

The effect of tension variability for sleep quality in headache patients

A Holter monitoring study

Esen Çiçekli, MD^{a,*} , Ender Emre, MD^b

Abstract

Background: Hypertension is one of the common causes of headaches. Disruption in the circadian rhythm of blood pressure (BP) also leads to some chronic diseases. Sleep disturbances have a relationship with neurologic and cardiac diseases. Our aim was to compare the sleep quality of patients with headaches showing dipper and nondipper BP patterns.

Methods: This retrospective study included 57 patients who applied to a neurology clinic due to headaches and were referred to the cardiology department for Holter monitoring. Chronic diseases, drugs used, smoking and exercise habits, and physical examination findings were recorded. The 24-hour Holter monitoring results were classified as dipper and nondipper. The Pittsburgh Sleep Quality Index scores were determined for each patient. The Pittsburgh Sleep Quality Index scores of patients with dipper and nondipper patterns were compared.

Results: The sleep quality of patients with dipper Holter patterns was better than that of patients with nondipper patterns ($P < .001$), and patients without chronic diseases had significantly better sleep quality compared with those with chronic diseases ($P = .029$). In the presence of chronic disease, the number of patients with a nondipper Holter pattern was higher ($P = .024$). There were no significant differences in Holter results or sleep quality between smokers and nonsmokers ($P > .05$).

Conclusion: Diagnoses of sleep disorders and BP abnormalities in the outpatient clinic are valuable in increasing the quality of life of patients and in preventing chronic diseases, especially cardiac diseases that may develop in the future.

Abbreviations: ABP = ambulatory blood pressure, BP = blood pressure, HPA = hypothalamus-pituitary-adrenal, PSQI = the pittsburgh sleep quality index, SNS = sympathetic nervous system.

Keywords: ambulatory blood pressure monitoring, dipper, hypertensive headache, nondipper, sleep quality

1. Introduction

Headache is one of the most common complaints of patients presenting to outpatient clinics. There are lots of underlying mechanisms of headache. Hypertension is a common cause when investigating the etiology of headaches. The relationship between elevated blood pressure (BP) and headache has long been acknowledged in the medical literature.^[1] Headache attributed to arterial hypertension is a secondary headache disorder of hemostasis according to the third edition of the International Classification of Headache Disorders.^[2,3]

Headaches attributed to arterial hypertension are generally bilateral and pulsatile. They are acute in onset and related to an abrupt rise in systolic BP of ≥ 180 mm Hg or diastolic BP of ≥ 120 mm Hg. This type of headache resolves once the BP is normalized.^[2-4]

After establishing patient's clinical history and physical examination, the clinician can work through the differential diagnosis

to establish the most likely cause of the acutely elevated BP and subsequent headache.^[5]

It is not always possible to detect high BP during the first examination of the patient. Increased BP, especially at night, can cause headaches and sleep disturbances. Therefore, more advanced examination methods are needed to diagnose the increased BP.

Ambulatory BP monitoring studies using noninvasive monitoring devices have demonstrated the presence of a distinct circadian rhythm, whereby BP falls during the nighttime sleep period. A normal healthy circadian BP profile includes a nighttime BP dip of 10% or more. In contrast, a nondipping circadian BP profile, typically defined as a $<10\%$ fall in average BP from daytime to nighttime, is a strong indicator of increased risk of cardiovascular morbidity and mortality for both hypertensive and normotensive individuals.^[6,7]

The relationship between headache and sleep disorders has been recognized in the literature for more than a century.

Informed written consent was obtained from all participants, and the study protocol was approved by the Ethics Committee of Sakarya University (reference number E-71522473-050.01.04-47674-405).

The authors have no funding and conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article (and its supplementary information files). The datasets generated during and/or analyzed during the current study are publicly available.

^a Department of Neurology, Akyazı State Hospital, Sakarya, Turkey, ^b Department of Cardiology, Ahi Evren Chest and Cardiovascular Surgery Education and Research Hospital, Trabzon, Turkey.

*Correspondence: Esen Çiçekli, Department of Neurology, Akyazı State Hospital, Batakköy, 54400 Sakarya, Turkey (e-mail: esencirit@gmail.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Çiçekli E, Emre E. The effect of tension variability for sleep quality in headache patients: a Holter monitoring study. *Medicine* 2022;101:30(e29876).

Received: 18 October 2021 / Received in final form: 31 May 2022 / Accepted: 8 June 2022

<http://dx.doi.org/10.1097/MD.00000000000029876>

The first observations about this association were made by Romberg^[8] in 1853. Some headache disorders are seriously influenced by sleep, with a group of them occurring exclusively in relation to sleep. Conversely, headache disorders can affect sleep.^[9]

In addition, sleep disturbances have been associated with coronary diseases, stroke, diabetes mellitus, and with or without sleep apnea.^[10]

The objective of this study was to compare dipper and nondipper patients with headache in terms of sleep quality, as well as the effects of health conditions such as chronic diseases, obesity, and exercise/smoking habits on sleep quality.

2. Materials and Methods

Ethics committee approval for this study was obtained from the Sakarya University Faculty of Medicine's Ethics Committee with decision number E-71522473-050.01.04-47674-405.

2.1. Participants

Participants included 24 men and 33 women. Patients who applied to the neurology clinic due to headache and were referred to cardiology for Holter monitoring were included in this study.

Exclusion criteria were body mass index of $>40\text{ kg/m}^2$, age of <18 years or >75 years, patients with cardiac or neurological diseases, current use of psychiatric or cardiovascular medications, previously diagnosed obstructive sleep apnea, oral contraceptive use, pregnancy, hormone replacement therapy, alcohol or drug abuse within the last 12 months, renal or hepatic dysfunction, and dementia.

2.2. Ambulatory blood pressure monitoring

Twenty-four-hour ambulatory BP (ABP) was assessed in the cardiology clinic for each participant. ABP was measured with the Bravo 24-HR ABP monitor (SunTech Medical, Morrisville, NC), which was validated previously. The monitor was programmed to take BP measurements every 20 minutes throughout the waking hours and every 30 minutes during the nighttime sleep period.

2.3. Subjective sleep quality

The Pittsburgh Sleep Quality Index (PSQI) was used to assess subjective sleep quality. The PSQI is a 19-item self-rated questionnaire for evaluating subjective sleep quality over the previous month.^[11] The PSQI provides a global subjective sleep quality score ranging from 0 to 21, with higher scores indicating worse sleep quality. A score >5 points indicate poor sleep quality. All participants' PSQI scores were recorded.

2.4. Statistical analysis

Statistical analysis of the data was carried out using SPSS 15.0 software (IBM, Chicago, IL). All results were reported as the mean \pm standard deviation. One way analysis of variance followed by Student's *t* test was conducted to compare statistical differences among the groups at a 5% significance level.

3. Results

There were 57 patients in our study, including 24 males and 33 females. The mean age of these patients was 43.2 ± 12.3 years. The mean age of the men was 45.6 ± 13.4 , and the mean age of the women was 41.5 ± 11.4 . There was no statistically significant difference in terms of the mean ages of men and

women ($P = .218$). In this study, 29 of the patients had no chronic diseases, while 28 had chronic diseases. Twenty of the 57 patients in the study were smokers. Twenty of the patients were exercising regularly, at least 3 days a week. The median PSQI score of patients was 6.4 ± 2.8 . The Holter results of 27 patients were dipper, whereas 30 patients were nondipper (Table 1).

PSQI levels of the patients with nondipper Holter results were found to be significantly higher than those with dipper results ($P < .001$). In patients with nondipper Holter results, the rate of chronic disease, the rate of nonexercise, and the rate of those with PSQI >5 were significantly higher than those with dippers ($P = .024$, $P = .002$, and $P < .001$, respectively). There was no statistically significant difference between the patients whose Holter result was dipper nondipper in terms of mean age, gender, and smoking ($P > .05$) (Table 2).

A statistically significant positive correlation was found between the PSQI score and the age of the patients ($P = .008$). The PSQI scores of the patients with chronic disease were significantly higher compared with that of patients without chronic diseases ($P = .029$). Patients who exercised had significantly lower PSQI scores than those who did not exercise ($P = .008$). Similarly, PSQI scores of dippers were significantly lower than that of nondippers ($P < .001$) (Table 3).

The rate of having chronic disease, hypertension, and nondipper Holter result in the patients with PSQI >5 was significantly higher than those with PSQI ≤ 5 ($P = .010$; $P = .044$; $P < .001$) (Table 4).

To examine the factors affecting the PSQI level, age and Holter results were found to be statistically significant factors in the model created from the variables with $P < .250$ in univariate analyzes ($P = .016$; $P = .001$) (Table 5).

In the model created from the variables with $P < .250$ in univariate analyzes to identify patients with PSQI >5 , nondipper Holter results were found to be a statistically significant factor compared with dipper ones ($P = .003$) (Table 6).

4. Discussion

In our study, we found that patients with dipper Holter results had better sleep scores. Recent studies are consistent with our findings where dippers were characterized by better subjective sleep quality than nondippers.^[7] In our study, the sleep scores of the patients who did not have a chronic disease and who

Table 1
Patient characteristics.

| | |
|--|----------------------------|
| Gender | |
| Female | 33 (57.9%) |
| Male | 24 (42.1%) |
| Age, mean \pm SD (min–max/median) | 43.2 \pm 12.3 (20–67/41) |
| Chronic disease | |
| None | 29 (50.9%) |
| Hypertension | 23 (40.4%) |
| Diabetes mellitus | 5 (8.8%) |
| Coronary artery disease | 2 (3.5%) |
| Obesity | 4 (7.0%) |
| Hyperlipidemia | 1 (1.8%) |
| Hyperthyroidism | 1 (1.8%) |
| Smoker | 20 (35.1%) |
| Exercise | 20 (35.1%) |
| PSQI score, mean \pm SD (min–max/median) | 6.4 \pm 2.8 (2–12/6) |
| PSQI | |
| ≤ 5 | 24 (42.1%) |
| > 5 | 33 (57.9%) |
| Holter | |
| Dipper | 27 (47.4%) |
| Nondipper | 30 (52.6%) |

PSQI = Pittsburgh sleep quality index; SD = standard deviation.

Table 2
Comparison of the characteristics of dipper and nondipper patients.

| Patient characteristics and PSQI results | Holter | | P |
|--|--------------|-----------------|-----------------|
| | Dipper n (%) | Nondipper n (%) | |
| Age, mean ± SD | 42.3 ± 13.1 | 44.1 ± 11.8 | .572 |
| Gender | | | |
| Female | 17 (63.0) | 16 (53.3) | .462 |
| Male | 10 (37.0) | 14 (46.7) | |
| Chronic disease | | | |
| Hypertension | 9 (33.3) | 19 (63.3) | .024 |
| Diabetes mellitus | 8 (29.6) | 15 (50.0) | .118 |
| CAD | 3 (11.1) | 2 (6.7) | .660 |
| Obesity | 0 (0.0) | 2 (6.7) | .492 |
| Hyperlipidemia | 2 (7.4) | 2 (6.7) | 1.000 |
| Hyperthyroidism | 1 (3.7) | 0 (0.0) | .474 |
| Smoker | 0 (0.0) | 1 (3.3) | 1.000 |
| Exercise | 9 (33.3) | 11 (36.7) | .792 |
| None | 12 (44.4) | 25 (83.3) | .002 |
| Yes | 15 (55.6) | 5 (16.7) | |
| PSQI, median (IQR) | 4 (3–6) | 7.5 (6–9) | <.001 |
| PSQI | | | |
| ≤5 | 18 (66.7) | 6 (20.0) | <.001 |
| >5 | 9 (33.3) | 24 (80.0) | |

Statistically significant values are bold.
IQR = interquartile range; PSQI = Pittsburgh Sleep Quality Index; SD = standard deviation.

Table 3
The relationship between the Pittsburgh Sleep Quality Index score of the patients with age and the comparison of the Pittsburgh Sleep Quality Index score in the patient characteristics.

| Patients characteristics and Holter results | PSQI | P |
|---|-----------------------|-----------------|
| | Median (IQR) | |
| Age | $P = .008; r = 0.347$ | |
| Gender | | |
| Female | 6 (4.5–8) | .801 |
| Male | 6.5 (3–9) | |
| Chronic disease | | |
| None | 5 (3.5–8) | .029 |
| Yes | 7 (5.25–9.75) | |
| Hypertension | | |
| None | 5 (4–8) | .063 |
| Yes | 6 (5–10) | |
| Smoker | | |
| None | 6 (4–8.5) | .321 |
| Yes | 7 (5–8.75) | |
| Exercise | | |
| None | 7 (5–9) | .008 |
| Yes | 4.5 (3–6) | |
| Holter | | |
| Dipper | 4 (3–6) | <.001 |
| Nondipper | 7.5 (6–9) | |

Statistically significant values are bold.
IQR = interquartile range; PSQI = Pittsburgh Sleep Quality Index.

exercised regularly were better. Previous studies have shown that exercise has an anti-inflammatory effect by reducing circulating pro-inflammatory cytokines, and with this mechanism, it has a positive effect on sleep.^[12]

Short sleep duration has been investigated in the context of chronic diseases. Many diseases such as hypertension, diabetes mellitus, coronary artery disease, obesity, and hyperlipidemia have been associated with short sleep duration and poor sleep quality.^[13–16] Sleep influences the 2 primary effector systems, the

Table 4
Comparison of characteristics of patients with the Pittsburgh Sleep Quality Index ≤5 and >5.

| Patient characteristics | PSQI | | P |
|-------------------------|-------------|-------------|-----------------|
| | ≤5 n (%) | >5 n (%) | |
| Age, mean ± SD | 39.7 ± 11.9 | 45.9 ± 12.2 | .061 |
| Gender | | | |
| Female | 13 (54.2) | 20 (60.6) | .627 |
| Male | 11 (45.8) | 13 (39.4) | |
| Chronic disease | | | |
| Hypertension | 7 (29.2) | 21 (63.6) | .010 |
| Diabetes mellitus | 6 (25.0) | 17 (51.5) | .044 |
| Coronary artery disease | 1 (4.2) | 4 (12.1) | .385 |
| Obesity | 0 (0.0) | 2 (6.1) | .504 |
| Hyperlipidemia | 1 (4.2) | 3 (9.1) | .631 |
| Hyperthyroidism | 1 (4.2) | 0 (0.0) | .421 |
| Smoker | 1 (4.2) | 0 (0.0) | .421 |
| Exercise none | 7 (29.2) | 13 (39.4) | .424 |
| Holter | | | |
| Nondipper | 13 (54.2) | 24 (72.7) | .147 |
| Dipper | 6 (25.0) | 24 (72.7) | <.001 |

Statistically significant values are bold.
PSQI = Pittsburgh Sleep Quality Index; SD = standard deviation.

Table 5
Multivariate linear regression analysis of factors affecting the Pittsburgh Sleep Quality Index score.

| Factors | B | Beta | P |
|--------------------------|--------|--------|-------------|
| Constant | -0.242 | | |
| Age | 0.068 | 0.298 | .016 |
| Chronic disease | 0.184 | 0.033 | .881 |
| Hypertension | 0.268 | 0.047 | .825 |
| Exercise | -0.466 | -0.079 | .551 |
| Holter | 2.358 | 0.420 | .001 |
| Dependent variable: PSQI | | | |

$R^2 = 0.367$. Statistically significant values are bold.
PSQI = Pittsburgh Sleep Quality Index.

Table 6
Multivariate logistic regression analysis of factors identifying patients with the Pittsburgh Sleep Quality Index >5.

| Factors | P | OR (95% CI) |
|--------------------------------|-------------|--------------------|
| Age | .080 | 1.06 (0.99–1.12) |
| Chronic disease | .193 | 6.60 (0.39–113.13) |
| Hypertension | .566 | 0.44 (0.03–7.25) |
| Exercise none | .306 | 0.43 (0.08–2.18) |
| Holter (ref: dipper) nondipper | .003 | 9.10 (2.16–38.43) |

Hosmer and Lemeshow test Chi-square: 3.535; $P = .831$; Cox & Snell R square: 0.292.
Statistically significant values are bold.
CI = confidence interval; OR = odds ratio.

hypothalamus-pituitary-adrenal axis and the sympathetic nervous system, which in turn regulate adaptive and innate immune responses. Chronic sleep disorder leads to activation of hypothalamus-pituitary-adrenal and sympathetic nervous system pathways. This results in an increased proinflammatory response.^[17,18]

Aging is associated with a reduced ability to initiate and maintain sleep.^[19] It may be related to the decrease in nocturnal melatonin secretion with age.^[20]

In support of this, there was a positive correlation between age and sleep scores in our study. The sleep quality of the patients tended to deteriorate with increasing age.

Chronic diseases, especially hypertension, and a lifestyle without exercise were more common in nondipper patients. Previous studies have clearly shown an association between a nondipper pattern and increased cardiovascular disease risk in hypertensive patients.^[21,22] Additionally, previous studies have suggested that normotensive individuals with nondipper patterns have increased target organ damage.^[23,24] Endothelial dysfunction and increased inflammatory markers, which are candidate mechanisms of atherosclerosis, were found in nondipper patients. As a result, an increase was detected in diseases with proinflammatory process and endothelial destruction, especially cerebrovascular diseases, cognitive destruction, and atherosclerotic diseases.^[25]

Smokers are more likely to experience sleep problems and poor sleep quality.^[26–28] However, we found no difference in sleep quality between smokers and nonsmokers. Sleep disturbances are often associated with conditions such as respiratory problems, sleep apnea, obesity, heart diseases, and various chronic diseases caused by smoking. Since we excluded most of these conditions at the beginning of the study, no difference could be found between smoking and sleep quality.

With the early diagnosis and treatment of sleep disorders, the life quality of patients increases. Sleep disorders can be a precursor to some chronic diseases, including cardiac and neurologic diseases. In addition to the relationship between hypertension and headache, asking patients with headaches about their sleep quality and examining risk factors will be helpful in preventing chronic diseases that may develop in the future. The results of this study suggest that patients with a nondipper pattern and poor sleep quality should be closely monitored by clinicians.

Our study was conducted with a small group of patients and retrospectively. These are among the limitations of our study. Patients suspected of hypertensive headache were included in our study. Headache grouping of the patients was not made. As the study was retrospective, patients were not grouped according to the severity of the headache. Also, no control group was included. These are the other limitations of our study. There is a need for more comprehensive and larger studies examining the relationship between BP, sleep, and headache and including sleep laboratory data in the future.

In conclusion, headache is one of the most common diseases seen in the neurology outpatient clinic and its association with hypertension is common. Both headache and hypertension are factors that impair sleep quality. High BP and circadian variability are closely related to sleep quality, and the disruption of this circadian rhythm impairs patients' quality of life and paves the way for future diseases. In our study, we found a significant relationship between impaired sleep quality and impaired circadian BP. We think that early diagnosis of sleep disorders in the outpatient clinic is an important factor in preventing chronic diseases that may occur.

Author contributions

Esen Çiçekli: Designing the study, collecting data, writing the article, statistical analysis of the data, making corrections. Ender Emre: Data collection, interpretation of holter monitoring results of patients, writing of the article.

References

- [1] Janeway T, CA. clinical study of hypertensive cardiovascular disease. *Arch Intern Med.* 1913;12:755–98.
- [2] Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia.* 2018;38:1–211.
- [3] Finocchi C, Sassos D. Headache and arterial hypertension. *Neurol Sci.* 2017;38(Suppl. 1):67–72.
- [4] Lagman-Bartolome AM, Gladstone J. Metabolic headaches. *Neurol Clin.* 2014;32:451–69.
- [5] Arca KN, Halker Singh RB. The hypertensive headache: a review. *Curr Pain Headache Rep.* 2019;23:30.
- [6] Sherwood A, Hill LK, Blumenthal JA, et al. The effects of ambulatory blood pressure monitoring on sleep quality in men and women with hypertension: dipper vs. nondipper and race differences. *Am J Hypertens.* 2019;32:54–60.
- [7] Lo K, Woo B, Wong M, et al. Subjective sleep quality, blood pressure, and hypertension: a meta-analysis. *J Clin Hypertens (Greenwich).* 2018;20:592–605.
- [8] Romberg M. *A Manual of the Nervous Diseases of Man.* London, UK: Sydenham Society; 1853.
- [9] Ferini-Strambi L, Galbiati A, Combi R. Sleep disorder-related headaches. *Neurol Sci.* 2019;40(Suppl. 1):107–13.
- [10] McDermott M, Brown DL, Chervin RD. Sleep disorders and the risk of stroke. *Expert Rev Neurother.* 2018;18:523–31.
- [11] Buysse DJ, Reynolds CF 3rd, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28:193–213.
- [12] Abd El-Kader SM, Al-Jiffri OH. Aerobic exercise modulates cytokine profile and sleep quality in elderly. *Afr Health Sci.* 2019;19:2198–207.
- [13] Dashti HS, Scheer FA, Jacques PF, et al. Short sleep duration and dietary intake: epidemiologic evidence, mechanisms, and health implications. *Adv Nutr.* 2015;6:648–59.
- [14] Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *J Hypertens.* 2010;28:896–902.
- [15] Chaput JP, Després JP, Bouchard C, et al. Association of sleep duration with type 2 diabetes and impaired glucose tolerance. *Diabetologia.* 2007;50:2298–304.
- [16] Nedeltcheva AV, Scheer FA. Metabolic effects of sleep disruption, links to obesity and diabetes. *Current Opinion in Endocrinology, Diabetes and Obesity.* 2014;21:293–8.
- [17] Vgontzas AN, Fernandez-Mendoza J, Liao D, et al. Insomnia with objective short sleep duration: the most biologically severe phenotype of the disorder. *Sleep Med Rev.* 2013;17:241–54.
- [18] Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. *Annu Rev Psychol.* 2015;66:143–72.
- [19] Mander BA, Winer JR, Walker MP. Sleep and human aging. *Neuron.* 2017;94:19–36.
- [20] Gursoy AY, Kiseli M, Caglar GS. Melatonin in aging women. *Climacteric.* 2015;18:790–6.
- [21] Palagini L, Bruno RM, Gemignani A, et al. Sleep loss and hypertension: a systematic review. *Curr Pharm Des.* 2013;19:2409–19.
- [22] Hermida RC, Ayala DE, Mojón A, et al. Blunted sleep-time relative blood pressure decline increases cardiovascular risk independent of blood pressure level—the “normotensive non-dipper” paradox. *Chronobiol Int.* 2013;30:87–98.
- [23] Wang C, Zhang J, Liu X, et al. Reversed dipper blood-pressure pattern is closely related to severe renal and cardiovascular damage in patients with chronic kidney disease. *PLoS One.* 2013;8:e55419.
- [24] Jennersjö PE, Wijkman M, Wiréhn AB, et al. Circadian blood pressure variation in patients with type 2 diabetes—relationship to macro- and microvascular subclinical organ damage. *Prim Care Diabetes.* 2011;5:167–73.
- [25] von Känel R, Jain S, Mills PJ, et al. Relation of nocturnal blood pressure dipping to cellular adhesion, inflammation, and hemostasis. *J Hypertens.* 2004;22:2087–93.
- [26] Cohrs S, Rodenbeck A, Riemann D, et al. Impaired sleep quality and sleep duration in smokers—results from the German Multicenter Study on Nicotine Dependence. *Addict Biol.* 2014;19:486–96.
- [27] Jaehne A, Unbehaun T, Feige B, et al. How smoking affects sleep: a polysomnographical analysis. *Sleep Med.* 2012;13:1286–92.
- [28] McNamara JP, Wang J, Holiday DB, et al. Sleep disturbances associated with cigarette smoking. *Psychol Health Med.* 2014;19:410–9.