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INSOMNIA WITH OBJECTIVE SHORT SLEEP DURATION AND INCIDENT HYPERTENSION: THE PENN STATE COHORT

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Abstract

Insomnia with objective short sleep duration appears to be a biologically more severe phenotype of the disorder. No longitudinal study to date has examined the association of this type of insomnia with incident hypertension using polysomnography. From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years and 786 did not have hypertension at baseline. Hypertension was determined by a self-report of receiving treatment for high blood pressure. Chronic insomnia was defined as a complaint of insomnia lasting ≥ 1 year, while poor sleep was defined as moderate-to-severe sleep difficulties. All subjects underwent 8-hour polysomnography. Sleep disordered breathing (SDB) was defined as an obstructive apnea/hypopnea index ≥ 5. We used the median polysomnographic percent of sleep time to define short sleep duration (i.e., < 6 hours). We controlled for gender, race, age, caffeine, cigarettes, alcohol consumption, depression, SDB, diabetes, obesity, and blood pressure in our analyses. Compared to normal sleepers who slept ≥ 6 hours, the highest risk for incident hypertension was in chronic insomniacs with short sleep duration (OR= 3.8, 95% CI=1.6–9.0). The risk for incident hypertension in poor sleepers with short sleep duration was significantly increased but became marginally significant after controlling for obesity (OR= 1.6, 95% CI=0.9–2.8). Chronic insomnia with short sleep duration is associated with an increased risk for incident hypertension in a degree comparable to SDB. Objective short sleep duration in insomnia may serve as a useful predictor of the biological severity of the disorder.

Keywords

Insomnia; Polysomnography; Hypertension; Incidence

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CONFLICT(S) OF INTEREST/DISCLOSURE(S)
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INTRODUCTION

Approximately 30% of the United States population has hypertension, which is associated with significant morbidity and increased mortality and great economic cost.[1] A large amount of literature has linked sleep disorders, particularly sleep disordered breathing (SDB), to hypertension.[2–4] However, insomnia, which is the most prevalent sleep disorder,[5] is traditionally associated with impaired occupational performance, increased work absenteeism, higher health care costs, and worse quality of life,but not with significant cardiovascular morbidity, i.e., hypertension risk. This leads some clinicians to view insomnia and the associated complaints of poor physical health as obsessions of otherwise healthy individuals.

Few studies that examined the association of insomnia with hypertension have reported modest and inconsistent effects.[6–11] More recent studies that used objective measures of sleep have shown that insomnia with objective short sleep duration is associated with significant morbidity, including hypertension,[12] diabetes,[13] and neurocognitive deficits,[14] and mortality,[15] suggesting that objective short sleep duration may be a marker of the biological severity of the disorder[16,17] and that insomniacs with short sleep duration are at high risk for adverse medical outcomes. A limitation of these previous studies is that they were cross-sectional and did not provide causality in terms of the direction of the association.

No study to date has examined whether insomnia with objective short sleep duration is associated with the development of hypertension. To test this hypothesis, we examined the joint effect of the complaints of chronic insomnia and poor sleep and objective sleep duration on the incidence of hypertension in a large, random, general population sample. We hypothesized that chronic insomnia is associated with a significant risk of incident hypertension, and that the association of chronic insomnia and incident hypertension is enhanced by objective short sleep duration.

METHODS

Participants

The data presented here were collected as part of a population-based study of sleep disorders, which used a two-phase protocol in order to recruit participants from various age groups.[10,18–21] In the first phase of the study, telephone interviews were conducted with 4,364 age-eligible men and 12,219 age-eligible women residing in the sample households, for a total sample of 16,583 with response rates of 73.5% and 74.1%, respectively. In the second phase of this study, a subsample of 741 men and 1,000 women, selected randomly from the first phase, were studied in our sleep laboratory, with response rates of 67.8% and 65.8%, respectively. After giving a complete description of the study to the subjects, written informed consent was obtained. Of the 1741 subjects who completed the sleep lab evaluation, 1395 subjects were followed up after an average duration of 7.5 years via telephone interview. The response rate of the follow-up study was 79.7%. After complete description of the follow-up study to the subjects, verbal informed consent was obtained. The whole study procedure was approved by the University's Institutional Review Board. Please see http://hyper.ahajournals.org for Online Data Supplements detailing the sampling procedure and the participant flow in the study.

Definition of Incident Hypertension

For the purpose of this study, the presence of hypertension at baseline was defined by a self-report of receiving treatment for high blood pressure, based on a standardized questionnaire completed by the subjects on the evening of their sleep laboratory visit. Commensurate with

the baseline definition, hypertension at follow-up was defined by a self-report of receiving treatment for high blood pressure. Of the 1395 subjects who were followed-up, 786 did not have hypertension at baseline and were selected for the present study. A total of 191 subjects were incident cases of hypertension while 595 did not have hypertension at follow-up. Twenty subjects had missing data on hypertension at follow-up.

Sleep Laboratory Evaluation

All subjects were evaluated for one night in the sleep laboratory in sound-attenuated, light- and temperature-controlled rooms. During this evaluation, each subject was continuously monitored for eight hours (fixed-time period) using 16-channel polysomnography (PSG) including electroencephalogram, electrooculogram, and electromyogram. Bedtimes were adjusted to conform to subjects' usual bedtimes, and subjects were recorded between 22:00–23:00 and 06:00–07:00. The sleep recordings were subsequently scored independently, according to Rechtschaffen and Kales criteria.[22] Percent of sleep time is total sleep time divided by recorded time in bed and multiplied by 100. From the objectively recorded sleep time data, we regrouped the entire study sample into two ordinal groups: the top 50% of persons above the median percent of sleep time ("longer sleep duration group"), and the 50% of persons in the bottom half ("short sleep duration group"). We then rounded the cutoff point to meaningful numbers and thus created the following two sleep duration groups: the "longer sleep duration group" consisted of those who slept ≥6 h (i.e., percent of sleep time ≥75%), and the "short sleep duration group" of those who slept <6 h (i.e., percent of sleep time <75%). This cutoff point has been shown in previous cross-sectional studies to be predictive of significant medical morbidity and mortality.[12–15] Respiration was monitored throughout the night by use of thermocouples at the nose and mouth and thoracic strain gauges. All-night recordings of hemoglobin oxygen saturation (SpO_2) were obtained with an oximeter attached to the finger. For the purpose of this study, the presence of SDB was defined as an obstructive apnea/hypopnea index (OHI) ≥ 5.[18,19] Body mass index (BMI) was based on measured height (cm) and weight (kg) during the subjects' sleep laboratory visit. Furthermore, blood pressure (BP) was measured in the evening, about 2 hours before the start of the sleep recording, using a pneumoelectric microprocessor-controlled instrument with the appropriate sized cuffs. The accuracy of this monitor is reported to be ± 3 mm Hg; in addition, internal calibration was performed before each use, and the machine was checked against a mercury sphygmomanometer at least annually. The recorded BP was the average of 3 consecutive readings during a 5-min period following 10 min of rest in the supine position. Based on these baseline BP measurements, a normal BP status was defined as systolic BP < 120 mm Hg and diastolic BP < 80 mm Hg, a pre-hypertensive BP status as systolic BP ≥ 120 and < 140 mm Hg and/or diastolic BP ≥ 80 and < 90 mm Hg, and a hypertensive BP status as systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg. BP measurements were not taken at follow-up.

Insomnia and Other Measurements

As part of the standardized questionnaire we also assessed the presence of all sleep disorders. The presence of sleep difficulty was established on three levels of severity. First, *chronic insomnia* was defined by a complaint of insomnia with a duration of ≥1 year. Second, *poor sleep* was defined as a moderate to severe complaint of difficulty falling asleep, difficulty staying asleep, early final awakening, or non-restorative sleep. Finally, *normal sleep* was defined as the absence of either of these two categories. In order to create three mutually exclusive categories, none in the poor sleep group reported having chronic insomnia and none in the normal sleeping group reported either chronic insomnia or poor sleep. Please see the Online Data Supplements for baseline characteristics of these three groups.

Additional information obtained from the standardized questionnaire included assessing other physical health conditions, depression, and substance use. The presence of diabetes at baseline was defined as a self-report of receiving treatment for diabetes or having a fasting blood sugar ≥126 mg/dl from blood drawn the morning after the subject's PSG. We also ascertained at baseline whether the respondent was currently treated for depression, including a history of suicidal thoughts or attempts. Participants' daily consumption of caffeine (number of cups/day), tobacco (number of cigarettes/day), and alcohol (number of drinks/day) was also assessed at baseline.

Follow-up measures taken through telephone interview included the standardized questionnaire that subjects completed at baseline during their sleep laboratory visit. Physical health questions were used to establish the presence of hypertension at follow-up.

Statistical Analyses

The design of this study included oversampling of those at higher risk for SDB and women with markedly higher BMI to increase the precision of the risk estimates. Because of this sampling strategy, numeric sampling weights were developed for the analysis so that the estimates could be inferred to the original target population.[18,19,21,23] We adjusted for the sampling weight in all of our statistical analyses, including those estimating the rate of incident hypertension. Please see the Online Data Supplements for details of the sampling weights.

Logistic regression models were used to assess the independent associations of the three-level sleep complaints and objective sleep duration with incident hypertension. The covariables we adjusted for included major confounding factors expected to affect this relation (i.e., gender, race, age, caffeine, cigarettes, and alcohol consumption, depression, SDB, diabetes, and obesity). We further tested the interaction between sleep complaints and objective sleep duration using the likelihood ratio test in logistic regression models. Because of the significant interaction between sleep complaints and objective sleep duration, we performed final logistic regression models to include five dummy variables to represent all six possible combinations of sleep complaints and objective sleep duration; we used normal sleepers with objective sleep duration ≥ 6 h as a common reference group. We calculated the odds ratios (OR) and the 95% confidence intervals (95%CI) from this model to estimate the risk of hypertension incidence associated with different combinations of sleep complaints and objective sleep duration, simultaneously adjusting for gender, race, age, caffeine, cigarettes, and alcohol consumption, depression, SDB, diabetes, obesity, and baseline SBP/DBP status. Please see the Online Data Supplements for more details. All analyses were conducted with IBM SPSS version 20.0 for Windows.

RESULTS

The overall incidence of hypertension was 18.0%. Table 1 presents the demographic, sleep, and clinical characteristics of the entire sample and stratified by the presence of hypertension at follow-up. As presented in Table 1, univariate analyses showed that chronic insomnia (p=.004) and objective short sleep duration (p=.003) were both significantly associated with incident hypertension, whereas poor sleep was not (p=.756).

The three sets of multivariable logistic regression models that examined the association of the three-level sleep difficulty alone or the two-level objective sleep duration alone with incident hypertension, after progressively adjusting for potential confounders, are presented in Table 2. Chronic insomnia was associated with a significantly higher risk for hypertension that was changed slightly as we increased the number of confounding factors that we adjusted for (OR ranged from 2.66, 95%CI = 1.45–4.88, p = .002, in the first model

to OR = 2.24, 95% CI = 1.19–4.19, p = .010, in the last model). In contrast, poor sleep was not associated with a significant increased risk for incident hypertension. Objective short sleep duration (i.e., < 6 h) was associated with a non-significant increased risk for incident hypertension after controlling for confounding factors (ORs across the three models were all about 1.3 and none of the 95% CIs excluded 1.00). As predicted, we found a statistically significant interaction between sleep difficulty and objective sleep duration on hypertension risk (OR=4.10, 95% CI=1.15–14.5, p=.029 for chronic insomnia and OR=3.36, 95% CI=1.42–7.94, p=.006 for poor sleep).

The logistic regression results presented in Table 3 examined the joint effect of sleep difficulty and objective sleep duration on incident hypertension. The odds ratios and the 95% confidence intervals presented in Table 3 estimated the risk of incident hypertension associated with different combinations of sleep difficulty and objective sleep duration, simultaneously adjusting for gender, race, age, caffeine, cigarettes, and alcohol consumption, depression, SDB, diabetes, obesity, and baseline SBP/DBP status. The risk for incident hypertension was synergistically and significantly increased among persons with both chronic insomnia or poor sleep and short sleep duration. Chronic insomnia with objective short sleep duration increased the risk for incident hypertension by about 4-fold (OR=3.75, 95% CI = 1.58–8.95, p = .012) compared to the group of normal sleepers who slept objectively ≥ 6 hours. For those subjects who complained of poor sleep and had short sleep duration, the joint effect on hypertension was OR = 1.80, 95% CI = 1.04–3.12, p = .036; however, this association became marginally significant after controlling for obesity (OR=1.62, 95% CI = 0.92–2.83, p = 0.09). In contrast, in subjects with a complaint of chronic insomnia or poor sleep who slept objectively ≥ 6 hours, the risk for hypertension was not significantly increased (see Table 3). The results remained significant, and the odds ratios very similar to those reported in Table 3 after we adjusted for hypnotic use and periodic limb movements at baseline.

DISCUSSION

This is the first study to demonstrate that chronic insomnia with objectively measured short sleep duration is a clinically significant risk factor for the development of hypertension. This increased risk is independent of comorbid conditions frequently associated with insomnia or hypertension, such as age, race, obesity, diabetes, smoking, caffeine, or alcohol consumption, SDB, and depression. Our findings provide further evidence that objective measures of sleep duration in insomnia may be a useful marker of the biological severity and medical impact of the disorder.

Few studies have assessed the association of insomnia with incident hypertension, and the results are inconsistent and modest. In a prospective, population-based study that included 8,757 participants, endorsement of either difficulty falling asleep or waking up repeatedly predicted a slightly increased risk of hypertension (OR = 1.2).[6] In that study, the investigators controlled for age, gender, smoking, diabetes, depression, and other comorbid conditions, but did not obtain objective measures of sleep or severity and chronicity of insomnia. In another prospective study, persistent (>4 years) complaints of difficulty initiating or maintaining sleep were associated with an increased risk of hypertension (OR = 1.96).[8] A recent prospective study found that insomnia severity in middle-aged subjects was associated with an increased risk of incident hypertension, and that insomnia possibly acted as a mediator of the relationship between depression and incident hypertension.[11] The stronger association found in these latter studies between insomnia and hypertension may be explained by the addition of severity and/or chronicity in their definition of insomnia. However, in these studies no polysomnographic measures were obtained and, therefore, the

potential confounder of SDB was not controlled for and the role of objective short sleep duration as a marker of the biological severity of the disorder was not examined.

In our study, the group with chronic insomnia, i.e., complaint of insomnia ≥1 year, was associated with a significant risk for incident hypertension (OR = 2.2), whereas the group with poor sleep, i.e., moderate-to-severe insomnia symptoms, was not associated with an increased risk for hypertension. When we introduced the criterion of objectively measured short sleep duration in the definition of insomnia, we showed a strong and significant joint effect on the association of insomnia with the incidence of hypertension. Chronic insomniacs who slept <6 h had 3.8 higher odds of developing hypertension than subjects who slept ≥6 h and had no sleep difficulties. In contrast, chronic insomniacs who slept ≥6 h did not show an increased risk for incident hypertension compared to the control group. Subjects with poor sleep had a significantly higher risk for incident hypertension when they slept <6 h (OR = 1.8) when compared to the control group; however, this increased risk became non-significant after controlling for obesity (OR=1.6). Thus, both chronicity of the disorder and objective short sleep duration, as a marker of a biologically more severe phenotype of insomnia, appear to have a strong effect on the association between insomnia and the development of hypertension.

Our findings on the additive or synergistic effect of insomnia and objective sleep duration on incident hypertension are consistent with previous reports that insomnia with short sleep duration is associated with hypercortisolemia,[16,17,24] increased sympathetic activity (e.g., increased catecholaminergic activity, 24-h metabolic rate, heart rate, and impaired heart rate variability)[25–29] and adverse impact on health (e.g., hypertension, type 2 diabetes, neurocognitive deficits, and mortality).[12–15] Also, a recent study showed that nighttime systolic BP was higher and day-to-night systolic BP dipping was lower in chronic insomniacs as compared to good sleeper controls.[30] Based on the data that insomnia is associated with physiological hyperarousal,[16,17,24–29] we speculated in our previous cross-sectional study that the most likely direction was that insomnia leads to hypertension.[12] This is consistent with previous longitudinal studies showing that hypertension is not a significant risk factor for the development of insomnia.[31, 32] Thus, the results of the present study further support the proposal that insomnia with objective short sleep duration is a premorbid, modifiable risk factor for hypertension.

In our study we found that chronic insomniacs or poor sleepers who slept more than 6 hours showed no or even a reduced risk for incident hypertension. This finding is consistent with our recent findings suggesting that poor sleep and chronic insomnia with normal sleep duration are not associated with cardiometabolic morbidity or mortality.[12–15]

In our previous studies, PSG-measured sleep duration was a strong predictor of HPA axis hyperactivity and medical morbidity among insomniacs.[12–17] However, PSG involves significant expense and efforts, tends to disturb a subject's sleep ("first night effect") and due to night-tonight variability of the subject's sleep, multiple night recordings are required to obtain a representative sample of an individual's typical habitual sleep duration and pattern.[33–35] More recently, night-to-night variability assessed with actigraphy for 1–2 weeks, has been indicated as a very useful marker of the severity of insomnia, i.e., there is significant increase in the night-tonight variability among chronic insomniacs than among the controls.[36] There was also a significant adverse association between intra-individual variability in sleep duration and fragmentation and psychosocial and physiological indices of stress, reflected as increased nighttime secretion of catecholamines.[36,37] These studies suggested the potential usefulness of other objective measures of sleep such as average sleep duration or night-to-night variability obtained with actigraphy for a period of days or weeks in the "habitual home environment"[38], which is impossible with traditional PSG.

The data on the association of insomnia with hypertension, as well as previous reports on insomnia and the stress system[16,17,24,25] and the autonomic system,[26–29] provide the basis for a meaningful phenotyping of chronic insomnia based on objective duration of sleep. One phenotype, the more biologically severe type of insomnia, is associated with physiological hyperarousal, i.e., short sleep duration, activation of the stress system, and significant medical sequelae, e.g., hypertension. The other phenotype, a less biologically severe form of insomnia, is not associated with physiological hyperarousal, i.e., normal sleep duration, normal activity of the stress system, and lack of significant medical sequelae.

Some limitations should be taken into account when interpreting our results. First, incident hypertension was defined by self-report and not by BP measurements. However, insomnia with objective short sleep duration remained strongly and significantly associated with incident hypertension even after controlling for baseline pre-hypertensive and hypertensive BP status. Moreover, two sensitivity analyses were performed. We entered SBP and DBP in two separate models as continuous variables, and the pattern of associations (data not shown) was very similar to that reported in Model 3. Also, we excluded individuals with baseline SBP ≥ 140 and/or DBP ≥ 90 and the pattern of associations (data not shown) remained very similar to that reported in Model 3. In addition, other large epidemiological studies have used self-reports to ascertain incident hypertension.[11] Thus, the consistency of the present findings with those of cross-sectional studies on the association of insomnia with objective short sleep duration and hypertension[12] and impaired heart rate variability[28,29] increases our confidence about the replicability of the present findings. Future studies should explore the association between insomnia, objective short sleep duration, and incident hypertension using BP monitoring at follow-up. Second, the objective sleep duration in this study was based on one night of polysomnography, which may not be representative of the subjects' habitual sleep duration. However, in our previous studies, the association between objective sleep duration and hypercortisolemia was based on a four consecutive night sleep laboratory protocol, which should represent better the typical sleep profile of the subjects.[16,17] The consistency of the findings on the role of objective sleep duration in predicting insomnia severity between these physiological studies with multiple night recordings and the current epidemiological study based on a single night recording increases our confidence about the replicability and generalizability of the present findings. Future studies should explore the association between insomnia, sleep duration, and hypertension using multiple night recordings. Finally, we performed further analyses to address the question whether receiving treatment for hypertension at follow-up relatively improved the sleep of chronic insomniacs and perhaps decrease their insomnia-related cardiovascular risk (see the Online Data Supplements for details). In fact, we found that a higher percent of those who persisted with chronic insomnia reported being treated for hypertension, which reinforces our findings that severe, persistent insomnia is a premorbid risk factor for incident hypertension.

PERSPECTIVES

In summary, insomnia with short sleep duration is associated with a high risk for the development of hypertension to a degree comparable with the other most common sleep disorder, i.e., SDB.[2–4] Given the high prevalence of insomnia in the general population and the widespread misconception of a disorder of the "worried well", its detection and diagnosis should become the target of public health policy. It appears that insomnia with objective short sleep duration may represent a biologically more severe phenotype of insomnia that may respond differentially to treatment. Finally, because polysomnographic measures of sleep are inconvenient and expensive, there is a need for validation of practical, easy to use, inexpensive methods to measure sleep duration outside of the sleep laboratory.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Writing Group Members; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics--2012 Update: A Report From the American Heart Association. Circulation. 2012; 125:e2–e220. [PubMed: 22179539]
2. Young T, Peppard P, Palta M, Hla KM, Finn L, Morgan B, Skatrud J. Population-based study of sleep-disordered breathing as a risk factor for hypertension. Arch Intern Med. 1997; 157:1746–1752. [PubMed: 9250236]
3. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Leiby BE, Vela-Bueno A, Kales A. Association of hypertension and sleep-disordered breathing. Arch Intern Med. 2000; 160:2289–2295. [PubMed: 10927725]
4. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD, Pickering TG. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. JAMA. 2000; 283:1829–1836. [PubMed: 10770144]
5. National Institutes of Health. NIH state of the science statement on manifestations and management of chronic insomnia in adults. J Clin Sleep Med. 2005; 1:412–421. [PubMed: 17564412]
6. Phillips B, Mannino DM. Do insomnia complaints cause hypertension or cardiovascular disease? J Clin Sleep Med. 2007; 3:489–494. [PubMed: 17803012]
7. Phillips B, Bůzková P, Enright P. Cardiovascular Health Study Research Group. Insomnia did not predict incident hypertension in older adults in the cardiovascular health study. Sleep. 2009; 32:65–72. [PubMed: 19189780]
8. Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. J Occup Health. 2003; 45:344–350. [PubMed: 14676413]
9. Janson C, Lindberg E, Gislason T, Elmasry A, Boman G. Insomnia in men a 10-year prospective population based study. Sleep. 2001; 24:425–430. [PubMed: 11403527]
10. Bixler EO, Vgontzas AN, Lin HM, Vela-Bueno A, Kales A. Insomnia in Central Pennsylvania. J Psychosom Res. 2002; 53:589–592. [PubMed: 12127176]
11. Gangwisch JE, Malaspina D, Posner K, Babiss LA, Heymsfield SB, Turner JB, Zammit GK, Pickering TG. Insomnia and sleep duration as mediators of the relationship between depression and hypertension incidence. Am J Hypertens. 2010; 23:62–69. [PubMed: 19893498]
12. Vgontzas AN, Liao D, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective short sleep duration is associated with a high risk for hypertension. Sleep. 2009; 32:491–497. [PubMed: 19413143]
13. Vgontzas AN, Liao D, Pejovic S, Calhoun S, Karataraki M, Bixler EO. Insomnia with objective short sleep duration is associated with type 2 diabetes: A population-based study. Diabetes Care. 2009; 32:1980–1985. [PubMed: 19641160]

14. Fernandez-Mendoza J, Calhoun S, Bixler EO, Pejovic S, Karataraki M, Liao D, Vela-Bueno A, Ramos-Platon MJ, Sauder KA, Vgontzas AN. Insomnia with objective short sleep duration is associated with deficits in neuropsychological performance: a general population study. Sleep. 2010; 33:459–465. [PubMed: 20394314]
15. Vgontzas AN, Liao D, Pejovic S, Calhoun S, Karataraki M, Basta M, Fernández-Mendoza J, Bixler EO. Insomnia with short sleep duration and mortality: the Penn State cohort. Sleep. 2010; 33:1159–1164. [PubMed: 20857861]
16. Vgontzas AN, Tsigos C, Bixler EO, Stratakis CA, Zachman K, Kales A, Vela-Bueno A, Chrousos GP. Chronic insomnia and activity of the stress system: a preliminary study. J Psychosom Res. 1998; 45:21–31. [PubMed: 9720852]
17. Vgontzas AN, Bixler EO, Lin HM, Prolo P, Mastorakos G, Vela-Bueno A, Kales A, Chrousos GP. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications. J Clin Endocrinol Metab. 2001; 86:3787–3794. [PubMed: 11502812]
18. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. Am J Respir Crit Care Med. 1998; 157:144–148. [PubMed: 9445292]
19. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, Kales A. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001; 163:608–613. [PubMed: 11254512]
20. Waksberg J. Sampling methods for random digit dialing. J Am Stat Assoc. 1978; 73:40–46.
21. Kish, L. Survey sampling. New York: John Wiley & Sons, Inc; 1965.
22. Rechtschaffen, A.; Kales, A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Bethesda, MD: National Institutes of Health; 1968.
23. U.S. Department of Health and Human Services (DHHS), National Center for Health Statistics. Third National Health and Nutrition Examination Survey, 1988–1994. NHANES III laboratory data file. Hyattsville, MD: Centers for Disease Control and Prevention; 1996.
24. Rodenbeck A, Cohrs S, Jordan W, Huether G, Rüther E, Hajak G. The sleep-improving effects of doxepin are paralleled by a normalized plasma cortisol secretion in primary insomnia. Psychopharmacology (Berl). 2003; 170:423–428. [PubMed: 13680082]
25. Irwin M, Clark C, Kennedy B, Christian Gillin J, Ziegler M. Nocturnal catecholamines and immune function in insomniacs, depressed patients, and control subjects. Brain Behav Immun. 2003; 17:365–372. [PubMed: 12946658]
26. Stepanski E, Glinn M, Zorick F, Roehrs T, Roth T. Heart rate changes in chronic insomnia. Stress Med. 1994; 10:261–266.
27. Bonnet MH, Arand DL. 24-hour metabolic rate in insomniacs and matched normal sleepers. Sleep. 1995; 18:581–588. [PubMed: 8552929]
28. Bonnet MH, Arand DL. Heart rate variability in insomniacs and matched normal sleepers. Psychosom Med. 1998; 60:610–615. [PubMed: 9773766]
29. Spiegelhalder K, Fuchs L, Ladwig J, Kyle SD, Nissen C, Voderholzer U, Feige B, Riemann D. Heart rate and heart rate variability in subjectively reported insomnia. J Sleep Res. 2011; 20:137–145. [PubMed: 20626615]
30. Lanfranchi PA, Pennestri MH, Fradette L, Dumont M, Morin CM, Montplaisir J. Nighttime blood pressure in normotensive subjects with chronic insomnia: implications for cardiovascular risk. Sleep. 2009; 32:760–766. [PubMed: 19544752]
31. Singareddy R, Vgontzas AN, Fernandez-Mendoza J, Liao D, Calhoun S, Shaffer ML, Bixler EO. Risk factors for incident chronic insomnia: a general population prospective study. Sleep Med. 2012; 13:346–353. [PubMed: 22425576]
32. Fernandez-Mendoza J, Vgontzas AN, Bixler EO, Singareddy R, Shaffer ML, Calhoun SL, Karataraki M, Vela-Bueno A, Liao D. Clinical and polysomnographic predictors of the natural history of poor sleep in the general population. Sleep. 2012; 35:689–697. [PubMed: 22547895]
33. Buysse DJ, Ancoli-Israel S, Edinger JD, Lichstein KL, Morin CM. Recommendations for a standard research assessment of insomnia. Sleep. 2006; 29:1155–1173. [PubMed: 17040003]
34. Wohlgemuth WK, Edinger JD, Fins AI, Sullivan RJ. How many nights are enough? The short-term stability of sleep parameters in elderly insomniacs and normal sleepers. Psychophysiology. 1999; 36:233–244. [PubMed: 10194970]

35. Scharf MB, Bixler EO, Kales A. Readaptation to the sleep laboratory. Psychophysiology. 1975; 12:412–415. [PubMed: 169540]

36. Buysse DJ, Cheng Y, Germain A, Moul DE, Franzen PL, Fletcher M, Monk TH. Night-to night sleep variability in older adults with and without chronic insomnia. Sleep Med. 2010; 11:56–64. [PubMed: 19962939]

37. Mezick EJ, Matthews KA, Hall M, Kamarck TW, Buysse DJ, Owens JF, Reis SE. Intra-individual variability in sleep duration and fragmentation: associations with stress. Psychoneuroendocrinology. 2009; 34:1346–1354. [PubMed: 19450933]

38. Lichstein KL, Steon KC, Donaldson J, Nau SD, Soeffing JP, Murray D, Lester KW, Aguillard RN. Actigraphy validation with insomnia. Sleep. 2006; 29:232–239. [PubMed: 16494091]

NOVELTY AND SIGNIFICANCE: 1) WHAT IS NEW, 2) WHAT IS RELEVANT?

What Is New?

- Although insomnia is a highly prevalent sleep disorder, it has not been consistently associated with significant cardiovascular morbidity.
- There is a lack of longitudinal studies examining the association between insomnia and incident hypertension and none has included objective measures of sleep to evaluate the biological severity of insomnia.

What Is Relevant?

- Insomnia is highly prevalent in the outpatient practice of general practitioners such as family doctors, internists, and cardiologists.
- Severe chronic insomnia is a risk factor for new-onset hypertension.
- Physicians should become aware that patients with hypertension may suffer from untreated severe chronic insomnia.

Summary

Insomnia with short sleep duration is associated with a high risk for the development of hypertension to a degree comparable with the other most common sleep disorder, sleep apnea. Given the high prevalence of insomnia in the general population its early diagnosis and appropriate management should become a target of public health policy in the prevention of hypertension.

Table 1

Demographic, Clinical, and Sleep Characteristics of Study Population at Baseline

		Hypertension Incidence	
Characteristics	**All (N = 786)**	**No (N = 595)**	**Yes (N = 191)**
Sex			
Female, %	51.3	79.5	15.1
Male, %	48.7	84.9	20.5 *
Race			
Caucasian, %	94.2	82.9	17.1
Non-Caucasian, %	5.8	71.9	28.1 *
Age, years	47.5 (12.7)	46.8 (12.9)	50.8 (11.4) †
≤ 40, %	30.6	89.3	10.7
41–59, %	51.4	78.9	21.1 †
≥ 60, %	18.0	79.8	20.2 †
BMI, kg/m^2	27.1 (4.8)	26.7 (4.5)	28.9 (5.7) †
< 30, %	79.0	85.4	14.6
≥ 30, %	21.0	70.1	29.9 †
SBP, mm Hg	126.1 (15.1)	123.7 (13.6)	136.9 (17.2) †
< 120, %	31.0	96.8	3.2
≥ 120, %	53.0	80.3	19.7 †
≥ 140, %	16.0	60.2	39.8 †
DBP, mmHg	78.8 (8.7)	77.6 (7.7)	84.5 (10.4) †
< 80, %	47.9	90.0	10.0
≥ 80, %	39.8	82.5	17.5 †
≥ 90, %	12.3	51.1	48.9 †
SBP/DBP status			
Normal, %	25.2	96.8	3.2
Pre-hypertensive, %	53.0	85.8	14.2 †
Hypertensive, %	21.8	57.1	42.9 †
Diabetes			
No, %	90.0	82.7	17.3
Yes, %	10.0	77.3	22.7
Depression			
No, %	93.8	82.8	17.2
Yes, %	6.2	73.5	26.5 *
OHI, events/h	2.0 (6.6)	1.6 (6.0)	3.8 (8.9) †
< 5, %	90.0	85.0	15.0
≥ 5, %	10.0	57.3	42.7 †
Caffeine, cup/day	2.4 (3.0)	2.3 (3.1)	2.8 (2.5) *

	Hypertension Incidence		
Characteristics	**All (N = 786)**	**No (N = 595)**	**Yes (N = 191)**
None, %	32.5	88.3	11.7
1–2 cups/day, %	31.8	80.6	19.4†
≥ 3 cups/day, %	35.7	78.1	21.9†
Cigarettes, n/day	4.4 (11.1)	4.4 (11.4)	4.0 (9.3)
None, %	77.7	81.7	18.3
1–20/day, %	9.7	88.0	12.0
≥ 20/day, %	12.5	81.2	18.8
Alcohol, drink/day	1.4 (6.5)	1.5 (7.1)	0.9 (2.6)
None, %	72.5	82.6	17.4
1 drink/day, %	10.5	74.8	25.2*
≥ 2 drink/day, %	17.0	85.1	14.9
Sleep Difficulty			
Normal Sleep, %	74.3	83.3	16.7
Poor Sleep, %	20.2	82.4	17.6
Chronic Insomnia, %	5.5	68.9	31.1†
Sleep Duration, hrs	6.0 (1.1)	6.0 (1.1)	5.7 (1.1)†
≥ 6 hrs, %	59.4	85.0	15.0
< 6 hrs, %	40.6	78.1	21.9†

All data are adjusted for sampling weight. Where appropriate the standard deviation is presented in parenthesis. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Normal BP status, SBP < 120 mm Hg and DBP < 80 mm Hg; Pre-hypertensive BP status, SBP ≥ 120 and < 140 mm Hg and/or DBP ≥ 80 and < 90 mm Hg; Hypertensive BP status, SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg; OHI, obstructive apnea/hypopnea index.

*p < .05;

†p < .01

Table 2

Multivariable Adjusted Odds Ratio (95% CI) of Incident Hypertension and Insomnia or Objective Sleep Duration

Predictors	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
Sleep Difficulty			
Normal Sleep	1.0	1.0	1.0
Poor Sleep	1.19 (0.78–1.79)	1.02 (0.66–1.57)	1.01 (0.65–1.55)
Chronic Insomnia	2.66 (1.45–4.88)†	2.29 (1.22–4.27)†	2.24 (1.19–4.19)†
Sleep Duration			
≥ 6h	1.0	1.0	1.0
< 6h	1.29 (0.91–1.81)	1.30 (0.91–1.84)	1.28 (0.90–1.82)

All data are adjusted for sampling weight.

Model 1 = sleep difficulty or objective sleep duration adjusted for gender, race, age, caffeine, cigarettes, and alcohol consumption, and depression.

Model 2 = sleep difficulty or objective sleep duration adjusted for gender, race, age, caffeine, cigarettes, and alcohol consumption, depression, SDB, diabetes, and BMI ≥ 30.

Model 3 = sleep difficulty and objective sleep duration adjusted for gender, race, age, caffeine, cigarettes and alcohol consumption, depression, SDB, diabetes, BMI ≥ 30. The interaction between sleep difficulty and objective sleep duration is statistically significant ($p < .05$).

* $p < .05$;

† $p < .01$

Table 3

Multivariable Adjusted Odds Ratio (95%CI) of Incident Hypertension Associated with Insomnia and Objective Sleep Duration

Predictors	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
Normal Sleep≥ 6h	1.0	1.0	1.0
Poor Sleep ≥ 6h	0.62 (0.33–1.18)	0.55 (0.28–1.05)	0.50 (0.26–0.98) *
Chronic Insomnia ≥ 6h	1.30 (0.49–3.43)	1.07 (0.40–2.88)	0.85 (0.30–2.40)
Normal Sleep < 6h	0.87 (0.57–1.32)	0.88 (0.58–1.34)	0.88 (0.57–1.37)
Poor Sleep < 6h	1.80 (1.04–3.12) *	1.62 (0.92–2.83)	1.34 (0.74–2.41)
Chronic Insomnia < 6h	4.50 (1.96–10.3) †	3.88 (1.68–8.97) †	3.75 (1.58–8.95) *

All data are adjusted for sampling weight.

Model 1 = adjusted for gender, race, age, caffeine, cigarettes and alcohol consumption, depression, SDB, and diabetes.

Model 2 = adjusted for gender, race, age, caffeine, cigarettes and alcohol consumption, depression, SDB, diabetes, and BMI ≥ 30.

Model 3 = adjusted for gender, race, age, caffeine, cigarettes and alcohol consumption, depression, SDB, diabetes, BMI ≥ 30, and baseline SBP/DBP status (i.e., SBP < 120 mm Hg and DBP < 80 mm Hg vs. SBP ≥ 120 and < 140 mm Hg and/or DBP ≥ 80 and < 90 mm Hg vs. SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg).

* $p < .05$;

† $p < .01$