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Ambulatory blood pressure monitoring: Is it mandatory for blood pressure control in treated hypertensive patients? Prospective observational study

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ABSTRACT

Objective: Twenty-four hour ambulatory blood pressure (ABP) is superior to office blood pressure (BP) in predicting cardiovascular events. However, its use to optimise BP control in treated hypertensive patients is less well examined.
Design and method: In this observational study conducted in 899 general practitioners' offices, 4078 hypertensive patients with uncontrolled office BP were included. Antihypertensive therapy was intensified and after 1 year office BP and 24-hour ABP were measured to categorise patients according to the ESC/ESH 2007 guidelines.
Results: In this cohort (mean office BP 156/90 mm Hg, mean ABP 146/85 mm Hg), 2059 out of 4078 patients (50.5%) had controlled office BP (<140/90 mm Hg) at 1 year examination. Of these apparently controlled patients (N = 2059), 1339 (65.8%) had 24-hour ABP ≥ 130/80 mm Hg, indicating masked hypertension (32.9% of all treated patients). In the prespecified subgroups the prevalence of masked hypertension was the following: diabetes 28.2%, CVD 29.1%, and CKD 32.1%. White coat hypertension (24 h-ABP < 130/80 mm Hg and office BP ≥ 140/90 mm Hg) was found in 12.4% (N = 233) of patients with elevated office BP (6.1% of all treated patients), and in 5.7% of the diabetic subgroup, 5.6% CVD and 7.1% CKD. Discrepancies in BP categorisation between office BP and 24-hour ABP were high; all subjects 52.8%, diabetes 50.0%, CVD 49.0% and CKD 50.4%.
Conclusion: In hypertensive patients on therapy, 2 out of 3 with apparently controlled office BP had masked hypertension, suggesting a more aggressive therapy, and 1 out of 8 with elevated office BP had white coat hypertension potentially falsely forcing physicians to intensify therapy.

The 3A Registry is listed under clinicaltrials.gov, NCT01454583.

1. Introduction

Hypertension is a major risk factor for cardiovascular morbidity and mortality. In epidemiological and clinical studies 24-hour ambulatory blood pressure (ABP) predicted cardiovascular events in untreated and treated hypertensive individuals, including myocardial infarction, sudden death, stroke, new episodes of angina pectoris, congestive heart failure, and peripheral vascular disease, even after adjustment for classic risk factors, including office blood pressure (BP) [1–4].

ABP components that have been related to the risk of cardiovascular events are mean 24-hour ABP, day-time and night-time ABP [5–8]. In particular, night-time BP emerged as the most significant prognostic marker of cardiovascular morbidity and mortality [9,10].

With ABP measurements in addition to office BP readings, it is possible to classify and categorise hypertensive patients. White coat hypertension, defined as hypertensive office BP but normotensive BP under ambulatory conditions and masked hypertension defined as normotensive BP in the office but hypertensive BP in daily life, have been shown to be associated with elevated cardiovascular risk in untreated [11,12] and also in treated hypertensive patients [13]. ABP offers the possibility of evaluating all these different components

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not only for initiation, but especially during follow-up for titration and adaptation of antihypertensive therapy, and is considered as a major criterion for therapeutic success [14]. However, only few data on ABP describe these phenomena of white coat effect and masked hypertensive effect in treated hypertensive patients and data about the prevalence and prognostic relevance are scarce [13].

Since the precondition of an effective BP therapy is the accurate assessment of the BP load, the purpose of the present study was to analyse the prevalence of discrepant categorisation of patients when the criteria for office BP and 24-hour ABP were applied in a large cohort of treated hypertensive patients.

2. Methods

2.1. 3A Registry

The analysis is based on the data of the 3A Registry. The Registry is a prospective, observational, non-interventional, multi-centre registry listed under clinicaltrials.gov, NCT01454583 and the VfA database is a resource for non-interventional studies (http://www.vfa.de/de/arzneimittel-forschung/datenbanken-zu-arzneimitteln/nisdb/nis-details/_616). Details of the study design and baseline data have been published in more detail elsewhere [15].

In brief, consecutive patients with known or newly diagnosed arterial hypertension were eligible for documentation in which the physician had decided independently and per best clinical judgement to initiate (13.8%) or modify antihypertensive therapy (86.2%). The only exclusion criteria were participation in a randomised controlled clinical trial and foreseeable problems to perform follow-up visits. Depending on the initiated medication, 14,988 patients were part of one of the three following study groups:

- 1. Treatment with the direct renin inhibitor aliskiren or
- 2. An ACE inhibitor (ACE-I) or angiotensin receptor blocker (ARB) or
- 3. Agents not blocking the renin–angiotensin-system (Non-RAS).

Reflecting the utilised medication of the three study groups, the registry was called 3A: *A*liskiren, *A*RB/ACE-I and others (in German called "*A*ndere"). Medication was given alone or on top of an existing drug regimen and patients were followed for 1 year. In 13,433 (89.6%) a complete follow-up after 1 year was obtained. In 6139 patients 24-hour ABP monitoring (ABPM) was performed at baseline visit and in 2/3 of these treated hypertensive patients (4078) 24-hour ABPM was repeated in parallel to office BP measurements at the 1 year examination.

The data were collected in web-based format with a standardised questionnaire (electronic case record form, eCRF). Measures of quality control included automated plausibility checks during data entry, queries after data entry, and in 10% of the patients, on-site monitoring with source data verification. All data, if available, were collected during the clinical examination or from the review of the patient's chart. Data were recorded at inclusion (baseline) and during follow-up visits.

2.2. Study cohort

At baseline and at 1 year examination, 4078 hypertensive patients underwent 24-hour ABPM in parallel to office BP measurements. For the analyses of the relationship of office BP and day- and night-time ABP respectively, only patients with the referring complete data set were considered, leading to the following numbers of patients: office BP vs. night-time ABP mean (N = 3798) and office BP vs. day-time ABP mean (N = 3907).

Office BP was assessed with the standard devices available at the physicians' office (manual sphygmomanometers or semi-automated devices), which according to German legislation must have a calibration validation. Furthermore, the German guidance for measuring office BP (sitting position, after 5 min of rest, at least 2 repeated measurements) had to be followed. 24-hour ABPM was also only performed with validated devices (see German guidelines: http://www.hochdruckliga.de/blutdruckmessgeraete-mit-pruefsiegel.html), routinely used in the respective office. Devices were preset from 6:00 to 22:00 h defined as day-time, and from 22:00 to 06:00 h as night-time, respectively, according to the recommendations of the German Hypertension Society. Average of office BP readings and means of 24-hour ABP, day-time ABP and night-time ABP were entered into the database.

2.3. Data analyses

Since at the time of inclusion patients had uncontrolled hypertension and the physician had decided to initiate or intensify antihypertensive therapy, we have selected the 1 year follow-up examination for our analyses when a stable situation, concerning the medication regimen, was achieved. This approach also avoids the bias of any exaggerated white coat effect during the first BP measurement in newly diagnosed hypertensive patients and has the advantage that patients have already been accustomed to 24-hour ABPM.

First we analysed all patients with reported ABP measurement at 1 year examination. Subsequently, patients were divided in predefined subgroups of patients with elevated cardiovascular risk, i.e. diabetes (treated diabetes or HbA1c ≥ 6.5%), cardiovascular disease (CVD) (known history of chronic heart failure, coronary artery disease, peripheral artery disease, cerebrovascular disease) and chronic kidney disease (CKD) (eGFR < 60 ml/min/1.73 m^2 calculated according to the CKD EPI formula which is more accurate than the commonly used MDRD formula [16]). Left ventricular hypertrophy was diagnosed on the basis of ECG criteria by the investigators.

According to the ESC/ESH 2007 guidelines [17], which were the latest guidelines during study performance, patients were categorised into 4 groups according to office BP: controlled office BP (<140/90 mm Hg) and uncontrolled office BP (≥140/90 mm Hg), and according to ABP 24-hour average: controlled ABP (<130/80 mm Hg) and uncontrolled ABP (≥130/80 mm Hg), leading to the general 2×2 categorisation (*used in figures and tables*).

2.4. Statistical methods

Continuous variables were summarised with descriptive statistics (absolute numbers, means, standard deviation, or medians with 25. and 75. percentile as appropriate). Categorical data were described by the number and percentage of subjects in each category. Univariate statistical comparisons between groups were performed by chi square for categorical variables, or Kruskal–Wallis test for continuous measures. Categorisation at baseline and at 1-year follow-up was compared with the Mc Nemar test. Percentages were calculated on the basis of patients with data for each respective parameter (i.e., no percentages for missing values provided). p-Values ≤ 0.05 (two-sided) were considered to be significant. The analysis was performed with SAS 9.2 (SAS Institute, Inc., Cary, NC, USA).

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3. Results

3.1. Patients characteristics

Clinical characteristics of the patients with 24-hour ABPM at 1 year examination (N = 4078) are set out in Table 1. In brief, mean age was 65.3 years, 45.6% were females, office BP was 138 ± 14/81 ± 8 mm Hg and the averages of ABP were for 24-hour 136 ± 13/79 ± 9 mm Hg, day-time 139 ± 13/82 ± 9 mm Hg and night-time 126 ± 15/73 ± 9 mm Hg, respectively, with patients receiving 3.0 ± 1.6 antihypertensive drugs. Of the 4078 patients, 29.4% had diabetes, 32.5% CVD and 20.3% CKD. Not unexpected in light of the nature of this study (registry data analysis), differences in various clinical characteristics were found between patients who had 24-hour ABPM as opposed to those who did not (data not shown). In our paper we refer with respect to data only to those with 24-hour ABPM at 1 year examination.

3.2. Office BP and ABP: BP control concordance

According to the ESC/ESH 2007 guidelines, [17] at 1 year examination 17.6% had controlled BP (office BP < 140/90 mm Hg and 24-hour ABP < 130/80 mm Hg) in the whole study group and 14.3%, 18.6% and 17.9% in the diabetes, CVD and CKD subgroups (Table 2a–2d), respectively.

3.3. Categorisation of patients by office BP and ABP

3.3.1. Whole study group

The percentage of patients with office BP values < 140/90 mm Hg was 50.5% and with 24-hour ABPM average < 130/80 mm Hg 23.7% (Fig. 1a). One third (32.9%) of all the patients, which corresponds to 65.8% of patients who had office BP values < 140/90 mm Hg, showed mean 24-hour ABP values ≥ 130/80 mm Hg, indicating masked hypertension. Thus, overall approximately 1 out of 3 treated hypertensive patients and 2 out of 3 patients with apparently controlled office BP, had masked hypertension. 6.1% of all the patients, corresponding to 12.4% of patients with elevated office BP ≥ 140/90 mm Hg, had mean 24-hour ABP < 130/80 mm Hg, indicating white coat hypertension (i.e. 1 out of 8 treated hypertensive patients) (Fig. 1a).