Periodic limb movements during sleep and risk of hypertension: A systematic review

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Abstract

Background—Several studies suggest an association between periodic limb movements during sleep (PLMS) and hypertension; however, a systematic evaluation of this relationship is lacking.

Methods—We conducted a systematic review and meta-analysis of observational studies that reported odds ratio, relative risk, hazard ratio, or standardized incidence ratio, comparing the risk of hypertension in persons with PLMS (defined by the level of periodic limb movements per hour of sleep depended on individual studies) versus those without PLMS. After assessing heterogeneity and bias, the pooled risk ratio and 95% confidence intervals (CIs) were determined using a random-effect, generic inverse variance method of DerSimonian and Laird.

Results—Out of 572 potentially relevant articles, six eligible studies were included in the data analysis. Studies (6 cross-sectional) included 8,949 participants. The statistical heterogeneity of this study was insignificant, with an I^2 of 0%. A funnel plot and Egger's regression asymmetry test showed no publication bias with P-value 0.05. The pooled risk ratio of hypertension in patients with PLMS was 1.26 (95% CI, 1.12–1.41).

Conclusions—Our analysis demonstrates an increased hypertension risk among patients with PLMS. Prospective or interventional studies are needed to confirm this association.

Keywords

Periodic limb movements during sleep; Hypertension; Epidemiology; Meta-analysis

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Introduction

Periodic limb movements during sleep (PLMS) are spontaneous movements of the legs that occur repetitively throughout the sleeping period (1). Although about 80–90% of individuals with restless legs syndrome (RLS) exhibit PLMS, they are not specific to RLS and are also frequently seen with aging and in other illnesses, such as narcolepsy(2), heart failure(3), obstructive sleep apnea(4), and Parkinson disease(3, 4). The clinical significance of PLMS is currently unclear and treatment to suppress movements is rarely indicated (5). A number of observational studies, however, have demonstrated an increase in heart rate and blood pressure with each individual movement that constitutes PLMS. The magnitude of heart rate and blood pressure increases during sleep are on the order of 7 to 10 beats per minute(6) and 22/11 mmHg, respectively(7). PLMS are also often associated with arousal and this combination results in an approximately 40% greater increase in heart rate and blood pressure than PLMS alone(7). Since the inter-movement interval for PLMS is between 15 and 35 seconds(8), frequent individual limb movements can number into the hundreds each night and thus may have an impact on daytime cardiovascular function.

PLMS are reported as the total number of periodic limb movements (PLMs) per hour of sleep in the periodic limb movement index (PLMI), and the periodic limb movement arousal index (PLMAI) representing the number of PLMs per hour of sleep associated with an arousal. PLMI greater than 15 events/hour is typically regarded as elevated(9)and occurs in nearly 30% of persons in the general population(10), but an even higher percentage of the elderly(1). Several conditions have been associated with PLMS, including obstructive sleep apnea, renal insufficiency, and peripheral neuropathy (11–13).

It is widely accepted that hypertension is one of the most potent risk factors for cardiovascular disease and death (14). While the presence of PLMS has recently been identified as a possible risk factor for hypertension, studies have shown conflicting results (1, 5, 15–18). It is important to systematically assess this relationship. Therefore, we conducted a systematic review and meta-analysis of observational studies that compared the presence of hypertension in individuals with to those without PLMS.

Methods

Search strategy

A systematic literature search of MEDLINE (1946-August 2022), EMBASE (1988- August 2022), Cochrane Central Register of Controlled Trials (database inception-August 2022), and Cochrane Database of Systematic Reviews (database inception-August 2022) was independently conducted by two investigators (N.S. and C.T.) to assess the association of PLMS and hypertension using the search terms of "periodic leg movement", or "periodic limb movement", or "PLMS", or "PLMD", and "hypertension", or "blood pressure" which is described in the supplementary data. Additionally, the references of selected articles were manually searched for potentially relevant studies, and there was no limitation on language. The reporting of this systematic review was guided by the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement(19). The

study protocol was registered in PROSPERO International prospective register of systematic reviews (CRD42022351882).

Inclusion criteria

Eligible studies were required to be clinical trials or observational studies (including cross-sectional, case-control, or cohort studies) which reported the association between PLMI and the risk of hypertension. We included studies that provided effect estimates by odds ratio (OR), relative risk (RR), hazard ratio (HR), or standardized incidence ratio (SIR) with corresponding 95% confidence intervals (CI), or sufficient raw data to calculate these ratios. Moreover, we included only studies that used a no PLMS group (or control group) to compare with those who had PLMS.

Retrieved articles were independently evaluated by N.S. and C.T. Any discrepancies in the determination of study eligibility were arbitrated by a third investigator (W.C.).

The quality of each study was independently appraised by each investigator using the Newcastle-Ottawa quality scale. This scale assesses each study in three domains, including 1) the selection of the participants, 2) the comparability between the study groups, and 3) the ascertainment of the exposure of interest for case-control studies and the outcome of interest for cohort studies. Maximal scores for the selection, comparability, and ascertainment of exposure/outcome of interest are four, two, and three, respectively and the final Newcastle-Ottawa scale score is the sum of these three component scores. A study is generally considered of good technical quality if the Newcastle-Ottawa scale score is more than or equal to six(20). A cross-sectional study was appraised using the modified version of the Newcastle-Ottawa quality scale.

Data extraction

A standardized data collection form was used to extract the following information: title of the article, name of the first author and his/her institution, year of publication, country of origin, year of study, the definition of elevated PLMI cut-off, definition of hypertension, method of the case and control identification, number of cases, number of controls, demographic data of patients, and confounders that were adjusted and adjusted effect estimates with 95% CI. This data extraction was independently performed by N.S. and C.T. Any discrepancies were resolved by referring to the primary studies.

Statistical analysis

All statistical analyses were conducted using Review Manager 5.3 software from the Cochrane Collaboration. Point estimates and their corresponding standard errors were extracted from each study and pooled together using the generic inverse variance method of DerSimonian and Laird (21). A random-effect model, rather than a fixed-effect model, was used given the high likelihood of study variance due to differences in study design, population, and the definition of PLMI. Statistical heterogeneity was assessed using Cochran's Q test, which is complemented with the I^2 statistic. This statistic quantifies the proportion of the total variation across studies, which is due to true heterogeneity rather than chance. A value of I^2 of 0–25% represents insignificant heterogeneity, more than 25% but

less than or equal to 50% low heterogeneity, more than 50% but less than or equal to 75% moderate heterogeneity, and more than 76% represents high heterogeneity(22). Publication bias was evaluated by 1) funnel plot (23) and 2) Egger's regression intercept. An intercept p-value of less than 0.05 was considered significant for potential publication bias.

Results

Our search strategy yielded 572 potentially relevant articles. After the exclusion of 188 duplicate articles, 384 unique studies underwent title and abstract review. Upon review of titles and abstracts, 296 studies were excluded for not fulfilling inclusion criteria based on the type of article, study design, population, or outcome of interest. Eighty-eight articles underwent full-length article review. Eighty-two articles were excluded (53 articles were not observational studies or RCT, and 29 articles did not report the outcomes of interest). Figure 1 outlines our search methodology and selection process.

The exposure (PLMS)

A cut-off of PLMI used to define the presence of PLMS depended on individual studies. Three studies (5, 15, 16) used a cut-off point of PLMI more than 15, 2 studies(1, 17) used a cut-off point of PLMI more than 30 and the other (18) used more than 26 events/hour respectively.

The outcome (Hypertension)

The outcome measurement was also dependent on the individual studies. Study by Mahmudova et al.(15) did not mention how hypertension was defined. The study by Shin et al.(16) defined hypertension as a documented diagnosis of hypertension on the medical record, self-report of a hypertension diagnosis, or self-report of taking anti-hypertensive medications. The study by Hein et al. (18) defined their outcome as resistant hypertension or uncontrolled hypertension (Systolic blood (SBP) 140 / Diastolic blood (DBP) 90) despite being on at least 3 anti-hypertensive medications or controlled hypertension (SBP<140 /<90) with at least 4 anti-hypertensive medications. The other three studies (1, 5, 17) defined hypertension as SBP 140 mmHg and/or DBP 90 mmHg or presence of drugs.

Study Characteristics

Table 1 displays the participant characteristics of the different studies. Most participants were male. Those in the PLM group tended to be older and have lower apnea- hypopnea indices except the study from Haba- Rubio et al. Other comorbidities such as diabetes mellitus, alcohol usage, depression or antipsychotic medication usage of the study subjects were not consistently reported among the studies. Table 2 describes the detailed characteristics and quality assessment of the included studies, and highlights the numbers from individual studies which were selected for the meta-analysis

Risk of hypertension in patients with PLMS

Six cross-sectional observational studies with a total of 8,949 participants were included in the data analysis for the risk of hypertension in participants with PLMS and high PLMI. The pooled risk ratio (RR) of hypertension in participants with PLMS was 1.26 (95%

CI, 1.12–1.41). The statistical heterogeneity was insignificant, with I^2 of 0%. Figure 2 shows the forest plot of the included studies. The first(1) and third (17) largest studies showed significant association between the presence of PLMS and hypertension, while the remaining four studies did not demonstrate a significant association between the presence of PLMS and hypertension. As the two studies which showed a significant association between PLMS and hypertension were weighted heavily and all other studies trended toward an association, the pooled RR was also significant. We conducted a sensitivity analysis by excluding Mahmodova et al. study in 2022(15) as it was the only study that did not provide a definition of Hypertension. As shown in Figure 3, the exclusion of this study did not change the results (RR 1.26; 95%CI 1.12 –1.42; I2 0%). We then conducted a sensitivity analysis by excluding Hein et al. study in 2019 (24) as it was the only study that defined the outcome as resistant hypertension, which is different from the other studies. As shown in Figure 4, the exclusion of this study did not considerably change the results (RR 1.26; 95%CI 1.12 –1.41; I^2 0%). Lastly, we excluded both studies by Mahmodova et al. (15) and Hein et al. (18) and again, it did not significantly alter results (RR 1.26; 95%CI 1.09 –1.45; I2 0%) as shown in Figure 5. The periodic limb movement with arousal was reported on 2 studies(1, 17) as PLMAI more than 5 compared with PLMAI less than 1, Koo et al(1) studied an older male population which revealed no increased risk of hypertension with PLMAI. The other study by Koo et al(17) in a multi-ethnic population showed increased risk of hypertension with PLMAI participants. We did not perform a meta-analysis due to insufficient original data.

Evaluation of publication bias

A funnel plot to evaluate publication bias for the risk of hypertension in patients with PLMS was summarized in Figure 5. Egger's regression asymmetry test was carried out and showed no publication bias with P   0.05 for all analyses.

Discussion

PLMS is a common finding in participants undergoing polysomnography and may be associated with adverse health outcomes, including hypertension. We conducted a systematic review and meta-analysis of observational studies to assess whether the presence of PLMS was associated with hypertension. We found a significant association between having PLMS and hypertension, with an overall 1.26-fold increased risk of hypertension compared with those who did not have PLMS.

While the mechanisms behind why participants with higher PLMI are at a higher risk of hypertension are not established, several observations support this relationship. First, PLMS originate from neuronal generators within the spinal cord, which is also the home of preganglionic sympathetic nerve fibers (25). Coupled activation of leg motor and sympathetic nerve fibers could cause both PLMS and blood pressure increases. Second, PLMS is associated with arousals, causing nocturnal blood pressure elevations (7, 17), which if chronic, may translate to daytime hypertension similar to what is seen in obstructive sleep apnea and hypertension(26). Additionally, PLMS and obstructive sleep apnea frequently coexist, with PLMS occurring in roughly 48% of people with obstructive sleep apnea(27). A cluster analysis by Zinchuk et al. identified several distinct polysomnographic

clusters (phenotypes), with the highest cardiovascular event rate occurring in a phenotype combining mild obstructive sleep apnea with high-frequency PLMS(28). These findings suggest that the cumulative impact of two sleep disorders may be associated with a greater risk of cardiovascular disease or death.

Blood pressure lability that occurs during leg movements (29) has been investigated as a mechanism that may explain the association between PLMS and risk of cardiovascular disease, stroke, and mortality (30, 31). This is particularly notable in heart failure where the presence of PLMS is linked to higher mortality rates (32). The mechanisms explaining the association between PLMS with vascular disease including repeated surges in blood pressure every night for years may cause repeated mechanical stress on the vasculature, leading to vascular remodeling; In addition, changes in blood flow caused by blood pressure oscillations induce sheer stress and platelet activation, which can lead to atherosclerosis and hypercoagulability(33).

Increased inflammation may be another mechanism linking PLMS with vascular disease. In a study of RLS, patients with higher PLMI (45 PLMS per hour of sleep) had more than a 3-fold likelihood of having an elevated C-reactive protein (CRP), a marker of systemic inflammation, compared to RLS patients with lower PLMI. In that study, the presence of RLS by itself was not reported to be associated with increased serum CRP levels, suggesting that PLMS were the main reason for the elevated CRP levels(34).

Our study may provide rationale to consider work up for or treatment of patients with high PLMI, particularly in patients with poorly controlled hypertension. Future research agenda includes large population-based studies with longer follow-up periods, a broad range of population demographic characteristics along with confounder adjustment especially obstructive sleep apnea, and standardized definitions of PLMS (level of PLMI) and hypertension. As such knowledge becomes available, we will better understand the potential prognostic role of PLMS in development of hypertension and determine to what extent PLMS are causal in the emergence of hypertension.

Strengths and limitations

Our article represents the most comprehensive and systematic review of the relationship between PLMS and hypertension and reveals that there is likely an association between PLMS and hypertension. The strengths include examination of five comprehensive databases (PubMed, Embase, Scopus, Web of science and the Cochrane Library). The strict and comprehensive inclusion and exclusion criteria ensured that the included study populations were as homogeneous as possible, and the results of our study demonstrated no potential publication bias. In addition, PLMS measured in each study used polysomnography recommended by American Academy of Sleep Medicine or the official World Association of Sleep Medicine standards.

Some limitations should also be noted. First, there was variation in the definition of the exposure as studies used different cutoffs for PLMI to define the presence of PLMS, which may lead to imprecision. Similarly, the definition of the outcome or hypertension differed among studies. Second, models that estimated hypertension risk did not consistently adjust

for potential confounders. Three studies (1, 15, 17) did not adjust for confounders, while the other 3 studies (5, 16, 18) used similar adjustment variables such as age, obesity, medical comorbidities, and antidepressant medication. Despite these differences among the studies, our analysis did not reveal statistically significant heterogeneity. Third, the included studies were only published in English, which could result in study selection bias. Last, this is a meta-analysis of observational studies, which can only demonstrate association but not causality. Therefore, our findings support a hypothesis that PLMS may pose an increased hypertension risk, however, prospective longitudinal or interventional studies are needed to help establish a causal relationship.

In conclusion, our meta-analysis demonstrated a statistically significant increased hypertension risk among patients with PLMS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlight

- An association between periodic limb movements during sleep (PLMS) and hypertension is controversial.

- This study is the most comprehensive and systematic review of the relationship between PLMS and hypertension

- Our study may give direction to work up or treat in patients who have PLMS, especially with poorly controlled hypertension
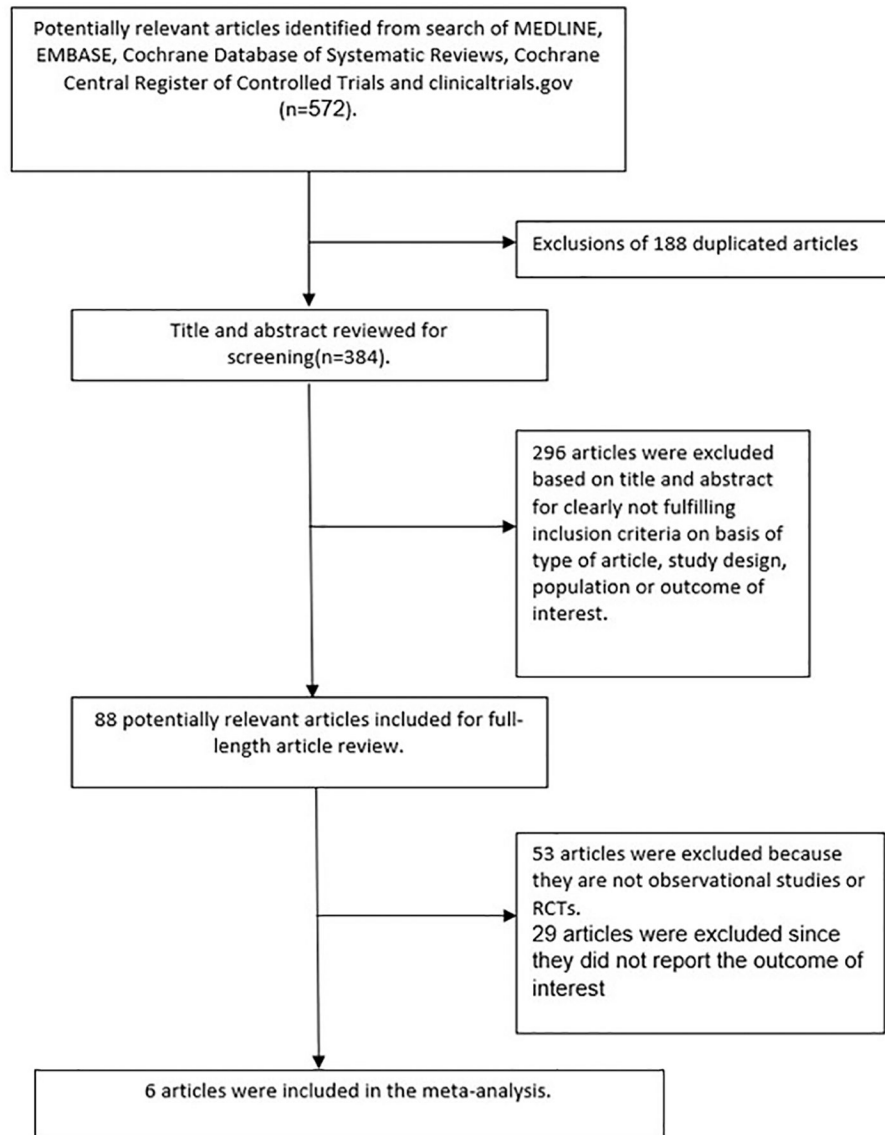
Figure 1:
Literature review process

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Hein et al.	0.25464222	0.32011	3.4%	1.29 [0.69, 2.42]
Mahmudova et al.	0.231112	0.233748	6.4%	1.26 [0.80, 1.99]
Shin et al.	0.11332868	0.20573364	8.3%	1.12 [0.75, 1.68]
Koo et al. (1)	0.43825493	0.13965188	17.9%	1.55 [1.18, 2.04]
Haba-Rubio et al.	0.10436002	0.11556277	26.2%	1.11 [0.89, 1.39]
Koo et al. (2)	0.2390169	0.0960402	37.9%	1.27 [1.05, 1.53]
Total (95% CI)			100.0%	1.26 [1.12, 1.41]

Heterogeneity: Tau² = 0.00; Chi² = 3.74, df = 5 (P = 0.59); I² = 0%
Test for overall effect: Z = 3.88 (P = 0.0001)

Figure 2:

Forest plot of the included studies comparing risk of hypertension in patients with PLMS and those without PLMS; square data markers represent risk ratios (RR). horizontal lines, the 95% confidence interval (CI) with marker size reflecting the statistical weight of the study using random-effects meta-analysis. A diamond data marker represents the overall RR and 95% CI for the outcome of interest. IV, inverse variance; SE, standard error.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Hein et al.	0.25464222	0.32011	3.6%	1.29 [0.69, 2.42]	
Shin et al.	0.11332868	0.20573364	8.8%	1.12 [0.75, 1.68]	
Koo et al. (1)	0.43825493	0.13965188	19.1%	1.55 [1.18, 2.04]	
Haba-Rubio et al.	0.10436002	0.11556277	27.9%	1.11 [0.89, 1.39]	
Koo et al. (2)	0.2390169	0.0960402	40.5%	1.27 [1.05, 1.53]	
Total (95% CI)			100.0%	1.26 [1.12, 1.42]	

Heterogeneity: Tau² = 0.00; Chi² = 3.74, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 3.75 (P = 0.0002)

Figure 3:

Forest plot of the sensitivity analysis excluding study that had no definition of the outcome (hypertension) comparing risk of hypertension in patients with PLMS and those without PLMS; square data markers represent risk ratios (RR); horizontal lines, the 95% confidence interval (CI) with marker size reflecting the statistical weight of the study using random-effects meta-analysis. A diamond data marker represents the overall RR and 95% CI for the outcome of interest. IV, inverse variance; SE, standard error.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Haba-Rubio et al.	0.10436002	0.11556277	27.1%	1.11 [0.89, 1.39]
Koo et al. (1)	0.43825493	0.13965188	18.5%	1.55 [1.18, 2.04]
Koo et al. (2)	0.2390169	0.0960402	39.2%	1.27 [1.05, 1.53]
Mahmudova et al.	0.231112	0.233748	6.6%	1.26 [0.80, 1.99]
Shin et al.	0.11332868	0.20573364	8.5%	1.12 [0.75, 1.68]
Total (95% CI)			100.0%	1.26 [1.12, 1.41]

Heterogeneity: Tau² = 0.00; Chi² = 3.74, df = 4 (P = 0.44); I² = 0%
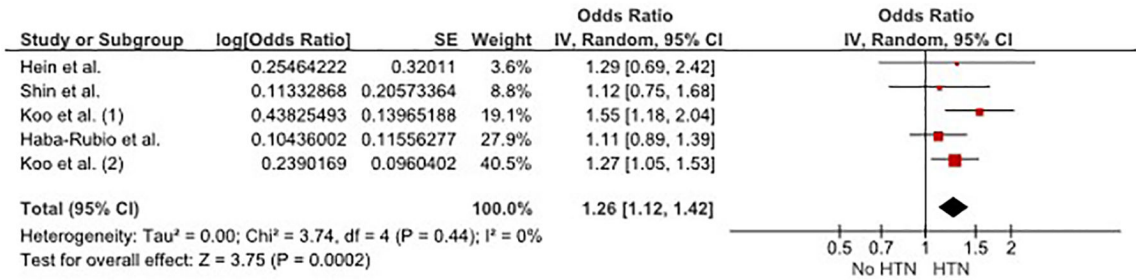Test for overall effect: Z = 3.80 (P = 0.0001)

Figure 4:

Forest plot of the sensitivity analysis excluding study that had different definition of the outcome (resistant hypertension) comparing risk of hypertension in patients with PLMS and those without PLMS; square data markers represent risk ratios (RR); horizontal lines, the 95% confidence interval (CI) with marker size reflecting the statistical weight of the study using random-effects meta-analysis. A diamond data marker represents the overall RR and 95% CI for the outcome of interest. IV, inverse variance; SE, standard error.
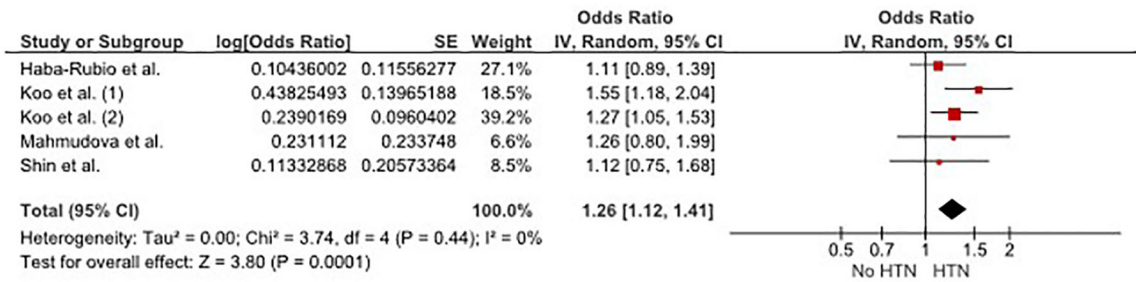
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Haba-Rubio et al.	0.10436002	0.11556277	29.2%	1.11 [0.89, 1.39]
Koo et al. (1)	0.43825493	0.13965188	21.6%	1.55 [1.18, 2.04]
Koo et al. (2)	0.2390169	0.0960402	38.2%	1.27 [1.05, 1.53]
Shin et al.	0.11332868	0.20573364	11.0%	1.12 [0.75, 1.68]
Total (95% CI)			100.0%	1.26 [1.09, 1.45]

Heterogeneity: Tau² = 0.00; Chi² = 3.74, df = 3 (P = 0.29); I² = 20%
Test for overall effect: Z = 3.21 (P = 0.001)

Figure 5:
Forest plot of the sensitivity analysis that excludes studies that had a different definition of the outcome comparing the risk of hypertension in patients with PLMS and those without PLMS and excluded the study that did not define the definition of hypertension; square data markers represent risk ratios (RR); horizontal lines, the 95% confidence interval (CI) with marker size reflects the study's statistical weight using random-effects meta-analysis. A diamond data marker represents the overall RR and 95% CI for the outcome of interest. IV, inverse variance; SE, standard error.
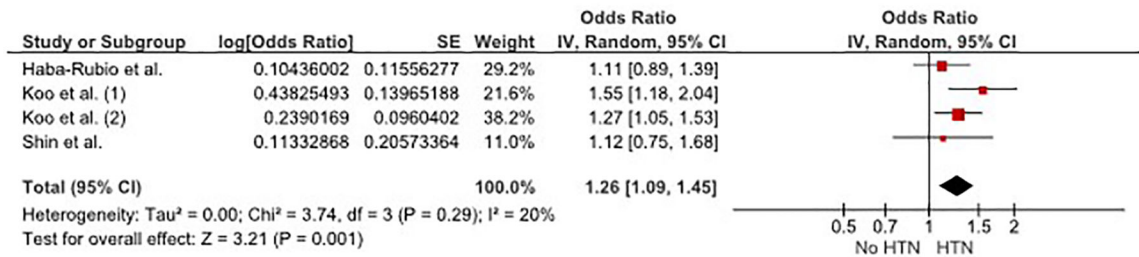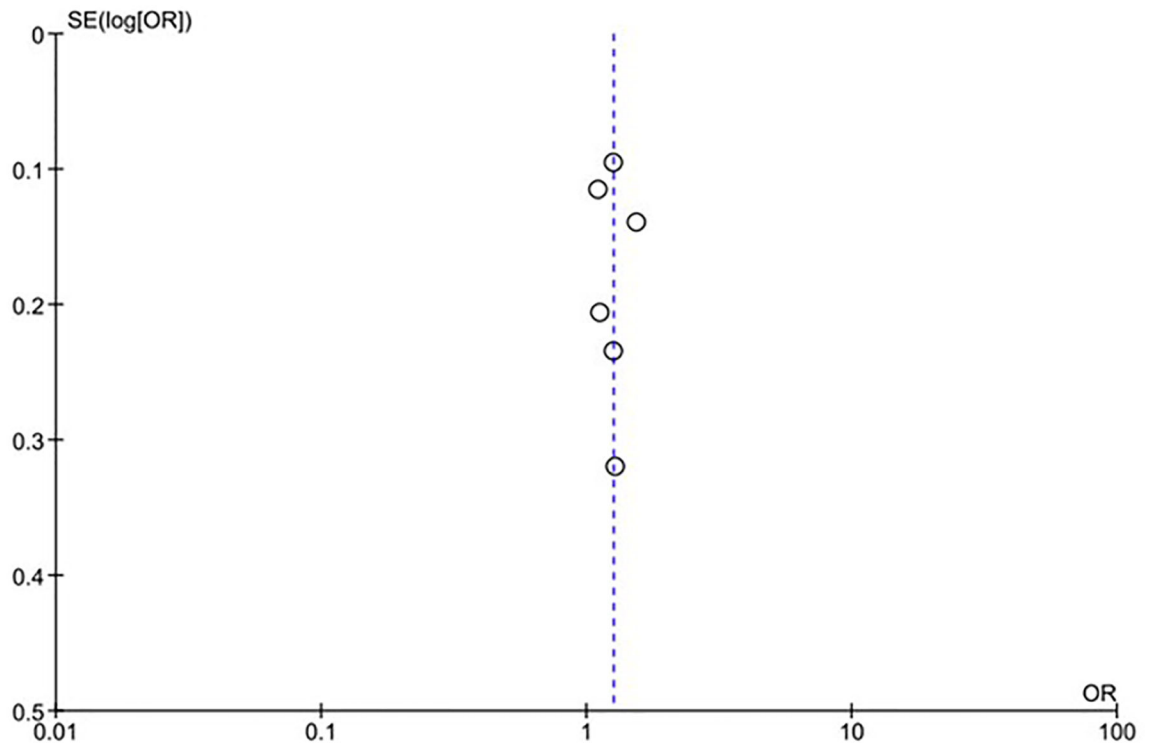
Figure 6:
Funnel plot of all studies included in the meta-analysis for the risk of hypertension in patients with PLMS and those without PLMS. RR, risk ratio; SE, standard error.

Table 1.

Participant characteristics.

Study	Sample Size(n)		Sex (Female, %)		Age (year)		Hypertension (%)		BMI (kg/m2)		Apnea/hypopnea index(n/h)	
	PLM	Non-PLM	PLM	Non-PLM	PLM	Non-PLM	PLM	Non-PLM	PLM	Non-PLM	PLM	Non-PLM
Mahmudova et al (14)	112	188	30.5	33.1	55.4	53.3	55	49.1	31.3	30.7	No data	No data
Haba-Rubio et al (5)	618	1544	46.6	53.0	64 ± 11	57 ± 11	54.5	36.3	No data	No data	17.3 ± 16.7	14.8 ± 16.12
Shin et al (15)	176	987	46.6	40.6	58.6 ± 0.9	49.1 ± 0.5	32.4	25.0	23.6 ± 0.2	24.3 ± 0.1	15.28 ± 1.49	19.47 ± 0.77
Koo et al (16)	293	1001	44.7	55.8	71.8±9.2	66.9±8.5	67.6	57.3	28.4 ± 5.5	29.0 ± 5.7	22.7±17.2	24.9±20.5
Koo et al (1)	1313	848	0	0	77.1 ± 5.7	75.6 ± 5.2	70.5	65.3	27.2± 3.7	27.1 ± 3.9	11.4 ± 12.9	12.5 ± 13.1
Hein et al (23)	53	384	32.5% total		54.7 ± 10.1		39.6	36.5	No data	No data	No data	No data

Abbreviations: PLM, periodic limb movement

Table 2.

Characteristics of included studies.

Study	Mahmudova et al(14)	Haba-Rubio et al (5)	Shin et al(15)	Koo et al(16)	Koo et al (1)	Hein et al(23)
Country	Turkey	Switzerland	South Korea	USA	USA	Belgium
Year	2022	2018	2018	2015	2011	2019
Study design	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional for prevalent hypertension The cohort for incident hypertension	Cross-sectional
Hypertension Definition	No mention	(SBP) 140 mmHg and/or (DBP) 90 mmHg or presence of drugs.	Self-reported that participants had been diagnosed with hypertension or if they reported that they receive or have received medicine for hypertension.	SBP) 140 mmHg and/or (DBP) 90 mmHg or presence of drugs.	1) SBP) 140 mmHg and/or (DBP) 90 mmHg 2) Self-reported receiving anti HTN med	1)Uncontrolled HTN (140 / 90) at least 3 meds 2) controlled HTN (<140 /<90) at least 4 meds
OR (95% CI)	**PLMI 15/ hour 1.26 (0.80– 2.00)** Persisting PLMS after PAP titration 15/hour 1.69 (1.05– 2.72)	**PLMI 15/ hour 1.11 (0.89– 1.40)**	**PLMI 15 1.12 (0.75–1.68)** PLMAI 1 1.21 (0.83–1.76)	PLMI 5–30 1.06 (0.84– 1.33) **PLMI 30 1.55 (1.18– 2.04)** PLMAI 1–5 1.13 (0.89– 1.43) PLMAI 5 1.62 (1.14– 2.32)	Prevalent hypertension PLMI 5–30 1.12 (0.91–1.38) **PLMI 30 1.27 (1.05–1.53)**	**PLMI 26 1.29 (0.69–2.42)** Occasional RLS + PLMI 26/hour 1.04 (0.64–1.69) Frequent RLS + PLMI 26/hour 2.20 (1.35–3.61)
Confounder adjustment for prevalence	None	Age, sex, BMI, alcohol use, smoking, and AHI	Age, sex, smoking, BMI, AHI, AI-overall, RLS	none	None for prevalent hypertension	Age, sex, BMI, hypertriglyceridemia, diabetes, sleep duration, snoring, OSA severity, BDI score, ISI score, ESS score, antidepressant therapy
Quality assessment	S4, C0, O3	S4, C2, O3	S4, C2, O3	S4, C0, O3	For cross-sectional S4, C0, O3	S4, C2, O3

Abbreviations: PLMI, periodic limb movement index; PLMS, periodic limb movements during sleep; PAP, positive airway pressure; PLMAI, periodic limb movement arousal index; BMI, body mass index; AHI, apnea hypopnea index; RLS, restless legs syndrome; AI-overall, overall arousal index; BDI, Beck depression inventory; ISI, insomnia severity index; ESS, Epworth sleepiness scale; OSA, obstructive sleep apnea; HTN, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure S, selection; C, comparability; O, outcome.