in Fig. 2. Table 2 shows the Pearson correlations between 24-h ABPM and the means of the four groups of office BP readings. No significant association between the different definitions of MUCH and LVH (by electrocardiogram) or microalbuminuria was found (Table 3).

Table 2 Pearson's correlations between ambulatory blood pressure and the four different office blood pressure (OBP) measurements, all $p < 0.001$.

	OBP_{123}	OBP_{234}	OBP_{345}	OBP_{456}
24 h systolic blood pressure	0.48	0.50	0.50	0.50
24 h diastolic blood pressure	0.50	0.52	0.54	0.55

OBP_{123}: definition based in the mean of the 1st, 2nd and 3rd office blood pressure readings; OBP_{234}: idem of 2nd, 3rd and 4th readings; OBP_{345}: idem of 3rd, 4th and 5th readings; OBP_{456}: idem of 4th, 5th and 6th readings.

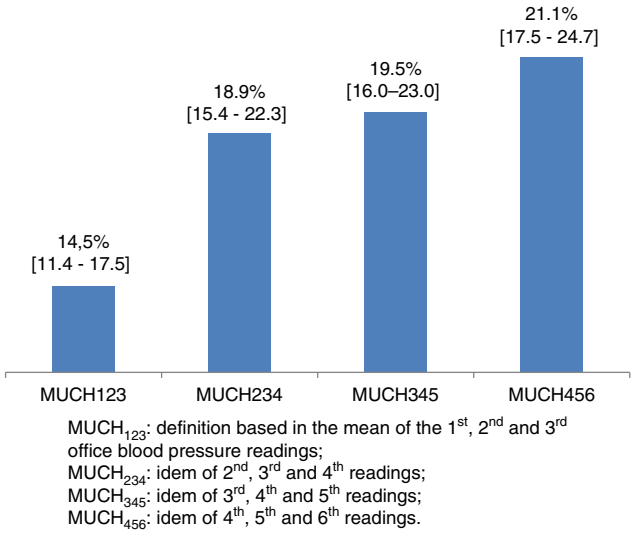

Figure 2 Prevalences [95% CI] of masked uncontrolled hypertension (MUCH) considering the four definitions based in successive office blood pressure readings.

Discussion

Correct diagnosis of hypertension currently requires the combined evaluation of office and ambulatory BP. This is particularly evident when a diagnosis of white-coat hypertension is made. However, the diagnosis of masked hypertension also requires an accurate assessment of office BP. The varying prevalences of masked hypertension found in different studies are related not only to variations in patient samples evaluated in each study, but also to aspects of the measurement of office BP. For example, the characteristics of BP measured repeatedly in a single clinic visit could be predictive of clinical differences in BP between repeated home and clinic measurements.[16] The interesting study of Banegas et al[10] included a high number of subjects. They performed only two office BP measurements and they found a MUCH prevalence of 31%. Considering the results of our study, it could be assumed that, if more BP readings had been made, the prevalence of MUCH would have been

Table 3 Association between the four definitions of masked uncontrolled hypertension (MUCH) and electrocardiographic left ventricular hypertrophy (LVH) and microalbuminuria.

	LVH OR [95% CI]	Microalbuminuria OR [95% CI]
$MUCH_{123}$	1.10 [0.65–1.84]	0.60 [0.27–1.33]
$MUCH_{234}$	1.10 [0.69–1.74]	0.84 [0.43–1.61]
$MUCH_{345}$	1.05 [0.66–1.66]	0.73 [0.37–1.43]
$MUCH_{456}$	1.08 [0.69–1.70]	0.83 [0.44–1.57]

$MUCH_{123}$: definition based in the mean of the 1st, 2nd and 3rd office blood pressure readings; $MUCH_{234}$: idem of 2nd, 3rd and 4th readings; $MUCH_{345}$: idem of 3rd, 4th and 5th readings; $MUCH_{456}$: idem of 4th, 5th and 6th readings; OR: odds ratio; CI: confidence interval.

even greater. Nevertheless, the differences between the prevalence of MUCH found by Banegas et al. and the prevalence in our study could be explained by differences between the two samples. Our sample is recruited just from a specialized hospital setting, with higher prevalence of associated cardiovascular disease and probably with longer duration of hypertension, more frequent evaluations of ambulatory blood pressure, and more number and higher doses of antihypertensive drugs.

Our results show that the method of measuring office BP influences the diagnosis of MUCH. Office BP was measured under optimal conditions by doctors and nurses from various specialized Spanish hypertension units. However, office BP decreased gradually in successive BP readings, even after initial rest and in the context of the baseline conditions of an experimental study. There was a reduction of up to 7 mmHg for systolic BP and up to 3.6 mmHg for diastolic between the first and sixth readings. Therefore, the prevalence of MUCH ranged between 14.5% in the first reading to 21.1% in the sixth reading in our study. Pearson correlations between ambulatory BP and each of the four groups of means office BP were quite similar. However, the best correlation was with diastolic 24-h ABPM and the mean diastolic office BP of the last three readings.

Thus, it seems that the inclusion or not of the first office BP readings is crucial in defining MUCH, especially the first reading. Most patients in our study had an alert reaction after the first office BP reading, despite the prior rest period. This alert reaction lessened progressively in successive readings. These reactions were similar when office BP was measured by physicians or nurses. However, the results might have differed if readings had been made using automatic BP monitors, without any medical intervention. That makes office BP values closer to the mean daytime BP (ABPM or HBPM).[17] However, it appears that the first BP readings are also higher in this case.[18] For example, Myers et al. found a BP reduction between the first and sixth automatic office measurements: 14 mmHg for systolic BP and 5 mmHg for diastolic BP.[19] And in our experience, an alert reaction is even detected in the first self-measurement by the patient, with an increase of systolic BP.[20]

None of the four groups of BP readings was significantly associated with subclinical organ damage, particularly with urinary albumin excretion or electrocardiographic criteria for left ventricular hypertrophy. It may be that a larger sample size would be needed to detect an association of this type, and this is a limitation of the study. Another potential limitation is the variability of BP measurement given the many investigators and participating centers.

It is known that the masked phenomena are higher in treated hypertensive patients than in untreated. This could be because there are other uncontrolled BP measurement and treatment aspects that could influence the office BP variability and therefore may affect the prevalence of MUCH: the time of office BP measurement, the time of taking the antihypertensive medication, the effect of postprandial hypotension in the elderly, the antihypertensive treatment nighttime noncompliance when ABPM is performed or unrecognized consumption of other drugs or alcohol.[21] However, we suggest that this variability reflects usual clinical practice and that our results are robust.

Conclusions

In conclusion, our results suggest that the first two office BP readings should routinely be discarded and a mean value should be taken from subsequent readings, except for patients whose first reading is <140/90 mmHg, because successive readings were even lower in 90% of cases.

Conflicts of interest

There are no conflicts of interest.

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