Sleep Medicine 15 (2014) 1302–1308

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Independent association of obstructive sleep apnea with left ventricular geometry and systolic function in resistant hypertension: the RESIST-POL study

Piotr Dobrowolski [a,*], Anna Klisiewicz [a], Elżbieta Florczak [b], Aleksander Prejbisz [b], Przemysław Bieleń [c], Paweł Śliwiński [c], Marek Kabat [b], Justyna Rybicka [a], Roman Topór-Mądry [d], Andrzej Januszewicz [b,†], Piotr Hoffman [a,†]

[a] Department of Congenital Heart Diseases, Institute of Cardiology, Warsaw, Poland
[b] Department of Hypertension, Institute of Cardiology, Warsaw, Poland
[c] IV Department of Respiratory Medicine, Institute of Tuberculosis and Lung Diseases, Warswa, Poland
[d] Institute of Public Health, Jagiellonian University Collegium Medicum, Faculty of Health Science, Wrocław Medical University, Wrocław, Poland

ARTICLE INFO

Article history:
Received 13 February 2014
Received in revised form 9 June 2014
Accepted 11 June 2014
Available online 19 August 2014

Keywords:
Obstructive sleep apnea
Hypertension
Left ventricular geometry
Left ventricular systolic function
Polysomnography
Echocardiography

ABSTRACT

Objective: We investigated the impact of obstructive sleep apnea (OSA) and night blood pressure (BP) on left ventricular geometry and systolic function in patients with resistant hypertension (RHTN).
Methods and Results: Data from 155 patients with RHTN were analyzed. All patients underwent biochemical evaluations, ambulatory blood pressure monitoring (ABPM), and polysomnography. Left ventricular mass index (LVMI), relative wall thickness (RWT), left ventricular ejection fraction (LVEF), midwall fractional shortening (mwFS) and global longitudinal strain (GLS) were measured. Patients were divided into four groups based on the presence of metabolic syndrome (MS) and OSA: group 1: OSA(–), MS(–) [$n = 42$]; group 2: OSA(+), MS(–) [$n = 14$]; group 3: OSA(–), MS(+) [$n = 46$]; and group 4: OSA(+), MS(+) [$n = 53$]. In group 3 and 4 concentric geometry was present in 53.2% and 79.6% respectively ($P = 0.004$). There were no differences in LVEF between groups. Group 3 and 4 had lower mwFS as compared with group 1 (16.40 ± 1.9 and 15.38 ± 2.2 vs 17.44 ± 1.9; $P < 0.049$ and $P < 0.0001$ respectively). Group 4 had significantly lower GLS as compared with group 1 (-12.64 ± 3.3 vs -15.59 ± 4.0; $P < 0.001$). In the multivariable analysis, factors independently associated with concentric geometry were age, nighttime SBP (OR –1.04; 95%CI 1.019–1.082; $P < 0.0001$) and OSA (OR –3.97; 95%CI 1.835–8.590; $P < 0.0001$). In the other multivariable analysis, factors independently associated with GLS were OSA (beta = 0.279; $P = 0.001$), and nighttime DBP (beta = 0.168; $P = 0.048$) whereas factors independently associated with mwFS were age, gender, nighttime SBP, concentric geometry, and metabolic syndrome.
Conclusions: In patients with true RHTN without diabetes concentric geometry and systolic dysfunction are independently associated with moderate and severe OSA and nighttime BP levels.

1. Introduction

Resistant hypertension (RH), occurring in 12–13% of treated hypertensive subjects, is of major clinical importance since it has been associated with higher cardiovascular risk [1,2]. It has also been shown that patients with RH are characterized by high incidence of target-organ damage, including left ventricular hypertrophy and concentric geometry [3–5].

The most frequently associated condition found in patients with RH is obstructive sleep apnea (OSA), often overlapping with metabolic syndrome (MS) [6]. Concentric geometry is associated with poor prognosis [7]. Several studies have shown that structural changes of left ventricular hypertrophy and concentric geometry are often found in patients with OSA [8,9].

In contrast to studies based on the assessment of left ventricular systolic function by means of ejection fraction [10], studies using speckle-tracking echocardiography (STE) have demonstrated that OSA patients may develop subclinical left ventricle systolic dysfunction [11,12].

We hypothesized that the high frequency of cardiac structure alteration in patients with RH might be related to common coexistence of OSA. We also evaluated whether this relationship is independent of blood pressure levels and frequently overlapping

* Corresponding author at: Department of Congenital Heart Diseases, Institute of Cardiology, Alpejska 42, 04-628 Warsaw, Poland. Tel.: +48 22 3434400; fax: +48 22 3434534.
E-mail address: p.dobrowolski@ikard.pl (P. Dobrowolski).
† Andrzej Januszewicz and Piotr Hoffman are equal senior authors.

http://dx.doi.org/10.1016/j.sleep.2014.06.015
1389-9457/

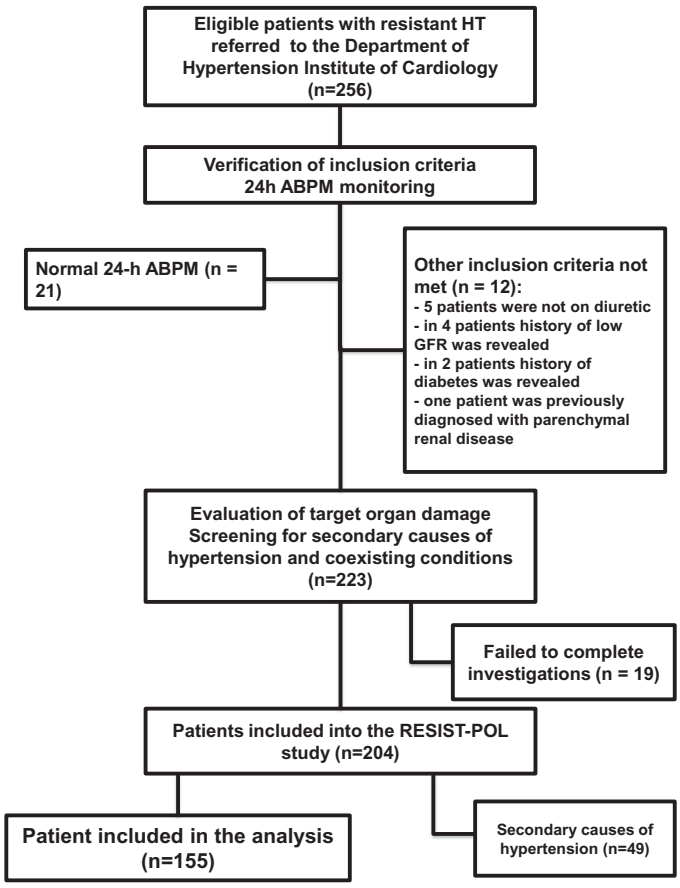

Fig. 1. Flow chart of the study population. HT, hypertension; ABPM, ambulatory blood pressure monitoring; GFR, glomerular filtration rate.

metabolic syndrome. Additionally, we evaluated the impact of OSA in patients with RH on systolic function, employing assessment of more accurate markers of systolic function such as midwall fractional shortening (mwFS) and global longitudinal strain (GLS).

2. Methods

2.1. Study population

Patients were enrolled in the RESIST-POL study in the Department of Hypertension, Institute of Cardiology, Warsaw, Poland between 2009 and 2011. The RESIST-POL study, based on the evaluation of 204 patients with RH, showed a high incidence of OSA and MS. The study revealed that different secondary causes of hypertension, including primary aldosteronism, renal artery stenosis, hyperthyroidism, and renal artery aneurysm were diagnosed in 49 patients (Fig. 1). Since the principle goal of the present study was to evaluate the relationship between OSA and left ventricle morphology and function in patients with RH, all cases with secondary causes of hypertension characterized by other underlying mechanisms that may independently influence the left ventricle structure and blood pressure pattern were ruled out. The inclusion criteria were as follows: age 20–65 years, and RH confirmed in 24 h ambulatory blood pressure monitoring (ABPM) [mean daytime blood pressure (BP) > 135/85 mmHg] while on three antihypertensive drugs in optimal doses (including diuretic). The exclusion criteria were: a history of other cardiovascular diseases (ischemic heart disease, heart failure, transient ischemic attacks and previous stroke), secondary causes of RH (for the purpose of this analysis), decreased estimated glomerular filtration rate <60 mL/min per 1.73 m^2), neoplastic diseases, previous diagnosis of diabetes mellitus, alcohol or medicine addictions, advanced changes in the skeletal system, malignant hypertension, pregnancy, and lack of cooperation or agreement to participation in the study.

It should be emphasized that the analyzed group consists only of patients without factors that may potentially alter morphology and function of the left ventricle, especially in patients with type 2 diabetes mellitus. Therefore patients included in our analysis were characterized as newly diagnosed, never-treated OSA, and by being free of diabetes, severe cardiovascular disorders, chronic kidney disease, and secondary causes of hypertension, thus limiting the influence of other factors on the evaluated relationship between OSA and cardiac structure and function.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. It was approved by the local Research Ethics Committee. Written informed consent was also obtained from each patient.

The full protocol and main results of the RESIST-POL study have been already published. In brief, patients with true RH were screened for coexisting conditions including metabolic abnormalities and OSA, secondary causes of hypertension as well as evaluated for target organ damage. As the methodology of the RESIST-POL study has been described previously, we summarize below the definitions and methods used for the purpose of this analysis [13].

2.2. Office blood pressure measurements

Blood pressure was measured by a trained nurse with a patient in the sitting position after a 5 min rest, using an automated device (Omron 705IT, Omron Co., Kyoto, Japan). Based on the upper arm circumference, an appropriately sized cuff was placed on the arm with the lower edge of the cuff 2 cm above the antecubital fossa. Three consecutive readings were performed. In cases where the difference between readings was >10 mmHg, further measurements were taken so as to obtain three consecutive consistent readings, the average of which was then recorded.

2.3. Ambulatory blood pressure monitoring

In all patients, the ABPM was recorded using Spacelabs 90207 or 90217 (Redmond, WA, USA). Readings were obtained every 15 min during the day (06:00–22:00) and every 30 min during the night (22:00–06:00). Average 24 h, daytime and night-time systolic blood pressure (SBP), daytime and night-time diastolic blood pressure (DBP), and average 24 h heart rate (HR) were analyzed. The nocturnal decrease in BP was quantified as the relative decrease in nocturnal BP for both systolic and diastolic BP: [(daytime pressure – night-time pressure)/daytime pressure] × 100 and expressed as a percentage.

2.4. Polysomnography

All patients irrespective of the symptoms of OSA were evaluated by standard polysomnography with an Alice 5 (Respironics Inc., Murrysville, PA, USA) device. The polysomnographic recordings were scored manually using 30 s epochs following Rechtschaffen and Kales' criteria for sleep and wake determination and sleep staging. Abnormal respiratory events were evaluated according to the standard criteria of the American Academy of Sleep Medicine Task Force [14]. Apnea–hypopnea index (AHI) indicating the number of apneic and hypopneic episodes per hour of sleep was calculated. Clinically significant OSA was diagnosed when AHI was >15.