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CLINICAL CHARACTERISTICS AND PROGNOSTIC SIGNIFICANCE OF NON-DIPPER HYPERTENSION

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ABSTRACT

Non-dipper hypertension, characterized by a nocturnal blood pressure (BP) decline of less than 10% relative to daytime means, represents a significant clinical phenotype associated with heightened cardiovascular morbidity and mortality. While conventional office measurements often fail to capture these variations, ambulatory blood pressure monitoring (ABPM) has emerged as the gold standard for assessing 24-hour BP variability and identifying circadian rhythm disruptions. This review synthesizes current evidence regarding the clinical profile, pathophysiology, and prognostic impact of the non-dipper pattern. The pathophysiology of non-dipper hypertension involves a complex interplay of autonomic dysregulation, nocturnal renin-angiotensin-aldosterone system hyperactivity, and impaired renal sodium handling. This profile is highly prevalent among patients with metabolic comorbidities, such as type 2 diabetes and obesity, where prevalence rates can reach up to 77%. Prognostically, the non-dipper pattern is a potent independent predictor of target organ damage, including left ventricular hypertrophy, stroke, and chronic kidney disease. Notably, each 5% reduction in nocturnal BP fall is associated with a 20% increase in cardiovascular mortality.

Therapeutic management emphasizes personalized chronotherapy specifically bedtime dosing of antihypertensive agents alongside novel pharmacological options like SGLT2 inhibitors and ARNIs. Furthermore, lifestyle interventions such as sodium restriction and the treatment of sleep disorders are crucial for restoring the physiological circadian rhythm. Ultimately, systematic use of ABPM is essential for accurate risk stratification and the implementation of targeted therapies to reduce the global burden of cardiovascular events.

KEYWORDS

Non-Dipper Hypertension; ABPM; Cardiovascular Risk; Circadian Rhythm

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Introduction

Hypertension continues to constitute a major worldwide health burden, impacting more than 1.3 billion individuals and remaining a principal contributor to cardiovascular morbidity and mortality [3]. Although office-based blood pressure measurements are fundamental for diagnosis, they have notable shortcomings, including their incidental nature, limited reproducibility, and vulnerability to the "white-coat effect" [34]. For this reason, ambulatory blood pressure monitoring (ABPM) has become the reference standard for assessing and managing blood pressure (BP), as it provides a comprehensive 24-hour profile of BP fluctuations [3,4,10]. Such continuous assessment is essential because it captures circadian BP variability, an indirect marker of autonomic cardiovascular regulation that correlates more closely with target-organ damage than conventional clinic measurements [4].

Under physiological conditions, blood pressure follows a circadian pattern, with higher values during daytime activity and lower levels during nocturnal rest [1,14]. In healthy subjects, this rhythm typically manifests as a "dipper" profile, characterized by an approximate 10–20% decline in both systolic (SBP) and diastolic blood pressure (DBP) during sleep compared with waking hours [18,20,33]. This nocturnal reduction largely reflects decreased sympathetic nervous system activity and relative dominance of parasympathetic (vagal) tone during sleep [8,33]. Preservation of this normal circadian BP variation plays a key protective role for vital organs such as the heart, brain, and kidneys [21,33].

Non-dipper hypertension represents a clinically relevant phenotype defined by an attenuated nocturnal BP decrease [10]. Operationally, it is identified when nighttime BP falls by less than 10% relative to mean daytime values [1,3,10,22]. This blunted decline indicates disruption of the normal circadian BP cycle and may coexist with more pronounced abnormalities, including "reverse-dipper" or "riser" patterns, in which BP fails to decrease or even rises overnight [3,10,33]. These atypical profiles frequently suggest underlying autonomic imbalance or secondary pathophysiological processes [8,10].

The non-dipping pattern occurs commonly across several clinical populations, particularly among individuals with metabolic or cardiovascular comorbidities [1,10]. It is estimated to affect roughly one quarter of patients with hypertension overall, yet its prevalence is markedly greater in those with obesity or diabetes mellitus [9]. Reports indicate rates ranging from 50% to 77% among patients with concomitant type 2 diabetes and hypertension [3,4,10]. Moreover, advanced age and coexisting renal or cardiovascular disease substantially increase the probability of an impaired nocturnal BP decline [10].

The prognostic importance of the non-dipper phenotype stems from its robust association with elevated cardiovascular risk and mortality [10,36]. Individuals with this pattern exhibit increased susceptibility to adverse outcomes such as left ventricular hypertrophy, stroke, heart failure, and chronic kidney disease, even when daytime BP remains within normal limits [1,3,10,14,25]. Persistent non-dipping is linked to target-organ injury and accelerated atherosclerosis, likely mediated by sustained sympathetic activation and endothelial dysfunction [14,20,22]. Evidence suggests that every 5% reduction in nocturnal BP fall corresponds to approximately a 20% increase in cardiovascular mortality risk, indicating that nighttime BP may predict adverse events more strongly than daytime or office measurements [2,10,22].

This review aims to characterize the clinical features and risk determinants associated with the non-dipper hypertension phenotype to improve patient risk stratification. By integrating current data on BP variability and its metabolic associations, we highlight the pivotal role of ABPM in identifying individuals at heightened risk [3,4]. Additionally, we examine the prognostic consequences of circadian BP disruption and the potential for targeted therapeutic strategies to re-establish normal dipping patterns and thereby mitigate the global burden of cardiovascular complications [4,10].

Materials and methods

To achieve the objectives of this review, a comprehensive literature search was conducted to identify relevant studies regarding the clinical profile and prognostic impact of non-dipper hypertension. The inclusion criteria were strictly limited to publications from the last 10 years, ensuring that the synthesized data reflects the most current medical knowledge and technological advancements in ambulatory blood pressure monitoring. Only works written in the English language were considered, encompassing various study types such as original research papers, clinical trials, and meta-analyses to provide a robust evidentiary basis. Following a rigorous screening process, a total of 45 papers were selected for inclusion, while 25 were excluded from the final analysis. Exclusion was necessitated by several predefined factors, including the lack of access to the full-text version of the publication and studies encompassing a narrow population of a non-European country. Furthermore, research focusing on animal models was omitted to prioritize human clinical data and its direct implications for patient care. To maintain the thematic integrity and focus of this review on circadian blood pressure variations, publications describing other specific types of arterial hypertension—such as white-coat hypertension, masked hypertension, or pre-eclampsia were also systematically excluded.

Pathophysiology of non-dipper hypertension

The pathophysiology underlying non-dipper hypertension reflects a marked disruption of the homeostatic processes governing the 24-hour blood pressure rhythm, predominantly due to abnormalities in autonomic regulation. In healthy subjects, the shift from wakefulness to sleep is accompanied by a substantial decline in sympathetic nervous system (SNS) activity and a relative predominance of parasympathetic (vagal) tone, producing the normal “dipper” pattern [8]. In contrast, patients with non-dipper hypertension exhibit an attenuated or absent nocturnal reduction in sympathetic outflow, often together with diminished parasympathetic activity [27,59]. Clinical evaluations employing heart rate turbulence and dynamic pupillometry confirm that nondippers have lower parasympathetic indices and heightened sympathetic drive compared with dippers [27,59]. Such autonomic imbalance is particularly apparent in neurodegenerative disorders, including Parkinson’s disease, in which loss of the circadian BP rhythm may represent an early manifestation of dysautonomia [31].

Sustained nocturnal sympathetic overactivity constitutes a key mechanism of the non-dipper phenotype and is closely associated with metabolic abnormalities. In obesity and type 2 diabetes mellitus, hyperinsulinemia and insulin resistance stimulate SNS activation and enhance catecholamine production [8]. This persistent adrenergic stimulation prevents the expected nighttime BP decline and elevates total peripheral resistance [8]. Moreover, autonomic impairment in these conditions is linked to reduced heart rate variability, further increasing susceptibility to cardiovascular complications and arrhythmias [4,59].

The renin–angiotensin–aldosterone (RAA) system serves as an important humoral pathway that aggravates the non-dipper profile through excessive nocturnal activity. Physiologically, the RAA system exhibits circadian variation influencing vascular tone and fluid homeostasis [5]. In nondipper individuals, however, RAA activation remains inappropriately elevated during sleep, sustaining hypertension [33]. In diabetes, hyperglycemia enhances intrarenal RAA activity, while hyperinsulinemia promotes sodium reabsorption, together exacerbating circadian BP disruption [8,33]. Chronotherapeutic strategies particularly bedtime administration of RAA-blocking agents have demonstrated greater efficacy in suppressing nocturnal RAA overactivity and may help re-establish a normal dipping pattern [5].

Impaired renal sodium handling and consequent sodium retention represent central contributors to the non-dipping phenotype. In many nondippers, the kidneys fail to maintain the normal circadian rhythm of natriuresis, leading to expansion of extracellular volume and increased nocturnal pressure load [6,17,28]. For example, in primary nephrotic syndrome, enhanced tubular sodium reabsorption driven by activated transporters plays a major role in the absence of nocturnal BP decline [17]. Elevated serum sodium concentrations have been correlated with a higher night-to-day BP ratio, supporting a direct role of renal sodium and water regulation in circadian BP abnormalities [17]. Accordingly, measures such as dietary sodium restriction or diuretic therapy can sometimes restore the physiological dipper pattern by correcting underlying volume excess [6,28].

Alterations in sleep architecture and endogenous circadian timing also interfere with normal nocturnal BP reduction. Melatonin, typically secreted at night, facilitates BP lowering by augmenting endothelium-derived nitric oxide production and reducing vascular tone [36]. Decreased nocturnal melatonin release or attenuation of its action by inhibitors such as asymmetric dimethylarginine (ADMA) is strongly linked with the non-dipper state [36]. Additionally, sleep disturbances, often provoked by stress or nocturnal sympathetic

activation, prevent adequate restorative sleep and maintain elevated nighttime BP [38]. In clinical practice, factors such as nocturia or discomfort from the ABPM device may further disrupt sleep and contribute to an apparent nondipping pattern [9].

Chronic low-grade inflammation and oxidative stress provide a vascular milieu that promotes the emergence and persistence of the non-dipper profile. Patients with nondipping commonly show increased circulating inflammatory markers, including C-reactive protein (CRP) and interleukin-37 (IL-37) [3,10,29]. Although IL-37 has anti-inflammatory properties, its elevation in hypertension may reflect a compensatory response aimed at limiting inflammation-related organ injury [29]. Concurrently, oxidative stress enhances endothelial dysfunction and platelet activation, abnormalities that are more pronounced in individuals with disrupted circadian BP rhythms [8,9,25]. Elevated homocysteine levels further contribute to vascular calcification and fibrosis, impairing normal BP variability and amplifying overall cardiovascular risk [9].

Clinical characteristics of patients with a non-dipper profile

Non-dipper hypertension is commonly observed in older individuals, as the normal physiological ability to lower blood pressure during sleep tends to decline with advancing age [3,10]. Although demographic patterns differ among studies, elderly patients consistently show a markedly higher prevalence of attenuated nocturnal BP reduction, a feature associated with increased cardiovascular risk [10,30]. Sex-related influences are also evident but complex: some data indicate a greater occurrence of nondipping in men, especially at younger ages, whereas older women may experience more pronounced increases in related indices such as pulse pressure [3,14,24]. Ethnic variability has likewise been described, with certain groups particularly Asian populations demonstrating a higher incidence of morning hypertension and abnormal nocturnal BP regulation compared with Western populations [15].

Diabetes mellitus, particularly type 2 diabetes (T2DM), is among the most significant clinical conditions linked to the non-dipper phenotype, with reported prevalence reaching 77.58% in affected cohorts [3,4]. Both disease duration and glycemic burden, reflected by elevated glycated hemoglobin (HbA1c), correlate directly with disturbed 24-hour BP variability and loss of normal circadian rhythmicity [10,11,37]. Chronic kidney disease (CKD) represents another major comorbidity; impaired renal sodium excretion and extracellular volume expansion frequently produce sustained nocturnal hypertension and diminished nighttime BP decline [10,17,28]. In such patients, nondipping is strongly associated with progressive target-organ injury, although some evidence suggests that strict overall BP control may be more critical for preserving estimated glomerular filtration rate (eGFR) than circadian normalization alone [3,10,22].

Excess adiposity particularly visceral fat accumulation assessed by body mass index (BMI) and waist circumference is an independent predictor of both non-dipper and reverse-dipper patterns [4,10,11,19]. Individuals with severe obesity often display reverse dipping, characterized by higher nighttime than daytime BP, a profile linked to the poorest cardiovascular outcomes and heightened sympathetic activation [19]. Obstructive sleep apnea (OSA) further amplifies this risk through nocturnal sympathetic surges, hypercortisolemia, and fragmented sleep, all strongly associated with absent nocturnal BP decline [2,19,38]. Sleep disruption and reduced sleep quality in these patients prevent adequate restorative rest, thereby sustaining elevated nocturnal pressure load [2,38].

Behavioral factors, including active smoking and alcohol intake, also modulate BP patterns by promoting arterial stiffening and autonomic imbalance [11,25,29]. Smokers exhibit increased circulating inflammatory mediators, which correlate with carotid atherosclerotic plaque presence in nondipper individuals [29]. Laboratory and clinical profiles in this group frequently indicate chronic systemic inflammation, with elevated C-reactive protein (CRP), total cholesterol, and homocysteine concentrations [3,10,11,29]. Hematologic markers such as higher mean platelet volume (MPV) and platelet distribution width (PDW) are likewise associated with nondipping, suggesting that augmented platelet activation contributes to increased risks of cardiovascular events and stroke [3,25]. Clinically, nondippers often present with greater 24-hour pulse pressure and increased carotid intima–media thickness (CIMT), findings indicative of advanced subclinical organ damage and vascular aging [10,29,40].

Prognostic significance of the non-dipper profile

The prognostic relevance of the non-dipper phenotype derives from its status as a strong independent determinant of cardiovascular events, frequently conferring greater risk than conventional office BP measurements. Clinical data indicate that patients with an attenuated nocturnal decline in blood pressure (BP) experience approximately a threefold higher incidence of cardiac events compared with individuals displaying a normal dipper pattern [41]. Absence of the expected nighttime BP reduction is closely linked to increased rates of acute coronary syndromes, myocardial infarction, and both silent and overt cerebrovascular disease [8,38]. Moreover, nondipping has been identified as an important risk factor for acute aortic dissection; studies show that loss of nocturnal BP fall is disproportionately common in these patients and may influence the temporal pattern of disease onset [24]. Elevated risk is also evident in stable coronary artery disease, where abnormal 24-hour BP variability functions as a key indicator of impending cardiovascular instability [3,8].

Left ventricular hypertrophy (LVH) represents a principal structural consequence of the sustained hemodynamic load characteristic of nondipper hypertension. Evidence demonstrates that left ventricular mass index (LVMI) and the prevalence of hypertrophy increase progressively with disruption of circadian BP rhythm, with LVH observed in about 9% of dippers, 17% of nondippers, and up to 31% of reverse dippers [8]. This remodeling is frequently accompanied by abnormalities in left ventricular rotational dynamics and diastolic function, reflected by an elevated E/Em ratio and delayed ventricular untwisting [7]. Among patients with heart failure with preserved ejection fraction (HFpEF), a “riser” profile defined by higher nocturnal than daytime BP serves as a significant independent predictor of adverse outcomes, underscoring the relationship between circadian BP disturbance and progressive myocardial injury [26].

Beyond cardiac involvement, the nondipper pattern contributes to widespread target-organ damage affecting the brain, kidneys, and vascular system. Within the central nervous system, nondippers demonstrate a greater prevalence of subclinical cerebrovascular injury, including silent lacunar infarctions and advanced deep white-matter ischemic changes [8,41]. Renal complications are also prominent: nocturnal hypertension and nondipping are strongly associated with the onset and progression of microalbuminuria and diabetic nephropathy [3,11,33]. Longitudinal observations in type 1 diabetes indicate that even normotensive patients with altered nocturnal BP are predisposed to microvascular sequelae, including worsening retinopathy [11]. Additionally, nondipper individuals often exhibit increased carotid intima–media thickness (CIMT) and more frequent carotid atherosclerotic plaques, highlighting the systemic vascular injury linked to this BP phenotype [8,29].

Overall, the non-dipper profile is a major determinant of both all-cause and cardiovascular mortality. The landmark Ohasama study established a dose–response relationship whereby each 5% reduction in nocturnal BP decline corresponds to roughly a 20% increase in cardiovascular mortality risk [20,35,36]. Importantly, this association is independent of mean 24-hour BP, making nighttime BP a more powerful predictor of survival than overall BP burden [20,29]. Prognosis is particularly unfavorable in reverse dippers, who carry the highest risk of total mortality and major adverse cardiovascular events (MACE), with risk levels approaching those of untreated hypertensive patients [3,19,29]. Accordingly, detection of nondipping through ambulatory blood pressure monitoring is crucial for precise risk stratification and for guiding chronotherapeutic strategies aimed at reducing global cardiovascular mortality [3,33].

Therapeutic implications

The principal therapeutic objective in non-dipper hypertension is the re-establishment of a normal nocturnal decline in blood pressure, with chronotherapy representing a central strategy. Administering long-acting antihypertensive medications at bedtime particularly renin–angiotensin system (RAS) inhibitors and calcium channel blockers (CCBs) has been shown to lower nighttime blood pressure (BP) more effectively than morning dosing and to facilitate conversion from a nondipper to a dipper pattern [5,24,41]. For example, evening intake of valsartan or nifedipine improves the day–night BP ratio [24]. Moreover, evidence indicates that divided twice-daily regimens (morning and evening) of agents such as perindopril or losartan may outperform a single nightly dose in correcting the nondipping profile [41]. Such timing ensures adequate drug levels throughout the night and during the early morning hours, thereby attenuating the morning BP surge [5].

Choice of pharmacological class is also critical for addressing mechanisms underlying circadian BP disruption, with SGLT2 inhibitors and angiotensin receptor–neprilysin inhibitors (ARNIs) emerging as particularly effective. Sodium–glucose cotransporter-2 inhibitors (SGLT2i) including empagliflozin, luseogliflozin, and dapagliflozin significantly reduce nocturnal systolic BP and can shift patients from a nondipper to dipper pattern in both experimental and clinical settings [1,16,20,35]. Their benefits are likely

mediated by enhanced natriuresis and reduced sympathetic activity during sleep [35]. Similarly, ARNIs such as sacubitril/valsartan are recommended for stabilizing morning BP and improving circadian regulation, especially in salt-sensitive individuals and those with heart failure [15,33]. Selective mineralocorticoid receptor antagonists, for instance esaxerenone, have likewise demonstrated substantial reductions in nocturnal systolic BP, particularly in patients with the extreme "riser" phenotype [15,18].

Optimal management also requires treatment of comorbid conditions frequently accompanying nondipper hypertension, notably diabetes, obesity, and autonomic dysfunction. Clustering of metabolic risk factors amplifies cardiovascular risk, making strict control of glycemia and lipid levels essential [3,10]. In individuals with type 1 diabetes complicated by cardiovascular autonomic neuropathy, high-dose vitamin D supplementation has been shown to lower total, morning, and daytime systolic BP and to attenuate the morning surge [13]. Correction of dyslipidemia is equally important, as elevated total cholesterol and triglycerides correlate with higher mean arterial pressure and greater arterial stiffness in nondippers [3,10,39]. For patients with metabolic syndrome, ambulatory blood pressure monitoring (ABPM) should be incorporated into risk assessment to guide individualized therapy [3,19].

Lifestyle modification and sodium restriction form the cornerstone of non-pharmacological treatment aimed at restoring normal BP circadian patterns. Reducing dietary salt intake to below 6 g/day can convert a nondipper profile to a dipper pattern by alleviating volume overload [6,15,20,28]. Additional key measures include weight reduction through dietary adjustment and structured physical activity programs [15,25,34]. Digital health interventions that support sodium reduction, stress control, and limitation of alcohol consumption have also demonstrated efficacy in lowering morning BP [15]. Regular exercise and weight loss further improve endothelial function and decrease arterial stiffness, both commonly impaired in nondipper patients [3].

Improvement of sleep quality and management of sleep-related disorders are essential therapeutic components, as disturbed sleep is a major contributor to nocturnal BP elevation. Disorders such as obstructive sleep apnea (OSA) are strongly linked to loss of the nocturnal dip and should be actively screened for and treated in patients with nighttime hypertension [4,5]. Psychological factors including anxiety and chronic emotional stress also raise nocturnal BP via sustained sympathetic activation [38]. When clinically indicated, the use of hypnotics or antidepressants alongside antihypertensive therapy may reduce excessive nocturnal BP by alleviating stress and sleep deprivation [38]. Therefore, optimization of sleep hygiene and treatment of underlying mental health conditions are key steps toward achieving comprehensive 24-hour BP control [15].

Discussion

The clinical profile of non-dipper hypertension reflects a marked disturbance of the normal 24-hour blood pressure rhythm and functions as a strong independent predictor of target-organ injury and unfavorable cardiovascular outcomes. Evidence consistently shows that an attenuated nocturnal blood pressure (BP) reduction defined as <10% relative to daytime levels is linked to an approximately threefold higher incidence of cardiac events [1,10]. This phenotype is especially frequent in metabolic and neurodegenerative disorders; reported prevalence reaches about 77% in type 2 diabetes (T2DM) and exceeds 71% in Parkinson's disease, where nondipping may represent an early manifestation of autonomic dysfunction [1]. The literature also indicates that the "riser" pattern—an extreme form in which nighttime BP surpasses daytime values—confers the poorest prognosis, predicting higher mortality and major adverse cardiovascular events (MACE) in conditions such as heart failure with preserved ejection fraction (HFpEF) and acute aortic dissection (AAD) [1]. Absence of nocturnal dipping is additionally associated with microvascular progression; for example, patients with type 1 diabetes (T1DM) show greater advancement of retinopathy and nephropathy when nocturnal diastolic BP remains elevated [1].

The clinical implications are reinforced by identification of emerging biomarkers and mechanistic pathways that enhance risk stratification. Beyond ambulatory blood pressure monitoring (ABPM) the diagnostic reference standard metabolic indicators such as the triglyceride-to-glucose ratio demonstrate meaningful ability to discriminate nondipper status [1,10]. Hematologic markers including increased mean platelet volume (MPV) and platelet distribution width (PDW) indicate a prothrombotic, proinflammatory milieu in nondippers, further supported by elevated mediators such as interleukin-37 and osteoprotegerin [1,10]. These signatures correlate with greater arterial stiffness assessed by the ambulatory arterial stiffness index (AASI), which independently associates with impaired left atrial mechanics and silent cerebrovascular injury [1,10]. The observation that asymmetric dimethylarginine (ADMA) weakens the BP-lowering effect of endogenous melatonin points to a biochemical mechanism whereby oxidative stress disrupts intrinsic circadian

BP regulation [10]. Collectively, these findings indicate that nondipper hypertension represents a systemic failure of autonomic and renal homeostasis rather than a simple numerical BP variation [1].

From a therapeutic perspective, management should move toward individualized chronotherapy aimed at restoring the physiological dipping pattern. Studies suggest that conventional once-daily morning dosing creates a therapeutic gap during the critical nocturnal and early-morning intervals [1]. Transitioning to twice-daily schedules or bedtime administration of long-acting agents such as perindopril, losartan, or nifedipine has proven more effective in correcting the nondipper phenotype [1,10]. Certain drug classes, including SGLT2 inhibitors (empagliflozin, luseogliflozin) and angiotensin receptor–neprilysin inhibitors (sacubitril/valsartan), show particular efficacy in lowering nighttime systolic BP by improving renal sodium handling and reducing nocturnal sympathetic activity [1]. In patients with cardiovascular autonomic neuropathy, high-dose vitamin D supplementation has also been proposed as a strategy to attenuate the morning BP surge [1]. These observations support the concept that normalization of circadian BP rhythm should be a central therapeutic goal to decrease hypertension-related mortality [1].

Nevertheless, interpretation of existing data is limited by several methodological constraints. Many studies involve small, single-center cohorts and cross-sectional designs that preclude definitive causal inference between dipping status and outcomes [1,10]. Another challenge is the limited reproducibility of nondipper classification based on a single 24-hour ABPM recording, as factors such as sleep quality, nocturia, and discomfort from the monitoring device can substantially affect nocturnal BP measurements [1,10]. Additionally, most research has focused on selected ethnic groups commonly Japanese or Caucasian populations restricting generalizability to broader populations [1]. Concomitant antihypertensive therapy at the time of monitoring may also confound results by obscuring patients' intrinsic circadian BP patterns [1].

Future investigations should emphasize large, longitudinal multicenter studies to validate these associations across diverse populations and to determine the long-term benefits of restoring normal dipping patterns. It remains essential to establish whether pharmacologically converting nondippers into dippers directly reduces cardiovascular mortality and organ damage [1,10]. Research into genetic determinants of circadian BP variation and the effects of lifestyle interventions such as digital stress-management tools and stringent sodium restriction may enable more comprehensive treatment strategies [1]. Exploration of novel biomarkers as predictors of therapeutic response could further support truly personalized antihypertensive regimens [1,10]. By clarifying the complex interactions among autonomic regulation, renal function, and metabolic factors, future work may inform optimized clinical guidelines tailored to the distinct risks of the nondipper population [1].

Conclusions

Key Observations

Clinical evaluation of non-dipper hypertension indicates that it represents a broad disturbance of autonomic, renal, and humoral regulatory systems rather than a simple quantitative BP abnormality. Available data show that loss of the normal circadian pattern defined by a nocturnal blood pressure reduction below 10% is largely attributable to sustained sympathetic activation and inadequate parasympathetic predominance during sleep. This phenotype occurs with particularly high frequency in individuals with metabolic comorbidities, notably type 2 diabetes and chronic kidney disease, with reported prevalence approaching 77%. Its pathophysiology is complex and multifactorial, encompassing nocturnal overactivity of the renin–angiotensin–aldosterone system, impaired renal sodium excretion, and persistent systemic inflammation. The "riser" or reverse-dipper variant represents the most severe circadian disruption and is linked to the poorest clinical outcomes.

Practical Implications for Clinicians

Successful treatment of non-dipper hypertension requires adoption of individualized chronotherapeutic strategies alongside rigorous management of associated disorders. Bedtime dosing or twice-daily administration of long-acting antihypertensive agents such as renin–angiotensin system inhibitors and calcium channel blockers should be considered to re-establish the normal nocturnal BP decline. Certain pharmacological classes, particularly SGLT2 inhibitors and angiotensin receptor–neprilysin inhibitors, are advantageous due to their capacity to promote natriuresis and reduce sympathetic overactivity. Nonpharmacological measures are equally important: strict dietary sodium limitation, weight reduction, and treatment of sleep disturbances (e.g., obstructive sleep apnea) form essential components of therapy. Management of psychological stress and optimization of sleep hygiene may further decrease excessive nocturnal BP load.

The Role of ABPM in Cardiovascular Risk Assessment

Ambulatory blood pressure monitoring (ABPM) remains the definitive method for detecting the non-dipper pattern and revealing cardiovascular risk not captured by office measurements. Because nighttime BP is a stronger predictor of cardiovascular mortality and overall survival than daytime or clinic BP, ABPM correlates more closely with target-organ injury, including left ventricular hypertrophy, silent cerebrovascular lesions, and progressive renal damage. The demonstrated dose–response relationship where each 5% reduction in nocturnal BP fall markedly elevates cardiovascular mortality risk highlights the importance of ABPM in precise risk stratification. Therefore, routine incorporation of 24-hour BP monitoring, particularly in high-risk metabolic populations, is essential for guiding targeted interventions and mitigating the global burden of cardiovascular complications.

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