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A Systematic Review of Publications on the Associations Between Sleep Architecture and Arterial Hypertension

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Sleep research has garnered substantial interest among scientists owing to its correlation with various diseases, particularly elevated blood pressure observed in patients with obstructive sleep apnea. This systematic review aims to identify and analyze publications exploring the associations between sleep architecture and arterial hypertension. A comprehensive search of PubMed (MEDLINE), Scopus, and Embase databases yielded 111 reports, of which 7 manuscripts were included in the review. Four of the studies reported a significant reduction in the duration of the N3 phase of sleep in hypertensive patients, while 2 studies found a statistically significant reduction in the duration of the N2 and rapid eye movement (REM) stages of sleep. Three studies indicated increased sleep fragmentation in hypertensive patients. They showed a longer duration of the N1 stage of sleep, shorter duration of overall sleep time, and an increased apnea-hypopnea index in hypertensive patients. These findings underscore the association between the duration of non-REM/REM sleep stages and elevated BP, providing substantial evidence. Moreover, a notable increase in sleep fragmentation was observed among patients with hypertension. However, further research is warranted to expand and deepen our understanding of this intricate relationship. This systematic review serves as a valuable resource, guiding future investigations and contributing to advancements in the field of sleep and arterial hypertension.

Keywords: **Arousal • Blood Pressure • Hypertension • Sleep Deprivation • Sleep Stages**

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Background

In recent years, sleep research has gained immense interest among scientists owing to its increasing prevalence and its correlation with various diseases, particularly in the cardiovascular system. The association between cardiovascular diseases and sleep disorders has been observed, which is possibly due to shared pathogenesis factors. Among these diseases, hypertension is a prominent condition, often undetected in its early stages. The contributing factors of hypertension development are the overactivation of the autonomic nervous system [1] and the inappropriate activation of the renin-angiotensin-aldosterone system [2]. The definition of sleep presented by Carskadon is as follows: “Sleep is a recurring, reversible neuro-behavioral state of relative perceptual disengagement from and unresponsiveness to the environment. Sleep is typically accompanied (in humans) by postural recumbence, behavioral quiescence, and closed eyes.” [3]. Scientists have observed that sleep can be categorized into stages of rapid eye movement (REM), in which humans spend around 75% of sleep, and non-rapid eye movement (NREM), with cycles of these stages occurring multiple times during the sleep period [4]. The NREM phase is further divided into the N1, N2, and N3 stages, presenting a progressively deeper sleep with each phase. The phases are selected with different sleep parameters that are recorded during a polysomnography examination. There is evidence that sleep deprivation leads to elevations in blood pressure and heart rate values [5]. The short sleep duration that appears especially during middle age is commonly associated with arterial hypertension, as well as with the higher blood pressure values present among patients with obstructive sleep apnea [6]. Moreover, disruptions in the timing and duration of sleep can contribute toward greater variability in blood pressure values and to the appearance of a non-dipping blood pressure pattern [7,8]. There is also a proven association between high blood pressure and sleep apnea [9]. Sympathetic, humoral, and cellular responses [10] to sleep apnea over time are responsible for vascular dysfunction and the consequent development of arterial hypertension [11]. These manifestations can be exacerbated by sleep deprivation [12,13], which commonly occurs in patients with sleep apnea because of their poor sleep architecture [14]. The apnea-hypopnea index has been found to have an association with blood pressure values and the arousal index. An elevated apnea-hypopnea index has been closely linked to higher blood pressure values [15]. Additionally, an elevation in blood pressure is seen not only among patients with obstructive sleep apnea but also in patients with restless leg syndrome [16], insomnia [17], or sleep bruxism [18].

Polysomnographic examination is the criterion standard tool for analyzing sleep architecture. It has shown that with the progressive deepening of the NREM phase of sleep, there is a

decrease in sympathetic nervous system activity [19]. In young healthy normotensive individuals, nocturnal blood pressure dipping has been observed during the shift to the deep slow wave sleep stage (NREM sleep stage N3) [20]. The association between slow wave sleep in the modulation of blood pressure was investigated in 2 community-based cohort studies. These studies showed that the percentage of slow wave sleep was inversely associated with the incidence of hypertension [21,22]. A link between sleep architecture and hypertension has also been uncovered. However, there is still a necessity to conduct further research in this context.

Therefore, this systematic review aims to identify and analyze publications on the association between sleep architecture and arterial hypertension, with a particular focus on sleep fragmentation and the duration of the non-REM/REM phases of sleep, to address the existing research gap.

Material and Methods

Eligibility Criteria

The inclusion criteria for this review included English-language research articles focusing on sleep architecture in the adult hypertensive population. Exclusion criteria consisted of pediatric patients, studies involving co-existing obstructive sleep apnea, animal research, genetic studies, hypertension in pregnancy, and studies lacking polysomnography data. Additionally, studies with sample sizes of less than 10 patients, case reports, reviews, letters to the editor, and those not reporting on sleep architecture and its association with hypertension were excluded.

Search Strategy and Sources Reviewed

A comprehensive search strategy was conducted, incorporating the following search terms: (sleep architecture, sleep stages, sleep structure) and/or (hypertension, and high blood pressure) in combination between the first and second term. These terms were searched within titles and keywords. The literature review was independently conducted by JK and HM, who reviewed PubMed (MEDLINE), Scopus, and Embase databases (access date January 20, 2022, 6: 45 p.m.). The search was limited to English-language publications going as far back as the year 2000. No other filter was applied during the search, but later on, the manual selection of the articles was performed. In addition to electronic searches, reference lists of relevant articles were manually searched to identify additional studies.

Data Collection Process

Data collection from the selected reports was performed independently by 2 researchers. The articles were manually selected

Table 1. List of investigated studies and their characteristics.

Author (Year)	Compared groups	Aim of the study	Polysomnography parameters					
			TST	REM	NREM			Other
					N1	N2	N3	
Berger (2022)	No hypertension at baseline Normotensives/ incident hypertension	Association between sleep macro and microstructure and incident hypertension	ns	ns	↑ p=0.002	ns	↓ p=0.008	↑ arousals (0.002) ↑ AHI (<0.001) ↑ ODI (<0.001) ↓ SpO2 (0.003)
Liu X (2021)	No comparison	Association between visit-to-visit blood pressure variability and sleep architecture	↓ p<0.001	↓ p<0.001	↑ p<0.001	ns	ns	↑ AHI (<0.001)
Kanclerska (2022)	Hypertensives/ normotensives	Blood pressure and sleep architecture association	–	ns	ns	↓ p<0.001	ns	↑ arousals (<0.01) ↑ AHI (<0.001) ↑ ODI (<0.001) ↑ SpO2 (<0.001)
Liao H (2016)	Mild/moderate HA vs control	Relation between arterial stiffness and sleep architecture	↓ p<0.001	↓ p=0.02	↓ p<0.001	↓ p<0.001	↓ p<0.001	↑ sleep latency (0.032) ↑ AHI (0.042) ↑ arousals (<0.001)
Li X (2018)	Hypertensives/ normotensives	Association between morning BP and sleep architecture	ns	ns	ns	ns	ns	↑ sleep latency
Fung MM (2011)	Hypertensives/ normotensives	Association between incident AH and PSG measures	ns	–	↑ p=0.013	↑ p=0.033	↓ p<0.002	↓ SpO2 <0.025
Grimaldi D (2014)	Hypertensives/ normotensives	Association between sleep parameters and AH	ns	ns	ns	↓ p<0.001	ns	Comparable values in wake-sleep fragmentation

BP – blood pressure; AH – arterial hypertension; PSG – polysomnography; TST – total sleep time; REM – rapid eye movement sleep stage; NREM – non-rapid eye movement sleep; N1 – N2, N3- adequate N1 NREM sleep, N2 NREM sleep, N3 NREM sleep; AHI – apnea-hypopnea index; ODI – oxygen desaturation index; SpO2 – oxygen saturation; ns – not statistically significant.

based on the title and abstract to ensure their relevance to this systematic review. No automation tools were used during the selection process. The data were extracted into Excel to perform further analysis. The characteristics of the considered studies, including author, publication year, study design, sample size, age and sex of participants, study setting, sleep and blood pressure measurement methods, and the main

findings are shown in **Table 1**. In case of discrepancies or disagreements between the 2 researchers, a third researcher was consulted to ensure accuracy and completeness of the data collection process. The data extraction process was carefully monitored to minimize errors or omissions, and the Excel spreadsheet was thoroughly checked for completeness and accuracy before proceeding with the analysis.

Table 2. Grading of recommendations, assessment, development, and evaluations (GRADE) assessment of evidence.

Study Author (year)	Design	Quality assessment						Summary of findings		
		Limitations	Inconsistency	Indirectness	Imprecision	Risk of bias	Other	No. of patients		Quality
								Intervention	Control	
Berger M (2022)	Prospective observational study	– No 24h ABPM – Single-night with no familiarization	Not serious	Not serious	Not serious	Not serious	+	974	198	+++ – Moderate
Liu X (2021)	Cross-sectional study	– Single-night – Lab-based PSG	Not serious	Not serious	Not serious	Not serious	+	3565		+++ – Moderate
Kanclerska J (2022)	Prospective observational study	– Single-night lab-based PSG – No ABPM	Not serious	Not serious	Not serious	Not serious	–	31	60	+++ – Moderate
Liao H (2016)	Cross-sectional study	– Small sample size – No follow-up	Not serious	Serious	Not serious	Not serious	–	86	20	++ -- Low
Li X (2018)	Cross-sectional study	– Couldn't exclude the effect of anti-hypertensive medication	Not serious	Serious	Not serious	Selection bias	+	82	62	++ -- Low
Fung MM (2011)	Prospective observational study	– No 24-h ABPM	Not serious	Not serious	Not serious	Not serious	+	243	541	+++ – Moderate
Grimaldi D (2014)	Case-control study	– Small sample – Sex differences (underrepresentation of women)	Not serious	Not serious	Serious	Not serious	+	14	28	++ -- Low

ABPM – ambulatory blood pressure monitoring; PSG – polysomnography.

Risk of Bias

The risk of bias in the included studies was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [23], which considers various factors, including study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias, to evaluate the

quality of evidence-based research. Specific criteria were used to assess the risk of bias in the included studies, such as selection bias, performance bias, detection bias, attrition bias, and reporting bias. Each study was independently analyzed by 2 researchers, with consensus reached through discussion. The results were assessed independently using the Risk of Bias-2 (RoB-2) tool for randomized studies [24] or the Risk of Bias in

Non-Randomized Studies – of Interventions (ROBINS-I) tool for non-randomized studies [25]. The results of the assessment are shown in **Table 2**. All 7 studies included in this systematic review demonstrated a statistically significant relationship between sleep architecture (at least 1 polysomnography parameter) and arterial hypertension.

Results

Selection of Studies

The study selection process involved a total of 111 initially identified publications. After removing duplicates ($n=7$) and excluding papers that did not meet the inclusion criteria, such as animal studies ($n=4$), studies involving patients with obstructive sleep apnea ($n=53$), studies focusing on pediatric populations or pregnant women, as well as case reports and medication effect descriptions, a 2-step process was followed. First, 2 reviewers independently screened the titles and abstracts of the retrieved studies to select appropriate publications. Of the remaining 20 full-text records that passed this stage, each was independently analyzed for eligibility by the researchers. No automation tools were used during this process. The same 2 reviewers examined the full texts of the research that had passed screening during the full-text evaluation stage. Discussion between the 2 reviewers helped to settle the differences in their assessments of the title/abstract and entire text. Finally, a total of 7 manuscripts were included in the systematic review (**Table 1**).

Quality of Studies

The risk of bias in each included study was assessed and is presented in **Table 2**. Most of the studies demonstrated no major issues with the comparability of participants among the examined patients. However, selection bias was detected in 1 of the analyzed papers by Li X et al. [26]. No detection bias, or problems with the measurement or classification of outcomes, were found in any of the studies. The statistical analysis provided in each study was deemed to have high methodological quality. Notably, among the 4 studies [21,26-28], a substantial improvement in the GRADE score was applied, as indicated in **Table 2**.

Study Description

In 3 out of 7 studies, there were statistically significant results showing a reduction in the N3 sleep stage [21,27-29], while in 2 others [30,31], there was statistical significance in the reduction of the duration of the N2 sleep stage. The duration of REM sleep was also observed to be reduced in 2 studies [26,28,29]. Furthermore, 2 papers reported statistical

significance in the reduction of total sleep time [28,29], and 3 papers noted more frequent arousals among the group of patients with hypertension [27,29,30].

One of the analyzed studies focused on microstructural and macrostructural parameters of sleep [27] that can be used to predict the development of hypertension. Berger et al investigated potential risk factors associated with sleep that increased the probability of developing arterial hypertension. The study followed 1172 participants who did not have hypertension prior to the study for an average of 5.2 years. Home-based polysomnography results and in-office measurements of blood pressure were analyzed. Among the microstructural changes observed during sleep, this study found that patients with diminished absolute delta and sigma power had a statistically significant probability of developing hypertension [27]. Furthermore, the study also explored macrostructural changes associated with sleep and demonstrated an inverse association between slow wave activity (N3 sleep stage) and the risk of developing incident hypertension. The N1 phase of sleep was observed to account for a greater percentage of sleep. Interestingly, Berger et al also noticed a statistically significant difference in the objective sleep parameters. During follow-up, it was observed that patients who had developed incident hypertension during the study had changes in sleep efficiency ($P=0.024$). Additionally, these patients were also found to have higher arousal and apnea-hypopnea indices.

A similar study design was conducted by Fung et al [21], focusing on 784 elderly men (age ≥ 65 years) with no hypertension at the time of in-home polysomnography screening. The study had a follow-up period of 3.4 years. Blood pressure was recorded (2 measurements on the right arm) at the beginning of the examination and at the time of follow-up. The results of the study were consistent with those of the Berger study, with higher percentages of the N1 and N2 stages of sleep, a higher apnea-hypopnea index, and a lower percentage of the N3 phase of sleep being observed. After adjusting for various factors, statistical significance was found for the N3 sleep stage ($P=0.002$) [21].

Blood pressure variability has been recognized as an independent risk factor for cardiovascular disease [29-33]. Sleep disturbances can also predict the onset of this group of diseases. In the third study we reviewed, conducted by Liu et al [28], the focus was on the association between blood pressure variability and sleep architecture. The study included a large sample of patients ($n=3565$) who underwent in-lab polysomnography and had at least 3 in-office blood pressure measurements taken 12 months before the polysomnography examination. Having regard for possible confounders, a statistically significant inverse correlation was seen between systolic blood pressure variability and duration of the REM stage of sleep. The results

indicated that patients with higher systolic blood pressure variability had shorter durations of REM sleep ($P=0.001$), as well as reduced durations of N2 and N3 sleep stages. Conversely, the N1 sleep phase was longer in patients with greater systolic blood pressure variability ($P=0.001$) than in those with normal blood pressure variability.

Kancłerska et al conducted a study that provided evidence for the differences in sleep structures between hypertensive and normotensive patients [30]. The study involved a 1-night polysomnography conducted in the sleep laboratory on 91 patients, along with ambulatory blood pressure monitoring. It was observed that the N2 phase of sleep was prolonged among hypertensive patients, which was a statistically significant finding consistent with the results of Liu et al [28]. Moreover, statistically significant differences in the apnea-hypopnea index and oxygen desaturation index were observed between the experimental and control groups. The study also revealed increased sleep fragmentation (measured according to the arousal index) in hypertensive patients, compared with normotensive patients.

A different approach to the analysis of the sleep architecture among patients with hypertension was presented by Liao et al [29]. The authors focused on pulse wave velocity, which is a key index for estimating arterial elasticity. Pulse wave velocity is recognized as a predictor for the development of cardiovascular diseases, including hypertension. In their study, a total of 86 hypertensive patients underwent ambulatory blood pressure monitoring and in-lab polysomnography and were compared with 20 normotensive individuals from the control group. The results of this study were consistent with the previously discussed papers, demonstrating that hypertensive patients had a longer sleep latency ($P<0.032$) and shorter duration of total sleep time ($P=0.001$). Additionally, the N3 phase of sleep was significantly shorter in the hypertensive group (19.93% in the control group vs 8.58% in the hypertensive group, $P<0.001$). This finding aligns with the previous research discussed. Interestingly, Liao et al also observed longer durations of the N1 and N2 phases of sleep, as well as higher apnea-hypopnea and microarousal indices in the experimental group. This result corresponds with the study outcomes of Kancłerska et al.

Li et al [26] conducted a study to investigate sleep architecture in relation to 24-h ambulatory blood pressure monitoring, with a focus on morning blood pressure values, among 144 hypertensive patients. A decrease in sleep efficiency, shorter slow wave sleep, and increases in the proportion of light sleep and the arousal index were observed. These results were consistent with the previously analyzed studies.

However, a study by Grimaldi et al [31] presented contrasting results to the aforementioned studies. The study included 14 patients with recently diagnosed untreated hypertension

(<1 year since the diagnosis), according to established guidelines [34]. These patients were compared with a normotensive control group consisting of 28 participants. Both groups underwent a 2-night polysomnography examination as well as 44-h ambulatory blood pressure monitoring. They found no statistically significant differences in total sleep time, slow wave sleep, or REM sleep. This might be attributed to the small sample size of patients or other individual factors, such as weight and family predisposition for developing hypertension. Interestingly, in contrast to previous studies, Grimaldi et al observed a statistically significant reduction in the percentage of N2 sleep among hypertensive patients ($P=0.03$). Furthermore, it appeared that hypertensive patients had particularly low systolic blood pressure values during the N1, N2, and REM phases of sleep, as opposed to the control group.

Indeed, the findings from the studies reviewed confirm that there is an existing association between changes in sleep architecture and blood pressure concerning REM and non-REM sleep phases. The evidence supports that hypertensive individuals exhibit alterations in their sleep patterns, compared with normotensive individuals. Increased sleep fragmentation, as indicated by a higher arousal index, was consistently observed in hypertensive patients across multiple studies. Additionally, several studies reported increased sleep latency and decreased total sleep time duration among hypertensive individuals. Furthermore, hypertensive patients exhibited higher apnea-hypopnea index values, indicating increased sleep-disordered breathing, and lower oxygen saturation levels than normotensive individuals. These findings collectively emphasize the relationship between sleep architecture and blood pressure regulation in the context of hypertension.

Discussion

The findings of the presented studies confirm the presence of an association between the duration of non-REM and REM stages of sleep and elevated blood pressure. Hypertensive patients were consistently found to have alterations in the duration of specific sleep stages, compared with normotensive individuals. Furthermore, a common finding across the studies was increased sleep fragmentation among hypertensive patients. Sleep fragmentation refers to disruptions in the continuity of sleep, often measured by indices such as the arousal index. Higher arousal index values reflect more frequent awakenings or disturbances during sleep. This increased sleep fragmentation observed in hypertensive patients suggests an association between disrupted sleep and elevated blood pressure. Overall, these findings highlight the importance of sleep architecture and sleep quality in relation to blood pressure regulation, emphasizing the potential impact of sleep disturbances on hypertension.

Sleep Disorders and Cardiovascular Risk

Sleep architecture disorders have become increasingly apparent in recent years. Obstructive sleep apnea, insomnia, and circadian rhythm disorders have been linked to an increased cardiovascular risk [7,8]. Researchers are recognizing the importance of identifying and treating sleep disorders as a way to reduce the risk of developing cardiovascular diseases. Screening for sleep disorders may become a routine part of the cardiovascular risk assessment. The reviewed papers investigated the relationship between changes in sleep architecture and blood pressure. Sleep architecture was analyzed using either at-home or sleep laboratory polysomnography, which is the criterion standard examination tool for the diagnosis of sleep disorders. Blood pressure measurements were recorded either by 24-h ambulatory blood pressure monitoring or were measured manually at the doctor's office. It is important to note that many studies on sleep disorders and hypertension have been conducted using respiratory polygraphy, which is a recognized, widely available, and inexpensive method used in the diagnosis of obstructive sleep apnea. However, it does not provide the capability to analyze sleep architecture, as it lacks the recording of electroencephalography. Consequently, publications that relied solely on polygraphy were excluded from this review, as the assessment of parameters such as total sleep time, sleep latency, and arousals cannot be accurately estimated with this method.

Arterial Hypertension

In 2019, the American College of Cardiology and American Heart Association [35] published new guidelines that updated the categories of arterial hypertension. The guidelines are as follows: (1) normal (<120 systolic and <80 mmHg diastolic), (2) elevated (120-129 systolic and <80 mmHg diastolic), (3) stage 1 hypertension (130-139 systolic or 80-89 mmHg diastolic), and (4) stage 2 hypertension (≥ 140 systolic or ≥ 90 mmHg diastolic). These measurements should be based on averaged measurements on at least 2 separate in-office visits, and should be correlated with at-home measurements. Alternatively, 24-h ambulatory blood pressure monitoring can be used. The studies that were analyzed in this review had either made use of in-office blood pressure measurements, as per the above mentioned guidelines, or ambulatory blood pressure monitoring.

Arterial hypertension is a disease encountered worldwide. In 2023, the WHO estimated that 1.28 billion adults aged 30-79 years had hypertension, with the majority living in middle to low income countries. Shockingly, approximately 46% of adults are oblivious to their condition [36]. Arterial hypertension presents a serious risk of developing end organ damage, which can affect the heart, brain, eyes, and kidneys [37,38]. These data convince us that hypertension is a global health problem that should be screened for more carefully. To avoid

the development of these complications, treatment should be started immediately after diagnosis.

The underlying pathomechanisms of hypertension involve the dysregulation of the renin-angiotensin-aldosterone system [2] leading to oxidative stress and, consequently, to renal tubular sodium reabsorption, vasoconstriction, vascular smooth muscle remodeling, and inflammation, ultimately resulting in endothelial dysfunction [39]. Moreover, overactivation of the autonomic nervous system (particularly the sympathetic nervous system) is also one of the proven pathomechanisms behind the development of arterial hypertension [1,40]. Its inappropriate activity can result in an increase in cardiovascular morbidity and mortality, as well as changes in various stages of sleep, ultimately affecting the quality of sleep [41-43].

There is a subtype of hypertension called resistant hypertension, which is associated with a particularly high cardiovascular risk. This subtype is often related to sleep disorders, most frequently, obstructive sleep apnea [44]. The importance of acknowledging the above-mentioned pathomechanisms is necessary to create new methods of treatment, as the effectiveness of current antihypertensive treatment is low [36].

Sleep Architecture

It has been postulated that sleep is essential for many vital functions, including energy conservation, modulation of immune responses, cognition, performance, vigilance, and the psychological state [45,46]. Human sleep architecture is primarily divided into 2 phases, namely the NREM and REM sleep phases. The non-REM phase of sleep is further subdivided into the N1, N2, and N3 stages. These 3 stages are associated with progressively deeper levels of sleep [47,48]. Researchers have emphasized the importance of sleep continuity for adaptive mental health functions [49]. Disturbances in sleep continuity have been associated with several negative health outcomes, including depression [50], activation of the sympathetic nervous system, elevation in heart rate [12], and an increase in the prevalence of hypertension [6]. Therefore, there is a known correlation between sleep and hypertension. In summary, the relationship between sleep and hypertension is well-established. Sleep disturbances, including sleep deprivation, sleep disorders (such as obstructive sleep apnea), and circadian rhythm disorders, can contribute to elevated blood pressure and increase the risk of developing hypertension. Maintaining healthy sleep patterns and addressing sleep disorders can have a significant impact on blood pressure control and overall cardiovascular health.

Sleep Disorders and Hypertension

Moreover, a strong connection between hypertension and obstructive disorders has been observed during sleep. Several

studies have linked the presence of sleep disorders and hypertension, focusing primarily on the correlation between obstructive sleep apnea and hypertension [51]. It has been hypothesized that the increase in blood pressure among patients with obstructive sleep apnea is due to hypoxia and its subsequent activation of the sympathetic nervous system [52]. While obstructive sleep apnea has been well-established as a risk factor for hypertension, in this review, we specifically excluded obstructive sleep apnea to focus on the relationship between essential hypertension (hypertension without obstructive sleep apnea) and specific sleep architecture disorders. There is also a large amount of research published on obstructive sleep apnea that was beyond the scope of this review. Even after the exclusion of obstructive sleep apnea, there appears to be strong evidence suggesting that hypoxia and respiratory events favor the appearance of hypertension. Interestingly, there is no safe level of respiratory obstruction. Even when the degree of respiratory obstruction is well within the normal range, there is a strong correlation with elevations in blood pressure. In addition, hypertension shares the same pathomechanism as other sleep disorders, namely sleep bruxism [30]. The increased variability of blood pressure values in sleep bruxism is accompanied by inflammation; therefore, sleep bruxism has recently been regarded as one of the risk factors behind the development of hypertension and other cardiovascular events [53]. It has also been proven that patients with sleep bruxism have a higher arousal index, consequently resulting in sleep fragmentation [54].

Fragmented sleep is less efficient than consolidated sleep and can often result in daytime sleepiness, fatigue, and a lack of concentration [55]. Frequent arousals during sleep are associated with longer wake after sleep onset, reduced sleep efficiency, and more frequent sleep phase shifts [56,57]. Ineffective sleep can lead to the development of hypertension as well as increased cardiovascular risk [15]. Most of the analyzed research correlates the fragmentation of sleep with arterial hypertension.

It has also been broadly discussed that there is a relationship between hypertension and the apnea-to-hypopnea index, even when the index is within the normal range [58], which we found in this systematic review [27-30]. Past studies have illustrated a linear association between the apnea-hypopnea index and blood pressure values and the prevalence of cardiovascular disease [59,60]. It appears that the apnea-hypopnea index may be a predictive parameter in the assessment of potential future cardiovascular disease development.

As stated in analyzed papers, a shorter N3 sleep stage can result in insufficient regeneration, a slower anabolic process, negligible cellular regeneration, impairment of immunological function, and an increase in oxidative stress [61]. Oxidative stress is one of the fundamental mechanisms responsible for the development of hypertension. Reactive oxygen species

play an important role in the homeostasis of the vascular wall. Overproduction of reactive oxygen species has been linked to the development of arterial hypertension [62]. The mechanism of activation of the sympathetic nervous system, the cytokine response, and the magnitude and extent of the proinflammatory immune response have been well documented in patients with hypertension [63].

Additionally, the N1 stage of sleep has been shown to be prolonged in individuals with sleep fragmentation and frequent arousals. The N2 sleep stage, on the other hand, appears to have the greatest discrepancies in the results of the analyzed studies in this review. We see a necessity for further research to be conducted on the N2 sleep phase among the hypertensive group of patients.

Although the REM stage of sleep is important for memory [64] and emotional processing [65], the relationship between REM and hypertension has been poorly described. Research suggests that patients with hypertension can have impaired emotional regulation, a greater risk of depression and anxiety, and difficulty regulating stress and emotions [66].

Among the analyzed research, sleep latency was increased and total sleep time was decreased in 2 studies. Studies have proven that there is a strong association between the reduced duration of sleep and hypertension [67]. It has been documented that a higher risk of unsatisfactory blood pressure regulation appears in adults habitually sleeping for less than 6 h a day [68].

Overall, while more research is needed to fully understand the relationship between sleep architecture and hypertension, as the existing evidence suggests that there is a connection between the two. It is important for individuals with hypertension, or at risk of developing hypertension, to prioritize good sleep habits and address any sleep disorders that are present.

There is also a great need for future research on the prevention of cardiovascular disease or the management of treatable sleep disorders. Early detection and treatment of sleep disorders can be a key strategy for reducing the risk of developing cardiovascular diseases and improving overall health and quality of life. Further research is needed to identify effective interventions for the prevention and management of cardiovascular diseases in people with sleep disorders.

The study had several limitations that need to be acknowledged. First, there was a limited number of studies available that specifically examined the association between hypertension and sleep architecture disorders in patients without sleep apnea. This scarcity of research in the field highlights the need for further investigation in this area. Additionally, some of the reviewed studies had a moderate risk of bias, which may have

influenced the validity of their findings. Furthermore, in some cases, the examined groups consisted of a small number of patients, which could limit the generalizability of the results. These limitations emphasize the need for larger scale, well-designed studies to provide more robust evidence on the relationship between hypertension and sleep architecture disorders in individuals without sleep apnea.

Conclusions

1. There is an association between the duration of the non-REM and REM stages of sleep and elevation in blood pressure. In patients with hypertension, there is a consistent reduction in the duration of N3 (deep sleep) and REM phases of sleep. This suggests that individuals with hypertension can experience less restorative and lower quality sleep in these stages. However, findings regarding the N2 (light sleep) stage are contradictory, with some studies showing elevations and others showing reductions in this sleep stage in patients with hypertension. Further research is needed to clarify the relationship between N2 sleep and hypertension.
2. Sleep fragmentation, as measured by the arousal index, is commonly observed in hypertensive patients. This indicates that individuals with hypertension experience frequent

awakenings or disruptions during sleep, leading to fragmented sleep patterns. Sleep fragmentation can have negative effects on overall sleep quality and may contribute to the development or exacerbation of hypertension. It highlights the importance of assessing sleep continuity and addressing sleep disturbances in the management of hypertension.

3. Airway obstruction and hypoxia, even within normal ranges, contribute to hypertension. Even subtle sleep-related breathing disturbances can activate the sympathetic nervous system and increase oxidative stress, promoting hypertension. Treating these underlying sleep-related breathing issues may help control blood pressure.
4. Further research is needed to expand and deepen our understanding of the relationship between arterial hypertension and sleep architecture, as the current body of evidence is limited by the small number of studies. More comprehensive investigations will provide valuable insights into the mechanisms and implications of sleep disturbances in hypertension, leading to improved diagnosis and treatment strategies.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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