CONTRIBUTION TO MASKED HYPERTENSION UNDERSTANDING:
ROLE OF AUTONOMIC CARDIOVASCULAR TESTS

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ABSTRACT

Background: Masked hypertension (mHT) is a frequent and poorly understood clinical form of primary HT but whose pathogenesis is not clear yet. The purpose of this study was to evaluate mHT using cardiovascular autonomic tests contributing to the understanding of this disease. Patients and methods: Inclusion criteria: This prospective study was conducted on 2 groups of 73 patients. Group 1 constituted of 40 Masked hypertensive patients (MHT) with normal office BP and with an impact of HT on heart such as left ventricular hypertrophy (LVH) detected by echocardiography. Group 2 was constituted of 33 Normotensive patients (NT). The cardiovascular autonomic tests performed have included Deep Breathing (DB), Hand-Grip (HG), orthostatic and Mental Stress (MS) tests. Exclusion criteria: the patients with severe HT, secondary or complicated HT, or being under any antihypertensive treatment, or in pregnancy. Results: alpha peripheral sympathetic response obtained on HG test was 27.0±5.4\% in MHT vs 16.4±4.5\% in NT (p<0.001), alpha central sympathetic response obtained during MS was 24.0±7.2\% in MHT vs 15.2±4.5\% in NT (p<0.001) and alpha peripheral adrenergic sympathetic response (Alpha PAS) obtained during OT was 40.4±2.8\% in MHT vs 15.2±3.7\% in NT (p<0.001). A univariate and multivariate logistic regression analysis showed that the odds of mHT increased with sympathetic hyperactivity in patients with mHT. Conclusion: The cardiovascular autonomic reflexes tests have shown a significant high sympathetic response in masked hypertensive patients when compared to normotensive subjects. The present data showed that this high sympathetic activity can be considered as a cardiovascular risk factor.
KEYWORDS: Masked hypertension, cardiovascular autonomic tests, home blood pressure self-measurement, ambulatory blood pressure monitoring.

INTRODUCTION
Hypertension (HT) is the leading cause of cardiovascular morbidity and mortality worldwide.\(^1\)-\(^3\) It’s defined as Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg, measured in supine position.\(^4\) In the recent decades, prevention, detection, and treatment of HT have significantly reduced HT-related mortality and morbidity. The variability of measurement of Blood Pressure (BP) leads up to develop the complementary measurement methods such as Home Blood Pressure Self-Measurement (HBPSM) and Ambulatory Blood Pressure Monitoring (ABPM).\(^5\) During these 15 last years, it has been shown that the basal Blood Pressure (BP) level was better defined by ABPM or by HBPSM than by conventional method in medical settings.\(^5\) Recently, several studies showed, as well for the ABPM than for the HBPSM, that both cardiovascular morbidity and mortality were better predicted by the BP level defined by these methods than by that measured in the medical consultation.\(^5\) The definition of normality of the BP or it’s control with treatment is different in consultation (<140/90 mmHg) and by HBPSM (<135/85 mmHg),\(^6\) the joint use of two different methods of measurement leads up to individualize four groups of patients,\(^5\) the patients whose BP is normal as well in consultation as by HBPSM are considered "normotensives" or "controlled" if taking an anti-hypertensive treatment. The patients whose BP exceeds the thresholds of normality of the two methods were considered as hypertensive or as uncontrolled hypertensive patients. The patients whose BP exceeds the thresholds of normality in consultation but proves normal at home were considered as hypertensive patients in consultation. Finally, those whose BP is normal in consultation but exceeds the thresholds of normality by HBPSM or by ABPM were considered as masked hypertensive patients. It’s important to recognize the Masked Hypertensive Patients (MHT) because their cardiovascular prognosis is as bad as uncontrolled hypertensive patients.\(^7\) In fact, primary HT can be Masked and be responsible of a severe impact on the target bodies. Masked HT (mHT) is a frequent and poorly understood clinical form of primary HT but whose pathogenesis is not clear yet. The purpose of this study was to find an explanation of the mHT using cardiovascular autonomic tests and thus to contribute to the understanding of this disease.
PATIENTS AND METHODS

Patients
All patients were recruited for cardiovascular autonomic testing at the Center for Cardiac Autonomic Studies at the department of cardiology A, University Hospital Center (UHC) Ibn Sina, Rabat, Morocco.

Inclusion Criteria
This prospective study was conducted on a total of 73 patients (68.5% of women and 31.5 % of men), ranging in age from 34 to 74 years (54.3 ± 10.6 years) divided into two groups:

Group 1: N = 40 Masked Hypertensive patients (MHT), mean age 51.6 ± 12.3 years, of which 62.5% were women. The patients with normal office BP and with an impact of HT on heart such as Left Ventricular Hypertrophy (LVH) detected by echocardiography. The LVH secondary to HTA (LVH symmetrical with a remodeling concentric) and interventricular septal thickness higher than 12 mm, detected by echocardiography, and not yet treated.

Group 2: N = 33 Normotensive patients (NT), mean age 49.4 ± 13.2 years, of which 75.8% were women.

Exclusion criteria
The patients with severe HT, secondary or complicated HT, or being under any antihypertensive treatment, or in pregnancy were excluded from the study.

All patients were referred to the unit of exploration of the Autonomic Nervous System (ANS) in the cardiology service A at Ibn Sina Hospital in Rabat during the period ranging from May 2014 to January 2015. The study was approved by the Ethics Committee of Ibn Sina Hospital after a thorough analysis. A written consent form was obtained from each patient before the tests. Each patient completed also a form recording the presence or the absence of functional signs.

The cardiovascular autonomic testing included Deep Breathing (DB), Hand-Grip (HG), orthostatic and Mental Stress (MS) tests were performed.

METHODS
Tests done in all patients included measurement of weight and height, cardio vascular autonomic tests, echocardiography and blood tests. In all patients, cardiovascular
examination, and electrocardiogram were requested, when necessary, others tests such as ABPM, exercise test, coronary catheterization, and scintigraphy were done and these tests were requested in all patients.

Weight and height were measured to calculate the Body Mass Index (BMI) of each subject using the usual formula weight / height$^2$. The result was expressed in kg/m$^2$.

**Cardiovascular autonomic testing**

Patients were initially lied on examination table in a quiet room for at least 30 min. Then monitoring of the BP, using a Dynamap (Critikon, 1846 SXP) and the Heart Rate (HR) (screen of posting LCD CS 503 E, HELLIGE, EK 512 E) was done. All the tests were carried in the morning, at fasting and under no anti-hypertensive treatment during at least 48 hours. The basal systolic BP (SBP) and HR were measured in both arms at rest of at least 10 min, then Ewing cardiovascular autonomic tests.

**Tests Description**

**The Deep Breathing Test (DB)**

This test analyzes the vagal response [8, 9]. The respiratory frequency has an influence on the variation of RR interval on the electrocardiogram (EKG). The procedure was the following: the patient breathes deeply at a frequency of six breaths for one minute [10]. It makes it possible to evaluate the vagal activity which is expressed as a percentage:

$$(RR_{\text{maximal}} - RR_{\text{minimal}}/RR_{\text{minimal}}) \times 100.$$  

**The Isometric Contraction or Hand Grip Test (HG)**

During three minutes the patient performs a manual pressure of 50% of the maximum with assistance of a dynamometer. The muscular contraction involves a rise in BP related to an increase of sympathetic nerve activity at the muscular level that is effort-dependent and time-dependent.[11, 12] The peripheral alpha sympathetic nerve response is given by the increase of the BP.

Alpha peripheral sympathetic response (alpha PS):

$$= (BP_{\text{after the test}} - BP_{\text{before the test}}/BP_{\text{before the test}}) \times 100.$$  

**The Mental Stress Test (SM)**

The patient performs mental arithmetic calculations by removing the number 7 successively from 200. The result is an increase in BP and in HR by activation of the central sympathetic
nerve. In mental stress, the central sympathetic nerves activities “α” was evaluated by measuring the variations of BP as bellow.\(^\text{[11, 12]}\)

Alpha central sympathetic response (alpha SC):

\[
\text{alpha SC} = \left( \frac{\text{BP after stimulation} - \text{BP before stimulation}}{\text{BP before stimulation}} \right) \times 100.
\]

The “β” central sympathetic nerves activities was evaluated by measuring the variations of HR as bellow.\(^\text{[11, 12]}\)

Beta central sympathetic response (beta SC):

\[
\text{beta SC} = \left( \frac{\text{HR after stimulation} - \text{HR before stimulation}}{\text{HR before stimulation}} \right) \times 100.
\]

**The Orthostatic Test (OT)**

The OT is a simple, non invasive and reproducible test included among the cardiovascular ANS tests, involving the measurement of the BP and the HR variation during the upright posture.\(^\text{[13]}\) The basal SBP and HR were measured in both arms after a rest of at least 10 minutes in supine position. Then we proceeded to the OT. Orthostatic SBP (ortho SBP) was recorded for 10 minutes at the rhythm of 3 measurements per minute.

The alpha peripheral adrenergic sympathetic response (Alpha PAS) obtained during OT was evaluated by measuring the variations of BP as bellow:

\[
\text{Alpha PAS} = \left( \frac{\text{BP orthostatic} - \text{BP supine position}}{\text{BP supine position}} \right) \times 100.
\]

**Echocardiographic Detection**

Pathological hypertrophy may be associated with an absence of symptoms for many years before the development of congestive heart failure or unexpected sudden death. Thus, in contemporary clinical practice and population studies, the diagnosis of LVH depends predominantly on echocardiographic measurements or novel noninvasive imaging techniques.

Methods for 2D targeted M-mode echocardiographic measurements of Left Ventricle (LV) dimensions and the calculation of LV mass are standardized.\(^\text{[14]}\) The detection of pathological LVH requires adjustments for sex, height, and body mass. Echocardiographic measurements were performed in accordance with the American Society of Echocardiography, and calculation of LV Mass (LVM) was done using the modified formula of:
LVM (g) = 0.8 x \[1.04 \times (LVID + LVPWT + IVST)^3 - LVID^3\] + 0.6
where LVID indicates LV internal diameter; LVPWT, LV posterior wall thickness; and IVST, intraventricular septal thickness.\[^{[15]}\]

**Blood tests**

Blood tests included Serum glucose, creatinine, triglycerides, High-Density Lipoprotein (HDL) cholesterol (HDL-cholesterol), Low-Density Lipoprotein (LDL) cholesterol (LDL-cholesterol) and uric acid.

Blood samples were collected from an antecubital vein in ethylene-diamine-tetraacetic acid (EDTA)-containing tubes (Miles Pharmaceuticals, Rexdale, Ontario, Canada) after a 12 hours overnight fast. Cholesterol and triglyceride levels were determined in plasma and lipoprotein fractions by the use of a Technicon RA-500 (Bayer, Tarrytown, NY). The HDL fraction was obtained after precipitation of LDL in the infranatant (density >1.006 g/ml) with heparin and MnCl2.

Glycated hemoglobin A\(_1c\) (HbA\(_1c\)) was measured using capillary zone electrophoresis, performed on a Beckman Coulter P / ACE 5000 or P / ACE MDQ (Beckman Coulter, Fullerton, CA).

Serum uric acid was measured by the uricase method.

To estimate renal function, the following equation Cochcroft and Gault was used to determine Creatinine Clearance (CrCl).

\[
CrCl (\text{mL/min}) = K \times [(140 - \text{age (year)}) \times \text{weight (kg)})/\text{creatinine (mg/ml)}], \text{with } k = 1.23 \text{ (if male)} \text{ or } 1.04 \text{ (if female)}.
\]

**Statistical analysis**

Descriptive statistics included the range, mean, and standard deviation for interval variables and the frequency and percentage for categorical variables. Group comparisons were carried out by independent samples Student’s t-test for interval variables and the \(\chi^2\) test for categorical variables, with 95% confidence intervals (CIs) calculated where appropriate. Univariate and multivariate logistic regression analysis were performed to assess the independent association of several variables with mHT. These effects were measured by odds ratios (OR), and their 95% CIs based on logistic regression models. P values were 2 sided and were considered statistically significant if less than 0.05. All analyses were performed using SPSS, version 15.0 (SPSS Inc., Chicago, Il).
RESULTS
Supine mean basal BP was 123.2 ± 9.0 mmHg in MHT vs 110.1 ± 7.6 mmHg in NT. Supine mean basal HR was 68.0 ± 8.6 beats/min in MHT vs 67.6 ± 10.0 beats/min in NT (table I). LVM was 187.3 ± 11.6 g in MHT vs 115.7 ± 13.4 g in NT (p = 0.03). IVST was 13.4 ± 1.2 mm in MHT vs 7.1 ± 2.5 mm in NT (p = 0.001). Cardiovascular autonomic reflexes responses were as follows: vagal response (XDB) obtained during DB was 30.5 ± 10.4% in MHT vs 32.7 ± 11.3% in NT, p = 0.1), alpha peripheral sympathetic response (Alpha PS) obtained on HG test was 27.0 ± 5.4% in MHT vs 16.4 ± 4.5% in NT (p<0.001), alpha central sympathetic response (Alpha CS) and beta central sympathetic response (Beta CS) obtained during MS were, respectively 24.0 ± 7.2% in MHT vs 15.2 ± 4.5% in NT (p<0.001), and 20.8 ± 8.0% in MHT vs 15.8 ± 3.4 % in NT (p=0.03). Alpha peripheral adrenergic sympathetic response (Alpha PAS) obtained during OT was 40.4 ± 2.8% in MHT vs 15.2 ± 3.7% in NT (p < 0.001) (table II).

Logistic regression analysis
Univariate and multivariate logistic regression analysis are in table III. Relationship between supine mHT and response to cardiovascular autonomic tests was made and also between mHT and some independent predictor factors such as, age, BMI, HbA1c value, triglycerides, HDL-cholesterol, LDL-cholesterol, creatinine, creatinine clearance and uric acid after excluding confusing factors.

Univariate logistic regression analysis showed that the odds of mHT increased with alpha peripheral sympathetic response (Alpha PS) (OR = 2.021, 95% CI: 2.001-7.139, P = 0.003), alpha central sympathetic response (Alpha CS) (OR = 1.170, 95% CI: 1.406-3.208, P = 0.006), beta central sympathetic response (Beta CS) (OR = 2.275, 95% CI: 2.002-5.134, P = 0.01) and Alpha peripheral adrenergic sympathetic response (Alpha PAS) (OR = 2.127, 95% CI: 1.125-4.793, P = 0.007) respectively, in MHT.

Multivariate logistic regression analysis showed that the odds of mHT increased with alpha peripheral sympathetic response (Alpha PS) (OR = 1.357, 95% CI: 1.301-3.618, P = 0.034), alpha central sympathetic response (Alpha CS) (OR = 2.380, 95% CI: 2.006-4.278, P = 0.01), beta central sympathetic response (Beta CS) (OR = 1.035, 95% CI: 1.012-3.624, P = 0.033) and Alpha peripheral adrenergic sympathetic response (Alpha PAS) (OR = 1.356, 95% CI: 1.101-3.469, P = 0.01) respectively, in MHT.
Table I: patients and diseases characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MHT (n = 40)</th>
<th>NT (n = 33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.6 ± 12.3</td>
<td>49.4 ± 13.2</td>
<td>0.21</td>
</tr>
<tr>
<td>Range (years)</td>
<td>(34-74)</td>
<td>(36-62)</td>
<td></td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>25(62.5%)/15(37.5%)</td>
<td>25(75.8%)/8(24.2%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Basal SBP (mmHg)</td>
<td>123.2 ± 9.0</td>
<td>110.1 ± 7.6</td>
<td>0.07</td>
</tr>
<tr>
<td>Basal DBP (mmHg)</td>
<td>83.3 ± 12.1</td>
<td>87.6 ± 10.4</td>
<td>0.51</td>
</tr>
<tr>
<td>Basal HR (beats/min)</td>
<td>68.0 ± 8.6</td>
<td>67.6 ± 10.0</td>
<td>0.8</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>187.3 ± 11.6</td>
<td>115.7 ± 13.4</td>
<td>0.03*</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>13.4 ± 1.2</td>
<td>7.1 ± 2.5</td>
<td>0.001*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 ± 3.9</td>
<td>25.7 ± 4.1</td>
<td>0.4</td>
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<tr>
<td>Triglycerides (g/L)</td>
<td>1.4 ± 0.6</td>
<td>1.2 ± 0.8</td>
<td>0.51</td>
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<tr>
<td>Cholesterol total (g/L)</td>
<td>2.10 ± 0.3</td>
<td>2.07 ± 0.44</td>
<td>0.5</td>
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<tr>
<td>HDL-cholesterol (g/L)</td>
<td>0.37 ± 0.004</td>
<td>0.32 ± 0.008</td>
<td>0.08</td>
</tr>
<tr>
<td>LDL-cholesterol (g/L)</td>
<td>1.31 ± 0.33</td>
<td>1.35 ± 0.35</td>
<td>0.34</td>
</tr>
<tr>
<td>Urea (g/L)</td>
<td>0.27 ± 0.004</td>
<td>0.25 ± 0.0017</td>
<td>0.6</td>
</tr>
<tr>
<td>Creatinine (mg/L)</td>
<td>11.4 ± 1.9</td>
<td>11.7 ± 1.6</td>
<td>0.06</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td>81.74 ± 16.7</td>
<td>83.6 ± 17.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Uric acid (mg/L)</td>
<td>45.0 ± 19.1</td>
<td>43.7 ± 15.6</td>
<td>0.07</td>
</tr>
</tbody>
</table>

SBP: Systolic Blood Pressure
DBP: Diastolic Blood Pressure
HR: Heart Rate
LVM: Left Ventricule Mass
IVST: Interventricular Septal Thickness
BMI: Body Mass Index
HDL: High-Density lipoprotein
LDL: Low-density lipoprotein

Values were expressed as mean ± SE, as median [quartiles], and as percentage; * : p significative if < 0.05.

Table II: Cardiovascular autonomic response

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MHT (n = 40)</th>
<th>NT (n = 33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>XDB (%)</td>
<td>30.5 ± 10.4</td>
<td>32.7 ± 11.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Alpha PS (%)</td>
<td>27.0 ± 5.4</td>
<td>16.4 ± 4.5</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Alpha CS (%)</td>
<td>24.0 ± 7.2</td>
<td>15.2 ± 4.5</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Beta CS (%)</td>
<td>20.8 ± 8.8</td>
<td>15.8 ± 3.4</td>
<td>0.03*</td>
</tr>
<tr>
<td>Alpha PAS (%)</td>
<td>40.4 ± 2.8</td>
<td>15.2 ± 3.7</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

vagal response (XDB) obtained during deep breathing, vagal response (XHG), alpha peripheral sympathetic response (Alpha PS) obtained on hand grip test, alpha central sympathetic response (Alpha CS), beta central sympathetic response (Beta CS) obtained
during mental stress and vagal response (XOT) obtained during orthostatic test. Values were expressed as percentage. *: P significative if < 0.05.

**Table III: Evaluation of relationship between masque HT and independent predictor factors by univariate and multivariate logistic regression analyses.** *: P significative if < 0.05.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratios (OR)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (year)</td>
<td>1.012</td>
<td>[0.843-1.053]</td>
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<tr>
<td>Range (years)</td>
<td>0.485</td>
<td>[0.173-1.047]</td>
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<tr>
<td>Sex (F/M)</td>
<td>0.217</td>
<td>[0.077-2.007]</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>1.204</td>
<td>[0.156-4.184]</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>0.823</td>
<td>[0.319-1.754]</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>2.123</td>
<td>[0.573-3.768]</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.716</td>
<td>[0.906-1.126]</td>
</tr>
<tr>
<td>XDB (%)</td>
<td>0.316</td>
<td>[1.117-4.162]</td>
</tr>
<tr>
<td>Alpha PS (%)</td>
<td>2.021</td>
<td>[2.001-4.193]</td>
</tr>
<tr>
<td>Alpha CS (%)</td>
<td>1.710</td>
<td>[1.406-2.208]</td>
</tr>
<tr>
<td>Beta CS (%)</td>
<td>2.275</td>
<td>[2.002-5.134]</td>
</tr>
<tr>
<td>Alpha PAS (%)</td>
<td>2.127</td>
<td>[1.125-4.793]</td>
</tr>
<tr>
<td>Triglycerides (g/l)</td>
<td>0.458</td>
<td>[0.316-1.675]</td>
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<tr>
<td>HDL-cholesterol (g/l)</td>
<td>0.006</td>
<td>[0.0003-3.117]</td>
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<tr>
<td>LDL-cholesterol (g/l)</td>
<td>0.813</td>
<td>[0.662-4.016]</td>
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<tr>
<td>Serum creatinine (mg/l)</td>
<td>0.712</td>
<td>[0.215-1.526]</td>
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<tr>
<td>Creatinine clearance (ml/min)</td>
<td>0.378</td>
<td>[0.246-1.264]</td>
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<tr>
<td>Serum uric acid (mg/l)</td>
<td>0.540</td>
<td>[0.053-1.351]</td>
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</table>

**DISCUSSION**

The purpose of this study was to find an explanation of the mHT. For that purpose, it was interesting to investigate the patients under vagal and sympathetic stimulation, using cardiovascular autonomic testing and thus to contribute to the understanding of this disease.

In the present study, our interest was focused on comparison of the Autonomic Nervous System (ANS) response to stimulation between those with mHT and those with normal BP by using cardiovascular autonomic testing to understand the etiopathogenesis of the mHT.

In this study, we reported a significant difference between MHT and NT in sympathetic response assessed by HG, MS and OT tests respectively. It was significantly higher in MHT than in NT. These findings suggest that mHT was related to the sympathetic system dysfunction, especially to sympathetic hyperactivity. In addition, a univariate and multivariate logistic regression analysis were performed in the present survey to determine
independent predictor factors of mHT in the patients whose mHT was detected. The analysis of the results indicates that alpha peripheral sympathetic (Alpha PS) hyperactivity, alpha central sympathetic (Alpha CS) hyperactivity, beta central sympathetic (Beta CS) hyperactivity, and alpha peripheral adrenergic sympathetic (Alpha PAS) obtained during HG, MS, and OT respectively, were significantly associated with mHT respectively, in patients with mHT. This data suggested that there was a linear association between the occurrence of mHT and these independent predictor factors in this group. A previous study showed that sympathetic hyperactivity might be involved in HT.\[16\] The sympathetic nerve hyperactivity observed in the patients with HT does not act solely on the cardiac system but it reaches also the other target bodies of the ANS.\[18, 19\] The excessive rise in the sympathetic nerve activity increases in an acute way of the BP while being responsible for cardiac, renal, and vascular stimulation by respectively increasing the cardiac flow, the sodium retention, and vascular resistance with hypertrophy of the vascular smooth muscular cells.\[18\] The sympathetic nerve hyperactivity was regarded as a risk factor of coronaropathy, cardiac insufficiency, cerebrovascular accident, and renal vascular attack.\[20\] Autonomic dysregulation plays a significant role in HT and acts as a coronary risk factor by severe metabolic complications.\[21\] In previous study, the microneurography has shown the increased activity of the sympathetic fibers specifically proportional to the severity of the primary HT, but not that of secondary HT. This could help to explain why some metabolic risk factors and some common diseases related with essential HT are not found in secondary HT. Mancia G and al showed that in hypertensive patients, the overactivation of the Sympathetic Nervous System (SNS) could be dependent on the circulating angiotensin II concentrations, because angiotensin II exerts excitatory effects on sympathetic outflow, to facilitate norepinephrine release from adrenergic nerve endings, and to amplify adrenergic receptor responsiveness to stimuli.\[17\] Previous papers showed that spectral analysis techniques provided important information regarding the alterations of the nervous control of primary HT and allowed an increase in sympathetic activity.\[22, 23\]

In this work, we also studied the vagal response between the two groups to know if parasympathetic nervous system was involved in the occurrence of mHT in patients with mHT. There was no significant difference between MHT and NT in parasympathetic response assessed by the DB test. It was normal in both groups. In addition, a univariate and multivariate logistic regression analysis showed that vagal response obtained during DB test
was not associated with mHT in patients with mHT. This data suggests that there was not a
linear association with the occurrence of mHT with decreased vagal in this group.

Several studies have compared office and ambulatory BP, and have found that the correlation
between the two is moderately close, with correlation coefficients in the region of 0.7.\cite{24, 25}
ABPM is a non-invasive method of obtaining BP readings over a 24-hour period, whilst the
patient is in their own environment, representing a true reflection of their BP.\cite{26, 27} The use of
ABPM at home can detect subjects with normal BP clinic but high ambulatory BP correspondent to a mHT. This type of HT is also as bad prognosis as uncontrolled HT.\cite{28}
mHT is a new emerging entity as previous studies have demonstrated that this prognosis joins
that of clinical HT.\cite{29} mHT not only does it occur frequently but by definition it also goes
undetected in consultation. It incurs a high risk of developing into permanent HT over a very
short period of time, which leads to the importance of HBPSM for patients so as to prevent
the risks of heart disease and stroke.\cite{30} However, the clinicians need to use careful clinical
judgment to identify and treat subjects with mHT. AMBP could be interesting at night.
During this period, the patients are at rest, and the measurement of the BP variability is
performed in a homogeneous way in all patients. Nevertheless, during the day, the activities
change from patient to patient, and thus the measurement of the BP variability change from
patient to other one. As a result, it could be difficult to confirm the presence or the absence
of the mHT in these patients. However, by measuring the variability of BP at rest and after
stimulation of the ANS using autonomic cardiovascular tests, the ANS assessment allows to
estimate the degree of both sympathetic and vagal response, which could be related to mHT.

Interestingly, in this study, we also noted that a sympathetic hyperactivity can’t restore the
sympathovagal balance in patients with MHT compared to patients without MHT. These
findings were comparable to the ones of the previous studies, which suggests that
sympathetic activity increases considerably in hypertensive patients.\cite{23, 31} Thus, the MHT
prognosis depends on the reduction of this sympathetic hyperactivity. This protective action
will disappear in patients with mHT.

Accordingly, a univariate and multivariate logistic regression analysis showed that LVM and
IVST were not significantly associated with mHT respectively in MHT.

In this research, we have performed also the blood tests in the two groups. The results have
shown that there was no significant difference between MHT and NT, in HbA$_1c$, in
triglycerides, in HDL-cholesterol, in LDL-cholesterol, in urea, in creatinine, and in uric acid
levels respectively. In addition, a univariate and multivariate logistic regression analysis demonstrated that these blood parameters were not significantly associated with mHT respectively, in patients with mHT, suggesting that the occurrence of mHT was only due to sympathetic hyperactivity in patients with MHT.

All in all, it would be interesting to conduct a further study focusing on a direct comparison that will include all the cardiovascular ANS tests between patients with mHT, patients with sustained HT and normotensive patients. The objective, therefore, was to determine the degree of involvement of the sympathetic nervous system in patients with mHT. To our knowledge, this is the first study focusing on comparison of ANS assessment between patients with mHT and those without mHT.

CONCLUSION
The cardiovascular autonomic reflexes tests have shown a significant high sympathetic response in masked hypertensive patients when compared to normotensive subjects. The present data showed that this high sympathetic activity can be considered as a cardiovascular risk factor. We also demonstrated that the cardiovascular autonomic reflexes can help to diagnose the association masked hypertension-high sympathetic response in patients with masked hypertension which prognosis depended on the reduction of the sympathetic hyperactivity.

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