

The current state of knowledge about the dipping and non-dipping hypertension

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Abstract

Ambulatory blood pressure monitoring provides information about the day-night blood pressure profile, which can be divided into dipping and non-dipping pattern. Non-dipping hypertension is recently thought to have increased cardiovascular risk and outcomes than dipping hypertension. The dipping pattern is explained by physiological changes in circadian rhythm, while the pathomechanism of non-dipping hypertension is not fully understood. Is it considered to be a result of many factors, such as: sympathetic nervous system overactivation, which can be accompanied by impaired parasympathetic nervous system response, obesity, concurrent diabetes mellitus and metabolic syndrome. Moreover abnormalities of hormones levels such as melatonin, catecholamines, thyroid and parathyroid hormones are connected to occurrence of non-dipping hypertension. Other widely discussed problem is obstructive sleep apnoea and its influence on circadian rhythm changes. Also dysfunction in activity of renin-angiotensin-aldosterone axis is thought to cause non-dipping pattern. There are some studies that indicate on role of inappropriate sodium intake in mentioned pathology. The chronic kidney disease and relationship with non-dipping hypertension will be also described. The last considered factor is influence of age on the development of non-dipping hypertension.

key words: circadian blood pressure profile, blood pressure regulation, chronobiology, nocturnal hypertension, non-dipping pathomechanism

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Introduction

Elevated blood pressure (BP) is recently thought to be one of the most important risk factors of cardiovascular diseases [1]. Therefore it is not surprising that there are a lot of studies about the pathology, complications and treatment of hypertension [2–4]. In this review we will focus on pathology of hypertension taking into account its dipping and non-dipping pattern. This is one of the fastest growing branches of interest in the field of hypertension.

Type of circadian BP rhythm is defined as proportion of the nocturnal average BP fall to daytime average BP value. If it is less than 10%, then it is referred to as a non-dipping pattern, if it is 10–20%, it is referred to as dipping pattern [1]. Nocturnal average BP fall above 20% of daytime average BP values is referred to as extreme dipper pattern. The increase instead of decrease of average BP values between average nighttime and daytime values is known as reverse dipper pattern [5, 6].

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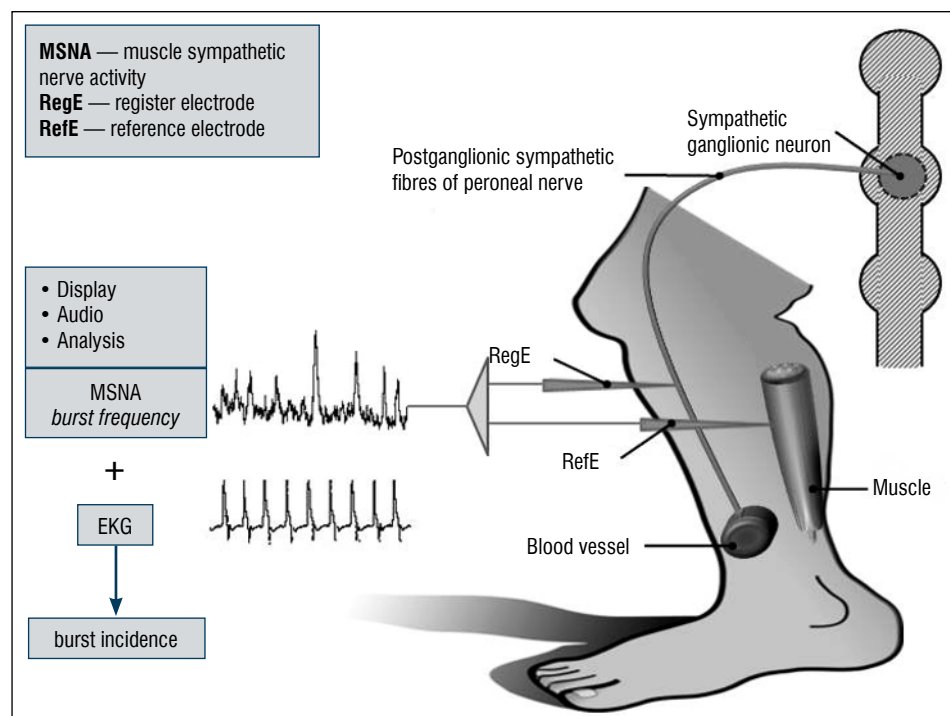


Figure 1. Microneurography is neurophysiological, invasive, direct method of postganglionic sympathetic nerves electric activity measuring. Usually it is used to visualize and record muscle sympathetic nerve activity

This division refers either to normotensive or hypertensive patients. To gather information about nocturnal BP fall ambulatory blood pressure monitoring (ABPM) is conducted. The data are collected from 24-hour period, which can be lengthened even up to 48 hours in order to increase reproducibility of the results. The ABPM is now accepted to have greater prognostic value than office BP measurements [7, 8]. The dipping pattern is explained by physiological sympathetic activity decrease and parasympathetic activity increase during the night [9]. This physiological change between day and night autonomic nervous system (ANS) activity is connected to suprachiasmatic nucleus and its ability to generate circadian rhythm [10–12]. On the other hand, the non-dipping pattern is connected with disorders and disturbances of the circadian rhythm as well as in situation where effects of regular circadian rhythm are too weak to manifest in front of existing pathology [12–21].

Autonomic nervous system

Despite many years of study on non-dipping pattern there is no one clear mechanism of its pathology. The ANS is believed to play the major role in non-dipping profile of hypertension [9, 13, 14, 22, 23]. To confirm such theory the ANS activity is measured and compared between dipper and non-dipper pa-

tients [12–15]. There are techniques that allow measurement only the sympathetic nervous system (SNS) activity or SNS and parasympathetic nervous system (PNS) activity [12–15, 24–28]. Modern medical technology offers direct and indirect SNS activity measurements [24–28]. One of them is measurement of the urinary concentration of norepinephrine (NE), the SNS neurotransmitter [29]. The Arita *et al.* found a correlation between the nocturnal fall in BP and the urinary NE concentration [15]. This correlation suggests that decrease in BP was associated with reduction in SNS activity [15]. Described method has some limitations, first one being that it provides information about the general SNS activity without information about regional ones [30]. Note that local SNS activity may increase, decrease or present no changes in different regions simultaneously. The regional SNS activity monitoring of particular organs (such as heart, kidneys, vessels) may be useful in localizing the cause and defining mechanism of blunted night BP drop [31]. The second limitation of the indirect measurement of SNS activity by the concentration of NE in urinary is its dependence of concentration of NE on its clearance from plasma [29]. Grassi *et al.* conducted a study on hypertension population and revealed negative correlation between the level of SNS activity and the magnitude of nocturnal BP [14]. They used microneurography, direct measurement of muscle sympathetic nerve activity [14] (Fig. 1).

Hojo *et al.* conducted a study which purpose was to show the correlation between disturbances in SNS and PNS activity by using the power spectral analysis of R-R interval [13]. The spectral components of analysed signal are related to different physiological mechanisms. Power spectrum of low frequency is related to SNS, PNS and renin-angiotensin system, while spectrum of high frequency (HF) reflects the efferent parasympathetic activity at the cardiac level and the low frequency to high frequency spectrum ratio is an index of sympathovagal balance at the cardiac level [13]. The authors revealed positive correlation in hypertensive patients between 24-hrs LF/HF power ratio and the percentage of nocturnal systolic BP reduction [13]. Results from all mentioned studies indicated the role of altered ANS activity in the occurrence of non-dipping hypertension pattern [13–15]. The first and the second one demonstrated the connection between excessive sympathetic activity and decreased nocturnal BP reduction, which correlated with non-dipping hypertension pattern [14, 15]. The third study showed an influence of disturbed sympathovagal balance on decreased reduction of nocturnal BP [13]. These results indicate the role of abnormal circadian rhythm of ANS on pathogenesis of non-dipping pattern. Okamoto *et al.* performed studies on patients with pure autonomic failure who had low and fixed sympathetic activity [12]. They suggested that jet another theory of pathogenesis of non-dipping pattern may be the inability to modulate sympathetic activity [12].

Orthostatic hypotension

Changes in body posture (horizontal to vertical) force our organism to adapt to different conditions. Autonomic nervous system is responsible for these adaptations [32]. The afferent autonomic nerves are activated and induce the baroreceptors unloading. The efferent sympathetic outflow and vasoconstriction is subsequently increased in order to increase venous return and keep resting BP value [33]. Impairment of this compensatory mechanism due to autonomic dysfunction results in orthostatic hypotension [32]. Very often patients with orthostatic hypotension may develop the supine hypertension which lead to non-dipping hypertension [34].

Obesity

The rapidly rising prevalence of obesity in highly developed countries has become the great challenge

to modern health care system [35]. Interlink between obesity and hypertension is well known both in adults and children. Overweight is a creditable risk factor of hypertension development [36]. There is a significant similarity between mechanism of obesity-induced hypertension and non-dipping causes considered in different studies [37–41]. Pathological factors of increased BP in obese individuals that may play role in impaired nocturnal BP drop include: SNS activation which is suggested as crucial, altered kidney functions, obesity-driven hormones elevation, endothelial dysfunction and vascular structural changes [16]. Moreover, obesity, increased BMI, visceral fat and neck circumference are the most established risk factors for occurrence of obstructive sleep apnoea [42].

Sympathetic nervous system activation

Autonomic nervous system activity changes may be essential for blunted nocturnal BP reduction [9, 13, 14, 22, 23]. Several studies provide evidence of SNS activation in obese patients and those with high-caloric intake [43, 44] High muscle SNS activity were detected by microneurographic methods (direct evidence) [43]. Plasma norepinephrine concentration and rise of norepinephrine turnover in peripheral tissues correlated positively with level of caloric intake (indirect evidence) [44].

Obesity may lead to increased rennin-angiotensin-aldosterone system (RAAS) activity, hyperinsulinaemia, impaired baroreceptor sensitivity and increased free fatty acids circulation and adipokines level [43, 45–47]. These factors are considered as those which result in increased sympathetic activity [48–51]. Animal models with high fat and carbohydrate intake developed significant rise in BP due to intensified peripheral alpha-1- and beta-adrenergic receptors sensitivity [52]. Corresponding results were reported in human studies, where BP of obese patients after one month of alpha- and beta-adrenergic receptors pharmacological blockade was noticeably more reduced than BP of lean ones [53]. It have also been noticed that abdominal obesity cause greater SNS activation than peripheral or subcutaneous obesity, though reason of this difference remains unknown [54].

Renal mechanism

Physiological balance of diuresis and natriuresis is disturbed in obese patients [55]. Sodium retention in obese patients is mainly caused by increased renal sodium reabsorption, and results with hypertensive adjustment of pressure natriuresis [56]. Excess weigh may be also associated with histological changes in

renal medulla that compress renal tubules, reduce their cross-section, which causes prolongation of the time given for sodium reabsorption [57].

Positive correlation between levels of plasma renin activity, plasma angiotensinogen, angiotensin II, aldosterone and obesity factor has been observed [58, 59]. Independently of fluid and sodium retention, this correlation can be explained with fat that surrounds kidneys and generates pressure inducing renin secretion [57].

Leptin

Leptin is considered as a mediator of SNS activation [56, 60]. Its amount of secretion from adipose tissue stays in direct proportion with adipose tissue mass [47]. After passing blood-brain barrier leptin binds to hypothalamus and brainstem, where it suppresses hunger drive and stimulates SNS [61]. SNS activation appears to mediate leptin-induced BP elevation, since after overall alpha and beta adrenergic blockade previous BP elevating effect of leptin is abolished [62]. This peptide hormone plays great role in modulating melanocortins production in central nervous system [63]. Leptin activity stimulates expression of pro-opiomelanocortin in hypothalamus, which in turn directly increases production of a melanocyte-stimulating hormone (MSH) [63]. Effects of MSH-3 and MSH-4 receptors blockade on rats are similar to those observed during alpha and beta-adrenergic blockade [64]. It seems that pro-opiomelanocortin-melanocortin 4 receptor system is necessary for leptin-induced BP elevation [65].

Diabetes mellitus and metabolic syndrome

Patients with diabetes mellitus also have higher risk of developing non-dipping hypertension [17, 66]. Spallone *et al.* showed that patients with neuropathic type 2 diabetes have blunted nocturnal BP decline [67]. The same correlation was found in type 1 diabetes patients with autonomic neuropathy [17]. The reduced vagal tone is suggested explanation of influence of autonomic neuropathy on decline in nocturnal BP fall. Reduced vagal tone causes increased cardiac output [67]. Hypertension development in patients with insulin resistance and hyperinsulinaemia is explained by anti-diuretic effect of insulin, activation of SNS, impaired endothelium-dependent vasodilatation, effect on vascular smooth muscle growth by insulin and augmented response to endogenous vasoconstrictors [68]. Insulin also affects kidney, which is manifested by increased sodium

reabsorption [69]. Related effect of described abnormalities is present in diabetes mellitus and contributes to the non-dipping hypertension pattern which we often diagnose in such patients [41].

Insulin resistance is the underlying mechanism of metabolic syndrome (MS) and previously described insulin resistance-induced hypertension [70]. Tartan *et al.* showed that high MS-Score predicted non-dipping BP [71, 72]. Hyperuricaemia is suggested to be a signal for clinician to intensify inspection of BP control [18]. Risk analysis revealed that hyperuricaemia is a risk factor of non-dipping hypertension development [18].

Hormones

Thyroid hormone

There is strong association between variation in serum thyroid hormones level and the occurrence of cardiovascular system diseases [73]. Free triiodothyronine directly affects smooth muscle cells as a vasodilator and free thyroxine induces relaxation of skeletal muscles resistance arterioles [74–76]. Hypothyroidism may cause impairment of muscle vasodilatation, endothelial dysfunction, hypercholesterolaemia associated with a reduction in aortic compliance and is also considered a risk factor for atherosclerosis [62, 77–81]. The fifth Tromsø study which included 5872 patients demonstrated modest, but significant positive association between serum thyroid-stimulating hormone range and BP levels [82]. Although results suggested that thyroid hormones played a role in regulating BP, it did not consider possible correlation between hormones levels and non-dipping hypertension. That type of correlation was reported by other study that indicated a graded independent negative relation between levels of free triiodothyronine and the risk of non-dipping hypertension [72, 74].

The relation between hypothyroidism and non-dipping hypertension might be caused by influence of thyroid hormones on sympathetic nervous system, probably by regulating adrenergic receptor function and their density [83–85]. The number of beta-adrenergic receptors is decreased, therefore, alpha-adrenergic responses increase what might result in the increase in systemic vascular resistance [86]. Probably, the endothelial dysfunction related to thyroid impairment plays an important role in the prevalence of sustained hypertension [87].

Parathyroid hormone

In the study performed by Kanbay *et al.* 190 patients were divided into 2 groups: dippers and non-dip-

pers. The analysis provided evidence that the second group had higher levels of parathyroid hormone (PTH), phosphate and calcium X phosphate product [88]. Those findings suggest correlation between higher levels of PTH and phosphate in hypertensive patients with normal mineral metabolism and glomerular filtration rate > 60 ml/min and the increased risk of having non-dipping hypertension pattern [88].

Primary hyperparathyroidism is correlated with high prevalence of hypertension [89]. Study by Fliser *et al.* demonstrated that in healthy volunteers subacute administration of physiological doses of human 1.34-parathyroid hormone causes BP increase [90]. Administration of 1.34-parathyroid hormone raised ionized calcium and intracellular calcium concentration of platelets [90]. Mechanism of BP increase may be a result of higher level of PTH, which causes a rise in intracellular ionized calcium in vascular smooth muscle cells [91, 92]. Investigation by Feldstein *et al.* revealed independent positive correlation between ionic calcium level and the risk of non-dipping pattern in subjects with nondialysis chronic kidney disease [93].

The function of PTH in pathogenesis of non-dipping hypertension might be related to direct effect on renin secretion [19]. Moreover, patients with primary hyperparathyroidism had the pressor response elevated as assessed in the norepinephrine test [19]. Activation of the RAAS and enhanced sensitivity to norepinephrine may contribute to hypertension prevalence and to vessels sensitization to pressor agents [19].

Other hormones

Melatonin is related to BP regulation [94]. Non-dipper patients have impaired nocturnal melatonin secretion in comparison with dippers [95]. Influence of melatonin on circadian BP profile may result from its direct effect on peripheral arteries by melatonin's antioxidative character and its interaction with the Ca²⁺-calmodulin complex in smooth muscle and endothelial cells, which decreases the level of Ca²⁺ [94]. Study by Lusardi *et al.* reported that exogenous melatonin ingestion can reduce BP [96]. Melatonin can alter ANS tonus [71].

Blood pressure regulation is also associated with cortisol and catecholamines [97, 98]. Impairment of the circadian BP rhythm has been reported in patients with Cushing's syndrome and pheochromocytoma [93, 99, 100]. Investigation by Krzyzanowska *et al.* revealed a correlation between hypopituitarism occurrence and abnormal circadian BP [101].

Renin-angiotensin-aldosterone system

Intrarenal RAAS is hyperactive in patients with essential hypertension [102]. Stimulation of the RAAS causes increased sodium and water retention. As a result, such stimulation extends blood volume. Moreover, when the RAAS is hyperactive, augmentation of peripheral vascular resistance occurs [103]. Experiments conducted mainly in rats reported that elevated intracellular sodium in neurons activates brain RAAS [104]. Angiotensin II administered into vertebral arteries causes sympathetic activation and pressor responses [105]. Westcott *et al.* consider major role of aldosterone in activation of central nervous system, but this finding requires further investigations [49].

Salt intake

Series of studies proved the importance of the role of salt intake and sodium retention as hypertension risk factors, and now it is accepted as common knowledge [106–108]. Over the years concept of salt sensitivity was established as a result of observing heterogeneous responses to salt intake. It resulted in dividing patients into two groups: salt sensitive (SS) and salt resistant [109, 110]. Salt sensitivity is proved to be important also in dipping and non-dipping type of hypertension [111]. Although influence of salt intake on circadian BP rhythm has been revealed, exact mechanisms are still not clear. In a group of patients with essential hypertension in response to high salt diet (HSD) SS patients with preserved nocturnal BP decline turned to non-dippers, which was not observed in SR group [111, 112]. Furthermore, in other study sodium restriction significantly decreased nighttime BP only in SS group [111]. Possible pathways of salt-induced non-dipping patterns are: SNS increased output, altered renal function and diminished inhibition of RAAS, impaired endothelial function, and genetic coupling factors [113–115].

Studies assessing the correlation between high salt intake and SNS activation showed that plasma norepinephrine concentration (PNEC), indirect index of SNS activity level, was elevated and significantly higher in SS patients compared with SR individuals [79]. In the face of PNEC elevation, nocturnal arousal effects of SNS may be also enhanced by not adequate urinary noradrenaline excretion, which in SS patients on HSD stays unchanged during the night and is increased in daytime [112]. Sodium intake affects RAAS and renal hemodynamic [112].

Table I. Salt sensitive and salt resistant patient's plasma renin activity (PRA), plasma aldosterone (PALD) and plasma angiotensin II (PAngII) levels were measured on the last day of both high and low salt intake study stages. Suppression of PRA, PALD, PAng II induced by high salt intake was poorer in SS patients. Adapted from reference [109]

	Sodium sensitive (N = 9)		Sodium resistant (N = 14)	
	High salt	Low salt	High salt	Low salt
PRA [ng/ml]	0.6 ± 0.2*	2.3 ± 0.9*	0.4 ± 0.2	3.0 ± 0.7
PALD [pg/ml]	70.3 ± 16.3*	252.2 ± 46.0*	55.0 ± 18.1	271.0 ± 51
PAng II [pg/ml]	42.8 ± 10.9	81.6 ± 17.0	40.1 ± 15.8	82.1 ± 14.6

*P < 0.05

As showed on Table I, plasma aldosterone level and plasma renin activity suppression was lower in SS than in SR group [109] (Table I).

Study conducted on large group of African individuals showed positive correlation between sodium urinary excretion in nighttime and level of nighttime systolic BP reduction [116]. Reduced sodium excretory capability, that occurred in SS patients, combined with HSD caused sodium overload during the day and resulted in blunted BP drop at night [59]. Night BP elevation was a compensative mechanism which increased natriuresis pressure [79]. Furthermore, patients with essential hypertension and non-dipping pattern during hydrochlorothiazide treatment, drug which increase sodium urinary excretion, showed significant reduction in both nocturnal systolic and diastolic BP, while this effect was not observed in dipping individuals [117]. The study conducted on G927R polymorphism of insulin receptor substrate-1 may help to understand association between HSD, SS and non-dipping in some patients [115].

In heterozygous carriers of G972R IRS-1, high daily salt intake resulted in significant increase in insulin level and insulin resistance [115]. Both mechanisms were considered as independent predictors and risk factors of lack of adequate nocturnal BP decline [68, 69]. Moreover, as predicted, heterozygous carriers on HSD more frequently developed non-dipping hypertension [115].

Chronic kidney disease

There are many studies in which kidneys are described as essential organ in BP regulation and their role in pathomechanism of hypertension development is crucial [118–120]. According to National Kidney Foundation, elevated level of BP may be either a consequence or a cause of chronic kidney disease (CKD) defined as a presence of, for 3 months or more, at least one of the following criteria: kidney damage or/and GFR < 60 ml/min/1,73 m² [121]. Among 264 patients with CKD involved in in-

vestigation by Fedecostante *et al.*, approximately all (97.8%) were hypertensive [122]. That study demonstrated also a relationship between prevalence of CKD and non-dipping pattern of hypertension. It indicated that CKD had direct influence on circadian BP profile [122]. That finding was in agreement with former study by Farmer *et al.*, who reported more frequent predominance of non-dipping in subjects with CKD than in controls with essential hypertension [123]. There were also associations between worsening of renal function and non-dipping pattern rise [123]. Arterial hypertension is also common in patients after renal transplantation (it affects 60–80% of them) [124]. A strong determinant of non-dipping hypertension pattern in those patients is the Doppler-derived renal resistive index [125].

Salt sensitivity (controlled by kidneys) is a potential mechanism causing non-dipping hypertension pattern [126]. High salt sensitivity was responsible for diminished BP fall in essential hypertension and salt restriction changed non-dipping pattern into dipping [111, 127]. According to study by Fujii *et al.* in non-dipping salt-sensitive type of hypertension, the circadian rhythm of natriuresis is disturbed [77]. Kimura *et al.* suggested that both, decrease in renal sodium excretory in patients with CKD and hypertension with sodium sensitive BP had influence on circadian alterations in BP [128].

Association between CKD and hypertension may be related to the activation of tissue renin-angiotensin system [129]. Aldosterone is associated with hypertension by its impact on BP elevation, cardiac fibrosis and vascular injury [130].

Metabolic changes in CKD are the cause of calcification of the wall of arteries and are associated with increased atherosclerosis [124]. As a result, the increase of arterial stiffness is observed, causing development of high BP [9].

Sleep disturbances

According to several studies high quality sleep is suggested as crucial for dipping pattern [131]. Noc-

turnal BP changes stay in close relation to sleep stages [132]. Years ago Portaluppi *et al.* extensively analysed that issue in the separate study [132]. The highest nighttime BP reduction occurred in the deepest sleep, which corresponded to 3 and 4 stage of non-rapid eye movement sleep, while during 1, 2 stage of NREM and rapid eye movement (REM) sleep BP was significantly higher [16, 132]. Central control of respiratory mechanism and respiration oscillations were also directly associated with nocturnal BP changes [132]. During deep NREM sleep breathing becomes regular and BP and heart rate decrease is observed [132]. Irregular respiration, apnoea periods, hypercapnia, oxygen saturation drop are characteristic for 1,2 stage of NREM and REM sleep, which results with arousal and BP elevation [132, 133]. Detailed study of these mechanisms may be a key to understanding association between several sleep disturbances and non-dipping pattern.

Stress status and sleep quality

Some studies revealed associations between poor sleep quality and impaired circadian BP rhythm [79, 134]. Other showed that sleep disturbances increase SNS activity and may cause blunted nocturnal BP drop [135]. The contribution of anxiety/stress disorders in decreased sleep quality was reported [79]. The examination of patients with posttraumatic stress disorders showed relationship between occurrence and severity of that disorder and lack of BP dipping [136]. Promising results were obtained from study carried out on Chinese cohort, a juxtaposition of stress and sleep quality proper assessment scales [the Perceived Stress Scale and Pittsburgh Sleep Quality Index (PSQI)] and nocturnal BP type [79]. Proportion of non-dippers, level of norepinephrine and epinephrine were higher in patients with higher PQSI and PSS score, which confirmed that stress and poor sleep quality could be reliable factors in non-dipping hypertension status. Even though controversies in the field remain [137]². Benign prostate hyperplasia, state in which sleep disturbances and nocturia occur, is as well in association with non-dipping pattern [138]. However, in that clinical scenario, mainly nocturia and following increase of arginine vasopressin secretion may affect directly nocturnal BP variability [139].

Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is a common disorder characterized by repetitive collapse of upper airways during sleep, resulting in recurrent apnoea episodes. Even mild OSA can manifest with transient hypoxaemia and hypercapnia, disruption of

normal sleep, increased SNS output and intra-thoracic pressure swings. Impaired nocturnal BP decrease was noted in 48–84% patient with OSA and was associated with OSA severity [140, 141]. Recent studies also showed 3% increase of mean arterial pressure per 1-unit increase of oxygen desaturation index (the number of oxygen desaturations > 3% per hour of estimated sleep time) [142]. Major factors in chronically increased BP are hypoxaemia and SNS outflow [74, 93, 142]. Moreover, these effects persist even after removal of hypoxaemic factor due to altered autonomic control [143]. The possible mechanism explaining persistence of these effects includes abnormal baroreceptor reflex function and impaired chemoreflex sensitivity [20, 21, 144]. Chen *et al.* suggested the role of endothelin (ET) in hypoxaemia-induced aroused chemoreceptor activity. Functional studies revealed chemoexcitatory action of ET [145]. Continuous hypoxaemia increases expression of ET A receptor and of preproendothelin in the carotid body, therefore enhance chemoreceptor activity [146]. Changes in mean BP from apnoea to ventilation periods stays in inverse correlation with age [16]. It explains why severe apnoea component of OSA is responsible for non-dipping only in young patients, while sleep disturbances are more meaningful in elderly non-dipping OSA individuals [86].

Wolf *et al.* discussed several factors involved in non-dipping pattern occurrence: impaired endothelium-dependent vasodilatation, blunted nitric oxide production, oxidative stress, increased plasma asymmetric dimethyl arginine concentration, elevated levels of L-selectin, vascular cell adhesion molecule-1, intercellular adhesion molecule-1 and low-grade inflammation [147]. Studies show that continuous positive airway pressure (CPAP) therapy and lateral pharyngoplasty reduce nocturnal BP and significantly increase prevalence of dipping pattern in OSA patients [148–150]. Treatment procedures show importance of OSA in triggering of non-dipping development.

Aging

Age is the next factor discussed in the context of non-dipping hypertension occurrence. Staessen *et al.* published analysis which showed that the number of non-dippers subjects increased with age [151]. In elderly patients the circadian sleep-wake rhythm is changed due to experiencing less slow-wave sleep and more frequent occurrence of awake periods [152]. The occurrence of non-dipping hypertension in elderly patients may be also caused by decreased para-

sympathetic nervous activity and impaired balance between sympathetic and parasympathetic nervous activity [135]. Kohara *et al.* suggested that atherosclerosis can participate in attenuation of ANS [153]. Furthermore, the study conducted on patients with OSA revealed that prevalence of non-dipping pattern in elderly patient group maintained higher than in younger group [86].

Conclusions

A lot of various factors are involved in development of hypertension. Its pathogenesis is associated with alteration in ANS activation e.g. disturbance in sympathetic and parasympathetic balance and changes in endocrine system. Risk factors for developing hypertension are: advanced age, obesity, diabetes mellitus, chronic kidney disease and obstructive sleep apnoea. They also correlate with the occurrence of non-dipping circadian blood pressure rhythm. Other important factor is overreaction for salt intake. The division of hypertension into dipping and non-dipping is clinically significant. Non-dippers have greater probability of cardiovascular events and have worse general prognosis. Exact pathomechanism of impairment of circadian blood pressure pattern is not fully understood and because of its importance related with raised general risk further studies are necessary.

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