



Original Article

Poor sleep quality and resistant hypertension



Rosa Maria Bruno^{a,d}, Laura Palagini^{b,*}, Angelo Gemignani^c, Agostino Virdis^d, Alessia Di Giulio^d, Lorenzo Ghiadoni^d, Dieter Riemann^e, Stefano Taddei^d

^a Institute of Clinical Physiology-CNR, Pisa, Italy

^b Department of Neuroscience, Sleep Center, University of Pisa, Via Roma 67, 56100 Pisa, Italy

^c Department of Surgical, Medical, and Molecular Pathology and of the Critical Area, University of Pisa, Pisa, Italy

^d Department of Clinical and Experimental Medicine, University of Pisa, Via Roma 67, 56126 Pisa, Italy

^e Department of Psychiatry and Psychotherapy, Freiburg University Medical Center, Freiburg, Germany

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ABSTRACT

Objectives: We aimed to determine the relationship between sleep quality and treatment-resistant hypertension (RH).

Methods: In our cross-sectional cohort study, 270 consecutive essential hypertensive patients were recruited at the Outpatient Hypertension Unit, University of Pisa, Italy. The Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI-Y2) were administered to all subjects. RH was defined as office blood pressure (BP) >140/90 mmHg with three or more antihypertensive drugs or controlled BP with four or more drugs. Poor sleep quality was defined as PSQI >5, depressive symptoms as BDI >10, and trait anxiety as STAI-Y2 >40. Patients with other sleep disorders were excluded.

Results: Complete data were available for 222 patients (50.9% men; mean age, 56.6 ± 12.5 y; RH, 14.9%). Poor sleep quality had a prevalence of 38.2% in the overall population. RH was associated with poor sleep quality, increased sleep latency and reduced sleep efficiency. No significant relationship was found between RH and short sleep duration or depressive symptoms and trait anxiety. Poor sleep quality was more prevalent in resistant vs nonresistant hypertensive women (70.6% vs 40.2%; $P = .02$) but not in resistant vs nonresistant men (43.8% vs 29.2%; $P = .24$). In women poor sleep quality was an independent predictor of RH, even after adjustment for cardiovascular and psychiatric comorbidities (odds ratio [OR], 5.3 [confidence interval {CI}, 1.1–27.6], explaining 4.7% of its variance. In men age, diabetes mellitus (DM), and obesity were the only variables associated with RH.

Conclusions: Poor sleep quality is significantly associated with resistance to treatment in hypertensive women, independent of cardiovascular and psychiatric confounders.

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1. Introduction

There is growing evidence of a relationship between sleep disorders and cardiovascular disease. In particular, sleep disorders are linked through several pathophysiologic mechanisms to cardiovascular risk factors, such as hypertension, diabetes mellitus (DM), and obesity, thus increasing the incidence of cardiovascular events [1,2]. This relationship is well-established for obstructive sleep apnea syndrome (OSAS) [3], but it also has been suggested for other sleep disorders such as insomnia and short sleep duration [4]. Indeed both insomnia and short sleep duration have been associated with increased prevalence and incidence of hypertension

and cardiovascular events [4–7]. In a cross-sectional population-based study, insomnia and short sleep duration were independently associated with a higher prevalence of hypertension, which further increased in the presence of both conditions [8]. Prospective studies also provided evidence of increased incidence of new-onset hypertension in subjects with insomnia or short sleep duration [5,6], though the relationship was attenuated or nonsignificant after considering confounding factors [4]. The question of causality between disordered sleep and cardiovascular disease is obscured by the fact that a variety of cardiovascular risk factors and psychiatric disorders might simultaneously contribute to both insomnia and hypertension [9–11], making it difficult to unravel if an independent cause-effect relationship that exists between these two conditions. Furthermore, the relationship appears to be gender-specific, being more prevalent in women than in men [12].

The role of global sleep quality in hypertension severity is even less established. In particular, the condition of resistant hyperten-

* Corresponding author. Address: Department of Neuroscience, Sleep Center, University of Pisa, Via Roma 67, 56126 Pisa, Italy. Tel.: +39 050 993165; fax: +39 050 992656.

E-mail addresses: lpalagini@tiscali.it, lpalagini@ao-pisa.toscana.it (L. Palagini).

sion (RH) is of interest, as it identifies a nonnegligible percentage of patients with a more severe form of hypertension, higher cardiovascular risk, and negative prognosis [13].

Thus we hypothesized that poor sleep quality or short sleep duration might be associated with increased hypertension severity. Accordingly, the aim of our study was to investigate the prevalence and features of poor sleep quality in a population of patients accessing a Hypertension Outpatient Unit for the first time, to assess if RH is associated with poor sleep quality or short sleep duration. Moreover, the role of gender and cardiovascular and psychiatric comorbidities in the relationship between RH and sleep quality also was evaluated.

2. Methods

2.1. Patients

Starting in May 2011, 270 consecutive patients attending their first visit to the Hypertension Outpatient Unit of the University Hospital of Pisa, Italy were enrolled. Inclusion criteria were age of >18 years, written informed consent, and diagnosis of essential arterial hypertension according to current guidelines [14]. Criteria of exclusion were: known or suspected (according to clinical judgment) secondary hypertension, including drug-induced hypertension; hypertension in pregnancy; previous diagnosis of OSAS or restless legs syndrome (RLS); severe chronic heart failure or hepatic insufficiency; end-stage renal disease; and active neoplastic disease. On the basis of these inclusion and exclusion criteria, 436 patients were screened to enroll 270 patients, with a rate of acceptance of 61.9%. Furthermore, patients with a score of 1 or more on item 10 of the Pittsburgh Sleep Quality Index (PSQI), regarding self-reported symptoms or symptoms reported by the patient's roommate that were compatible with OSAS or RLS (i.e., snoring), were excluded from the analysis after enrollment.

The study conformed to the Declaration of Helsinki and was approved by the local Ethical Committee. All patients provided written informed consent prior to entering the study.

2.2. Measurements

After enrollment, patients were asked to come to the Hypertension Outpatient Unit after an overnight fasting period. A blood sample was drawn for routine examination (e.g., lipid profile, blood fasting glucose, serum creatinine, urinalysis), determined according to standard laboratory procedures. Hypercholesterolemia and DM were defined according to current guidelines [15,16] or in the presence of current lipid-lowering or glucose-lowering treatment, respectively. Glomerular filtration rate was estimated using the Modification of Diet in Renal Disease formula, and chronic kidney disease was defined as glomerular filtration rate <60 mL/min/1.73 m².

Office blood pressure (BP) was measured at the brachial level in the sitting position by a trained physician, with the patients resting for at least 10 min under quiet environmental conditions. BP measurement was repeated at least three times at 2-min intervals using an automatic oscillometric device (OMRON-705IT, Omron Corporation, Kyoto, Japan). Average BP was then calculated for the last two measurements. On this basis of these measurements, RH was defined as office BP >140/90 mmHg with three or more antihypertensive drugs or controlled BP with four or more drugs, including a diuretic, according to current guidelines [13,14]. Weight and height were measured and a complete clinical examination was performed; obesity was defined as a body mass index (BMI) >30 kg/m².

Medical and pharmacologic history was recorded to identify cardiovascular risk factors and disease. Habitual physical activity was defined as brisk walking or sports activities for at least 1 h per week. Current use of cardiovascular and psychiatric drugs also was recorded.

2.3. Questionnaires

2.3.1. Pittsburgh Sleep Quality Index

The PSQI is a widely used, self-rated, standardized questionnaire assessing sleep quality in the previous month [17]. The 19 questions are grouped in seven component scores, each exploring a different sleep feature; the sum yields a global PSQI score used to define poor sleep quality when >5. On the basis of the sleep duration component of the PSQI score, self-reported short sleep duration was defined as <6 h of sleep per night. The following PSQI-derived data also were analyzed: increased sleep latency (>30 min), reduced sleep efficiency (<85%), sleep disturbance (sleep disturbances component score >1), and daytime dysfunction due to sleepiness (daytime dysfunction component score >1).

2.3.2. Beck Depression Inventory

To consider the frequent comorbidity of sleep disorders with depression, the Beck Depression Inventory (BDI) was administered. The BDI is a 21-question inventory for self-assessment and is one of the most widely used instruments for measuring the severity of depression. The presence of depressive symptoms was defined with a BDI score >10 [18,19].

2.3.3. State-Trait Anxiety Inventory

To consider the frequent comorbidity of sleep disorders with anxiety, trait anxiety was assessed using the State-Trait Anxiety Inventory (STAI-Y2) and was defined as a score >40 [20].

2.4. Statistical analysis

Statistical analysis was performed using NCSS 2008 (NCSS: Kaysville, Utah, USA). For normally distributed data, results were expressed as mean ± standard deviation (SD), whereas median value and 25% to 75% interquartile range were used for abnormally distributed data. Differences in means between groups were analyzed using analysis of variance for normally distributed variables or the Kruskal–Wallis *z* test for abnormally distributed variables; categorical variables were analyzed using the χ^2 test. Questionnaire results and cardiovascular risk factors were expressed as binary discrete variables to build multiple logistic regression models including RH as a dependent variable. We analyzed the effects of age, gender, and of a panel of cardiovascular (e.g., previous cardiovascular events, DM, obesity) and psychiatric comorbidities (e.g., psychiatric medications use, depressive symptoms, anxiety) as well as of short sleep duration, chosen according to a significant association with RH in our population or in previous studies. Chronic kidney disease was not inserted in the model, despite significant association with RH for high collinearity correlation with DM. For the same reason, menopause status could not be considered as a confounding factor (resistant hypertensive women were 100% in postmenopause). The analysis was then stratified by gender.

3. Results

Among the 270 patients enrolled, those with self-reported (or reported by roommate) sleep apneas, snoring, and leg restlessness (*n* = 35) or with incomplete data (*n* = 13) were excluded. The final

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