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Is there any relation between arterial stiffness and insomnia? A challenging question

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Abstract

Purpose Insomnia is a common sleep disorder which has high comorbidity with a number of cardiovascular diseases (CVD). As a possible risk factor for the CVDs, arterial stiffness may be assessed non-invasively by pulse wave velocity (PWV) and augmentation index (AI). The aim of this study was to evaluate any relation between insomnia and arterial stiffness.

Methods Patients with insomnia were included in the study after the exclusion of other sleep disorders by polysomnography. Sleep quality and the degree of insomnia symptoms were evaluated by the Pittsburgh sleep quality index (PSQI) and insomnia severity index (ISI), respectively. PWV and AI were assessed by Mobil-O-Graph arteriograph system.

Results Consecutive patients with insomnia (n = 72, 56 women, mean age 55.8 ± 9.1 years) were included. Patients were grouped as those with severe ISI scores (22–28) and those with mild to moderate ISI scores (8–21). Despite no significant difference in characteristics and clinical data, patients with severe ISI scores had significantly higher total PSQI scores and NREM-2 with significantly lower REM duration. They also had significantly higher systolic blood pressure, mean blood pressure, pulse pressure, PWV, and AI compared to patients with mild and moderate ISI scores. Correlation analysis revealed that PWV and AI were significantly correlated with the ISI score and PSQI score.

Conclusion There is a close relation between arterial stiffness and insomnia suggesting a risk for CVD in patients with insomnia.

Keywords Arterial stiffness · Insomnia · Sleep apnea · Pulse wave velocity

Introduction

The definition of insomnia includes a difficulty in falling asleep or maintaining sleep or the perception of uncomfortable sleep. Insomnia is a common sleep disorder in developed countries having high comorbidity with a number of cardiovascular diseases (CVD) [1]. Sleep duration is shown to be associated with CVD [2] due to the increased risk of hypertension, diabetes, and obesity [3, 4]. Insomnia increases morbidity and mortality risk in patients with CVD [5].

Arterial stiffness has been implied in the pathophysiology of CVD related with multiple cardiovascular risk factors including older age, hypertension, hypercholesterolemia, diabetes, obesity, smoking, kidney disease, and stroke [6–8]. Although underlying pathogenesis is not clear yet, hemodynamic, mechanical, metabolic, and enzymatic mechanisms are some of the potential hypothesis [9]. Arterial stiffness may also increase the risk of mortality and morbidity due to its hemodynamic effects [10]. Arterial stiffness may be assessed non-invasively by pulse wave velocity (PWV) and augmentation index (AI), which helps in the evaluation of cardiac risk and early vascular damage [11, 12].

There are several potential mechanisms about the link between insomnia and arterial stiffness such as increased risk hypertension and systemic inflammation. There is a close relationship between insomnia and hypertension [13]. Activation of hypothalamic–pituitary–adrenal axis [14] that may lead to increased sympathetic tone, stress-diathesis model [15] that biological diatheses interact with environmental stressor factors to result in a pathophysiologic effect,

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and a neurobiological model [16] that insomnia results from activation of wake-promoting neural pathways during non-rapid eye movement sleep are potential mechanisms for the relation between insomnia and hypertension. Recent studies have supported that there are some evidence linking insomnia with elevated levels of systemic inflammation [17]. Arterial stiffness is associated with systemic inflammation and hypertension [18, 19]. There is no study that has evaluated the relation between arterial stiffness and severity of insomnia until now. The aim of the study was to explore any relation between insomnia and arterial stiffness.

Methods

Study population

All study procedures were approved by the local ethic committee and are compliant with the Declaration of Helsinki. All study population gave written informed consent prior to participation.

We included patients with DSM-5 chronic insomnia disorder [20]. The patients were included if they had self-reported mean wake after sleep onset (WASO) of ≥ 1 h on ≥ 3 nights per week or mean WASO of ≥ 45 min across 2 nights on polysomnography (PSG). All patients underwent polysomnography to exclude other sleep disorders. Patients with prior/current DSM-5 major depression and sleep or circadian disorders determined by patient report or PSG (obstructive sleep apnea defined as apnea–hypopnea index ≥ 5, periodic limb movements defined as arousal frequency ≥ 15), WASO < 30 min, and usage of medications that may affect sleep including sleep aids, antidepressants and herbal supplements) were excluded. Sleep quality was determined by the Pittsburgh questionnaire, while the degree of insomnia was assessed by insomnia severity index (ISI).

Evaluation of arterial stiffness parameters

A single cardiologist assessed arterial stiffness non-invasively by Mobil-O-Graph arteriograph system (Mobil-O-Graph NG, Stolberg, Germany) in a quiet, temperature-controlled room (22–24 °C) in the morning after a fasting period of 12 h with the patients lying in supine position. The contraction of the myocardium creates a pulse wave (early systolic peak) running down the aorta, which is reflected by the aortic wall at the distal branching point resulting in a second wave (late systolic peak). The shape of this reflected wave depends on the stiffness of the large artery. The system detects the signals from the brachial artery when cuff pressure exceeds systolic pressure more than 35 mmHg. The AIx (AIx adjusted for heart rate 75 bpm) and PWV are calculated from amplitude and time difference of the first and second waves according to current guidelines [21].

The Pittsburgh sleep quality index (PSQI)

All patients were given the Pittsburgh questionnaire for determination of sleep quality. It is a self-report questionnaire including 19 items to evaluate 7 aspects of sleep quality (sleep onset latency, sleep duration, efficiency, quality, disturbances, medication, and daytime dysfunction). Each aspect is assigned a value from 0 to 3 where their sum gives global score of sleep quality (0–21) with high scores associated with poor sleep quality. The cut-off score is > 5 to differentiate patients with primary insomnia [22].

The insomnia severity index

The degree of insomnia including insomnia severity, noticeability of sleep impairment, sleep interference with day-time functioning, sleep satisfaction, and distress caused by insomnia over the last 2 weeks was determined by Insomnia severity index. It includes 7 items with each item rated on a 5-point Likert scale. Their sum gives global score (0–28) with high scores indicating severe (scores 22 to 28) and moderate (scores 15 to 21) insomnia and a low score (scores 0 to 7) pointing no significant insomnia. A score of 8 to 14 indicates sub-threshold insomnia, and a score of > 14 is used to detect primary insomnia [23]. In our study, we divided the patients into two groups as those with mild to moderate ISI scores (8–21) and those with severe ISI scores (22–28) to evaluate the effect of disease severity on arterial stiffness.

Statistical analysis

SPSS 20.0 statistical package for Windows was used for statistical analyses. Categorical variables were presented as percentage and compared with Chi-square test. Continuous data were expressed as mean ± standard deviation, and normal distribution was assessed by the Kolmogorov–Smirnov test. The Student *t* test or Mann–Whitney *U* test was used to compare the parametric or non-parametric continuous parameters, respectively. Pearson or Spearman's correlation tests were used for correlation analysis. A value of $p < 0.05$ was considered statistically significant. The minimum required sample size was calculated with anticipated effect size of 0.10, alpha 0.05 (probability), and 90% power (10% type 2 error) [24].

Results

We studied 85 patients seen in the outpatient clinics who had complaints of insomnia. After the exclusion of 13 patients due to the usage of medications affecting sleep,

Table 1 Baseline characteristics and clinical data of study population

Age (years)	55.8 ± 9.1
Sex (female/male)	56/16
Smoking (n)	19 (26%)
Alcohol (n)	16 (22%)
Married (n)	54 (75%)
Working (n)	13 (18%)
Onset of symptoms (years)	12.4 ± 6.7
Diagnosis of insomnia (years)	3.6 ± 2.8

Table 2 PSQI score of study population

Component 1 score	2.6 ± 0.6
Component 2 score	2.5 ± 0.7
Component 3 score	2.7 ± 0.7
Component 4 score	2.6 ± 0.8
Component 5 score	2.4 ± 0.7
Component 6 score	2.6 ± 0.7
Component 7 score	2.0 ± 0.9
Total PSQI score	17.5 ± 3.4

Component 1, subjective sleep quality; *Component 2*, sleep latency; *Component 3*, sleep duration; *Component 4*, sleep efficiency; *Component 5*, sleep disturbance; *Component 6*, use of sleep medication; *Component 7*, daytime dysfunction; *PSQI*, Pittsburgh sleep quality index

previous sleep disorder, and diagnosis of major depression, the remaining 72 patients (mean age 55.8 ± 9.1 years, 56 women) were included in the study. Table 1 shows characteristics and clinical data of the patients. The mean duration of insomnia was 3.6 ± 2.8 years. Components of the PSQI score of the patients are shown in Table 2. The total PSQI score of the patients was 17.5 ± 3.4. While 50 patients had mild and moderate ISI score, 22 patients had severe ISI score.

A comparison of baseline characteristics and clinical data according to ISI scores is shown in Table 3. The patients with severe ISI scores had significantly higher total PSQI score. Table 4 shows the comparison of polysomnography parameters between patients with mild or moderate ISI scores and patients with severe ISI scores. The patients with severe ISI scores had significantly higher non-rapid eye movement (NREM-2) and significantly lower rapid eye movement (REM) duration than patients with mild or moderate ISI scores. Arterial stiffness parameters between the patients with mild or moderate ISI scores and the patients with severe ISI scores are shown in Table 5. The patients with severe ISI scores had significantly higher systolic blood pressure, mean blood pressure, pulse pressure, PWV, and AI compared to the patients with mild or moderate ISI scores.

Correlation analysis was performed to demonstrate the association between arterial stiffness parameters, ISI score, and PSQI score (Table 6). PWV and AI were significantly correlated with the ISI score and PSQI score.

Discussion

In this study, we found that patients with severe ISI scores had significantly higher PWV and AI compared to those with mild or moderate ISI scores. Furthermore, PWV and AI were significantly correlated with the ISI score and PSQI score. To the best of our knowledge, this is the first study to demonstrate an association between arterial stiffness and severity of insomnia.

Sleep quality has an important role in promoting health. Insomnia is shown to be associated with hypertension [25, 26], atherosclerotic CVD [27], and heart failure [28]. Although the underlying pathogenesis of insomnia and CVD is not clear, there are several mechanisms that proposed this association such as dysregulation of the hypothalamic-pituitary axis, abnormal activation of the autonomic system, increased sympathetic system activity, and triggered systemic inflammation [29, 30]. Chronic insomnia and short sleep duration are found as significant risk factors for the

Table 3 Comparison of baseline characteristics and clinical data of study population

	Mild and moderate ISI (n = 50)	Severe ISI (n = 22)	p
Age (years)	55.1 ± 9.6	57.5 ± 7.9	0.304
Sex (female)	38	18	0.584
Smoking (n)	16	3	0.148
Alcohol (n)	12	4	0.761
Married (n)	38	16	0.768
Working (n)	10	3	0.742
Onset of symptoms (years)	12.5 ± 7.4	12.2 ± 5.2	0.837
Diagnosis of insomnia (years)	3.7 ± 3.1	3.6 ± 1.9	0.873
Total PSQI score	16.5 ± 3.6	19.7 ± 0.8	**< 0.001**

ISI, insomnia severity index; *PSQI*, Pittsburgh sleep quality index

Bold value indicates $p<0.05$

Table 4 Comparison of polysomnography parameters between groups

	Mild and moderate ISI (n = 50)	Severe ISI (n = 22)	p
AHI	1.7 ± 1.6	1.8 ± 1.8	0.762
TST	215.4 ± 56.6	216.9 ± 80.6	0.476
SOL	58.0 ± 55.4	78.5 ± 75.0	0.336
WASO	137.6 ± 48.5	119.6 ± 50.8	0.109
Sleep efficiency	49.0 ± 11.8	50.1 ± 15.6	0.786
REM sleep latency	257.0 ± 107.3	254.4 ± 124.8	0.926
NREM-1	11.1 ± 8.3	9.6 ± 9.4	0.227
NREM-2	25.8 ± 12.2	36.5 ± 9.9	**< 0.001**
NREM-3	40.0 ± 31.9	31.7 ± 26.2	0.901
REM	76.7 ± 24.9	53.3 ± 37.8	**0.026**

ISI, insomnia severity index; *AHI*, apnea–hypopnea index; *TST*, total sleep time; *SOL*, sleep onset latency; *WASO*, wake time after sleep onset; *NREM*, non-rapid eye movement sleep stage; *REM*, rapid eye movement sleep stage

Bold values indicate $p<0.05$

development of hypertension [25, 26]. Mendoza et al. [25] has showed that increased risk of hypertension due to insomnia is independent from comorbid conditions including age, race, obesity, diabetes, smoking, caffeine or alcohol consumption, sleep-disordered breathing, and depression.

Arterial stiffness can be simply and non-invasively assessed by PWV and AI [12, 31]. In our study, we used oscillometric method, which is more reliable in assessing PWV compared to tonometric and piezo-electronic methods as those techniques are time-consuming and require trained operators [32]. PWV and AI are good markers of the vascular damage, endothelial dysfunction, and early atherosclerosis. A high PWV is independently associated with CVD [33]. Cardiovascular morbidity and mortality increase with increased arterial stiffness [10]. Decline in arterial elasticity is related with hypertension, left ventricular hypertrophy, and stroke [34]. Therefore, assessment of arterial stiffness has gain attention. Our study demonstrated that patients with severe ISI scores had increased arterial stiffness parameters correlating with the ISI and PSQI scores. Our results suggest that increased arterial stiffness may lead to an increased risk of CVD in patients with insomnia.

Possible underlying mechanisms linking insomnia and CVD are increased sympathetic activity and impaired vascular endothelial function, which have been found in healthy population with sleep deprivation and patients with chronic insomnia [14, 35]. Insomnia is also associated with non-dipping of blood pressure, which may place these patients at increased risk for CVD [36]. There is a higher risk for development of hypertension and dyslipidemia in patients with sleep disturbance, which further increases the risk for CVD [37]. Poor sleep quality is in relation with metabolic disturbances through sympathetic activation or inflammatory cytokines [38]. Chronic sleep problems can trigger the

Table 6 Correlation analysis between arterial stiffness parameters, ISI score, and total PSQI score

	ISI score	Total PSQI	PWV	AI
ISI score		r = 0.563 **p < 0.001**	r = 0.754 **p < 0.001**	r = 0.341 **p = 0.003**
Total PSQI	r = 0.563 **p < 0.001**		r = 0.605 **p < 0.001**	r = 0.249 **p = 0.035**
PWV	r = 0.754 **p < 0.001**	r = 0.605 **p < 0.001**		r = 0.485 **p < 0.001**
AI	r = 0.341 **p = 0.003**	r = 0.249 **p = 0.035**	r = 0.485 **p < 0.001**	

ISI, insomnia severity index; *PSQI*, Pittsburgh sleep quality index; *PWV*, pulse wave velocity; *AI*, augmentation index

Table 5 Comparison of arterial stiffness parameters between groups

	Mild and moderate ISI (n = 50)	Severe ISI (n = 22)	p
Systolic blood pressure (mmHg)	121.2 ± 11.7	141.3 ± 16.0	**< 0.001**
Diastolic blood pressure (mmHg)	76.2 ± 6.3	75.5 ± 9.5	0.724
Mean blood pressure (mmHg)	96.8 ± 7.5	105.7 ± 11.2	**0.002**
Pulse rate (beat/min)	74.2 ± 9.5	70.6 ± 8.4	0.121
Pulse pressure (mmHg)	45.0 ± 10.4	65.9 ± 12.3	**< 0.001**
Stroke volume (ml)	63.6 ± 11.1	64.2 ± 8.9	0.828
Cardiac output (l/min)	4.6 ± 0.7	4.5 ± 0.6	0.317
Cardiac index (l/min × $1/m^2$)	2.6 ± 0.4	2.7 ± 0.4	0.408
Pulse wave velocity (m/s)	7.7 ± 1.3	10.3 ± 1.0	**< 0.001**
Augmentation index (%)	26.9 ± 10.5	33.1 ± 7.1	**0.013**
Body mass index (kg/m^2)	26.1 ± 3.4	25.8 ± 0.9	0.684

ISI, insomnia severity index

Bold values indicate $p<0.05$

hypothalamus–pituitary–adrenal axis and the sympathetic nervous system pathways, leading to an increased pro-inflammatory process [39]. There is strong evidence that inflammation is associated with arterial stiffness [40]. Our results demonstrated that in patients with severe insomnia, arterial stiffness parameters may be used as a non-invasive parameter to evaluate cardiovascular risk. The clinician should give more importance to evaluate patients with severe insomnia in outpatient clinics and should consult those patients to cardiology clinics to prevent future cardiac events.

Lack of a control group and the small sample size were major limitations. A possible effect of medical treatment on arterial stiffness parameters could not be evaluated. The lack of follow-up of the patients with higher PWV and AI has limited to identify the predictors associated with development of CVD. Further large-scale, prospective studies are needed to elucidate whether severe insomnia has clinical reflections of cardiovascular events through increased arterial stiffness parameters.

Conclusions

There is a close relation between arterial stiffness parameters and insomnia suggesting a higher risk for CVD in patients with insomnia and severe ISI.

Declarations

Ethics approval All procedures in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

References

1. Ohayon MM (2002) Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 6:97–111
2. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA (2010) Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. Sleep 33(5):585–592
3. Knutson KL, Van Cauter E (2008) Associations between sleep loss and increased risk of obesity and diabetes. Ann N Y Acad Sci 1129:287–304
4. Patel SR, Blackwell T, Redline S et al (2008) The association between sleep duration and obesity in older adults. Int J Obes (Lond) 32(12):1825–1834
5. Sofi F, Cesari F, Casini A et al (2014) Insomnia and risk of cardiovascular disease: a meta-analysis. Eur J Prev Cardiol 21(1):57–64
6. Greenland P, Alpert JS, Beller GA et al (2010) 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 56:e50–e103
7. Franklin SS (2008) Beyond blood pressure: arterial stiffness as a new biomarker of cardiovascular disease. J Am Soc Hypertens 2:140–151
8. Payne RA, Wilkinson IB, Webb DJ (2010) Arterial stiffness and hypertension: emerging concepts. Hypertension 55:9–14
9. Palombo C, Kozakova M (2016) Arterial stiffness, atherosclerosis and cardiovascular risk: pathophysiologic mechanisms and emerging clinical indications. Vascul Pharmacol 77:1–7
10. Mitchell GF, Hwang SJ, Vasan RS et al (2010) Arterial stiffness and cardiovascular events: the Framingham heart study. Circulation 121:505–511
11. Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 55(13):1318–1327
12. Mattace-Raso F, Hofman A, Verwoert GC et al (2010) Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values.' Eur Heart J 31:2338–2350
13. Jarrin DC, Alvaro PK, Bouchard MA et al (2018) Insomnia and hypertension: a systematic review. Sleep Med Rev 41:3–38
14. Vgontzas AN, Bixler EO, Lin HM et al (2001) Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications. J Clin Endocrinol Metab 86:3787–3794
15. Drake CL, Pillai V, Roth T (2014) Stress and sleep reactivity: a prospective investigation of the stress-diathesis model of insomnia. Sleep 37:1295–1304
16. Buysse DJ, Germain A, Hall M et al (2011) A neurobiological model of insomnia. Drug Discov Today Dis Models 8:129–137
17. Dolsen MR, Crosswell AD, Prather AA (2019) Links between stress, sleep, and inflammation: are there sex differences? Curr Psychiatry Rep 21:8
18. Dumor K, Shoemaker-Moyle M, Nistala R et al (2018) Arterial stiffness in hypertension: an update. Curr Hypertens Rep 20:72
19. Jain S, Khera R, Corrales-Medina VF et al (2014) Inflammation and arterial stiffness in humans. Atherosclerosis 237:381–390
20. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn. Arlington, VA, American Psychiatric Association
21. Van Bortel LM, Duprez D, Starmans-Kool MJ et al (2002) Clinical applications of arterial stiffness, task force III: recommendations for user procedures. Am J Hypertens 15:445–452
22. Backhaus J, Junghanns K, Broocks A et al (2002) Test-retest reliability and validity of the Pittsburgh sleep quality index in primary insomnia. J Psychosom Res 53:737–740
23. Smith S, Trinder J (2001) Detecting insomnia: comparison of four self-report measures of sleep in a young adult population. J Sleep Res 10:229–235
24. Ledolter J, Kardon RH (2020) Focus on data: statistical design of experiments and sample size selection using power analysis. Invest Ophthalmol Vis Sci 61:11
25. Mendoza JF, Vgontzas AN, Liao D et al (2012) Insomnia with objective short sleep duration and incident hypertension: the Penn State cohort. Hypertension 60(4):929–935
26. Vgontzas AN, Liao D, Bixler EO et al (2009) Insomnia with objective short sleep duration is associated with a high risk for hypertension. Sleep 32(4):491–497

27. Cappuccio FP, Cooper D, D'Elia L et al (2011) Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J. 32(12):1484–92
28. Laugsand LE, Strand LB, Platou C et al (2014) Insomnia and the risk of incident heart failure: a population study. Eur Heart J 35(21):1382–1393
29. Castro-Diehl C, Roux AV, Redline S et al (2015) Association of sleep duration and quality with alterations in the hypothalamic-pituitary adrenocortical axis: the multi-ethnic study of atherosclerosis (MESA). J Clin Endocrinol Metab 100(8):3149–3158
30. Irwin MR (2015) Why sleep is important for health: a psychoneuroimmunology perspective. Annu Rev Psychol 66:143–172
31. Oliver JJ, Webb DJ (2003) Noninvasive assessment of arterial stiffness and risk of atherosclerotic events. Arterioscler Thromb Vasc Biol 23:554–566
32. Baulmann J, Schillings U, Rickert S et al (2008) New oscillometric method for assessment of arterial stiffness: comparison with tonometric and piezo-electronic methods. J Hypertens 26:523–528
33. Liu CS, Li CI, Shih CM et al (2011) Arterial stiffness measured as pulse wave velocity is highly correlated with coronary atherosclerosis in asymptomatic patients. J Atheroscler Thromb 18:652–658
34. Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 55:1318–1327
35. Carreras A, Zhang SX, Peris E et al (2014) Chronic sleep fragmentation induces endothelial dysfunction and structural vascular changes in mice. Sleep 37(11):1817–1824
36. Lanfranchi PA, Pennestri MH, Fradette L et al (2009) Nighttime blood pressure in normotensive subjects with chronic insomnia: implications for cardiovas- cular risk. Sleep 32(6):760–766
37. Clark AJ, Salo P, Lange T et al (2016) Onset of impaired sleep and cardiovascular disease risk factors: a longitudinal study. Sleep 39(9):1709–1718
38. Copinshi G (2005) Metabolic and endocrine effects of sleep deprivation. Essent Psychopharmacol 6:341–347
39. Vgontzas AN, Fernandez-Mendoza J et al (2013) Insomnia with objective short sleep duration: the most biologically severe phenotype of the disorder. Sleep Med Rev 17:241–254
40. Mozos I, Malainer C, Horbańczuk J et al (2017) Inflammatory markers for arterial stiffness in cardiovascular diseases. Front Immunol 8:1058

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