

Characteristics and control of the 24-hour ambulatory blood pressure in patients with metabolic syndrome

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Funding information

Y Li was financially supported by grants from the National Natural Science Foundation (81770455 and 82070432), and Ministry of Science and Technology (2018YFC1704902), Beijing, China.

Abstract

Asian countries are facing an increasing prevalence of metabolic syndrome (MetS), which may aggravate the burden of cardiovascular diseases in this region. MetS is closely associated with ambulatory blood pressure (BP). Patients with MetS, compared to those without, had a twofold higher risk of new-onset office, home, or ambulatory hypertension. Furthermore, the risk of new-onset MetS in patients with white-coat, masked and sustained hypertension was also doubled compared to normotensives. High-risk masked hypertension and blunted nighttime BP dipping are common in patients with MetS, suggesting perfect 24-hour BP control with long-acting antihypertensive drugs and early initiation of combination therapy might be especially important for patients with MetS.

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1 | INTRODUCTION

Metabolic syndrome (MetS), which had been coined as “x syndrome”¹ and “syndrome of insulin resistance,”² is characterized as the clustering of multiple cardiovascular risk factors including central obesity, dyslipidemia, and elevated levels of fasting blood glucose and office blood pressure (BP).³ Prior studies have demonstrated that MetS was associated with left ventricular hypertrophy, arterial stiffness, microalbuminuria, and long-term risk of cardiovascular morbidity and mortality.⁴⁻⁶ Along with rapid economic development and urbanization, Asian countries are facing a significant epidemic of MetS. Around 20%-40% of the adult population were affected by MetS depending on the study population and the diagnostic criteria applied.⁷ Tailored strategies for the prevention and management of MetS are required to reduce the associated cardiovascular disease burden in this region.

In the last three decades, ambulatory BP monitoring has been established and increasingly recommended as the method of choice for the assessment of BP.⁸ It captures diurnal BP variations and allows identification of masked hypertension from office normotension and differentiating white-coat hypertension from office hypertension. Although the recommended definitions of the BP component of MetS still rely on office BP measurement, a closer association of MetS with the 24-hour ambulatory BP has been observed.^{9,10} This article will concisely review the characteristics of the 24-hour ambulatory BP in patients with MetS and discuss the rational use of antihypertensive drugs in patients with MetS to achieve a perfect 24-hour BP control.¹¹

2 | LITERATURE SEARCH

We searched PubMed for articles published in English from 2000 to 2020 on ambulatory BP monitoring and antihypertensive treatment in MetS, using the key word “metabolic syndrome” and the following terms related to ambulatory BP monitoring, including “ambulatory blood pressure,” “white-coat hypertension,” “masked hypertension,” “dipping,” “morning hypertension,” and “morning blood pressure surge.” In total, 603 articles were identified. After removal of duplicates and screening abstracts and references of the identified articles, 72 full-length articles were assessed. From these assessed articles, 38 (52.8%) were removed, because of outcomes not of interest ($n = 20$), data had been reviewed before¹² ($n = 15$) or incomplete data ($n = 3$). Finally, a total of 34 studies were included in the present review.

2.1 | A close relationship between MetS and ambulatory BP

There is a close relationship between MetS and ambulatory BP. Irrespective of the definition of MetS, patients with white-coat, masked and sustained hypertension had a higher prevalence of MetS compared to normotensives in both populations and patient cohorts (Table 1).^{10,13-21} On the other hand, patients with MetS, compared

with those without, had a higher 24-hour, daytime or nighttime BP, albeit not in all reports (Table 2).²²⁻²⁸

In the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study,⁹ 193 (13.9%) patients with MetS according to the 2003 National Cholesterol Education Program Adult Treatment Panel (ATP) III criteria, compared to the 1201 patients without MetS, were older, and had higher office BP as well as 24-h and home BPs at baseline. After 10 years of follow-up, the age- and sex-adjusted risk ratios (95% confidence interval [CI]) of new-onset office, home, or ambulatory hypertension were, respectively, 3.52 (1.56-7.90), 2.94 (1.49-5.83), and 3.19 (1.75-5.79) ($p < .005$) in patients with MetS relative to those without.⁹ Furthermore, the PAMELA researchers observed a greater age- and sex-adjusted incident risk of new-onset MetS in patients with white-coat hypertension (1.75 [1.01-3.04], $p = .0046$), masked hypertension (2.58 [1.26-5.30], $p = .009$), and sustained hypertension (2.14 [1.20-3.79], $p = .009$) defined with office and ambulatory BPs.¹⁰ However, when hypertension was defined with office and home BPs, only patients with white-coat hypertension showed a greater risk of new-onset MetS (2.16, [1.28-3.63], $p = .003$). Similar associations were observed for single components of the MetS such as abdominal obesity and hyperglycemia.¹⁰

2.2 | High prevalence of masked hypertension in MetS

Masked hypertension is a special subtype of hypertension, characterized as out-of-office hypertension in the presence of a normal office BP and was associated with an adverse cardiovascular outcome.⁸ One of the MetS components is an elevated office blood pressure of $\geq 130/85$ mmHg, but quite a number of patients with MetS do not have hypertension based on office BP measurement according to the current hypertension guidelines in Asian countries. However, elevated office BP in the high normal range, increased waist circumference, and other components of MetS were significantly associated with a high risk of the presence of masked hypertension.²⁹

In the Jackson Heart Study,²⁸ the prevalence of masked hypertension was compared between African Americans with and without MetS, who all had an office BP of $< 140/90$ mmHg. Among the 359 participants not taking antihypertensive medication, the prevalence of masked hypertension was 62.3% and 43.6% among participants with and without MetS, respectively. After multivariate adjustment, the prevalence ratio of masked hypertension for MetS versus non-MetS was 1.38 (95% CI, 1.10-1.74). However, when the components of MetS were analyzed separately, only office BP of 130-139/85-89 mmHg was significantly associated with masked hypertension (OR, 1.90, 95%CI, 1.56-2.32). In the 393 participants who were treated with antihypertensive medication, there was no significant association between masked hypertension and MetS.²⁸

TABLE 1 The prevalence of metabolic syndrome according to hypertension subtype

Study	First author, RefN	N	Population	Mean age (years)	Male sex (%)	Mets (n, %)	OBP/ABP (N, %)			
							NBP	WCH	MHT	SHT
Baguet JP ¹³		126	Patients with obstructive sleep apnea syndrome	48.2	84.9	34 (27.0) ^b	6 (15)	/	9 (24)	19 (41)
Konstantopoulou AS ¹⁴		300	Outpatients in hypertension clinic	59.7	56.7	137 (45.7) ^c	/	48 (48)	41 (41)	48 (48)
Thomopoulos C ¹⁵		328	Outpatients in hypertension clinic	48.0	52.4	69 (21.0) ^a	16 (12)	10 (17)	12 (29)	31 (30)
Hermida RC ¹⁶		3344	Spanish subjects with normotension, untreated hypertension, or resistant hypertension	52.6	51.4	1915 (57.3) ^a	466 (44.0)	598 (64.1)	184 (52.1)	667 (66.8)
Afsar B ¹⁷		309	Outpatients in nephrology clinic	55.3	67.0	86 (27.8) ^a	3 (3.5)	28 (25) [*]	9 (29) [*]	46 (57) [*]
Mancia G ¹⁸		1921	Hypertensive patients in the ELSA trial	56.1	53.6	568 (29.6) ^a	/	77 (30.8)	/	491 (29.4)
Mancia G ¹⁹		1256	Part of the general population of the PAMELA Study	46.4	46.5	107 (8.5) ^a	33 (3.8)	74 (19.8) [*]	/	/
Saeed S ²⁰		298	Ischemic stroke survivors	49.0	67.2	103 (34.6) ^b	19 (16)	/	12 (33)	72 (50)
Kenny IE ²¹		323	Obesity patients without CVD	49.1	44.0	167 (51.7) ^b	19 (21.6)	/	30 (50.9) [*]	118 (67.3) [*]
Cuspidi C ¹⁰		2024	The general population of the PAMELA Study	43.4	44.4	326 (16.2) ^a	/ (6.0)	/ (27.5)	/ (14.7)	/ (30.6)

Abbreviations: ABP, Ambulatory blood pressure; HBP, Home blood pressure; MetsS, Metabolic syndrome; MHT, Masked hypertension; NBP, Normal blood pressure; OBP, Office blood pressure; RefN, Reference number; SHT, Sustained hypertension; WCH, White coat hypertension.

Definition of MetS applied:

^aAdult Treatment Panel (ATP) III;

^bAmerican Heart Association/National Heart, Lung and Blood Institute guidelines (AHA/NHLBI);

^cNot specified.

*P < .05 vs normotension

TABLE 2 Ambulatory blood pressure and dipping status in patients with and without metabolic syndrome*

Study	Without MetS					With MetS								
	N	Mean age (Years)	Daytime BP (mmHg)	Nighttime BP (mmHg)	24-hour BP (mmHg)	Nighttime BP fall (%)	Non-dippers (%)	N	Mean age (Years)	Daytime BP (mmHg)	Nighttime BP (mmHg)	24-hour BP (mmHg)	Nighttime BP fall (%)	Non-dippers (%)
Hermida RC ²²	1588	50.9	128/81	115/68	124/77 [‡]	10/16	39.5 [†]	1764 ^a	56.3	129/79	118/68	126/76 [‡]	9/14	52.0 [†]
Shivpuri S ²³	224	49.1	118/74	102/62	/	14/16	/	62 ^a	51.4	124/75	108/65	/	13/13	/
Nazzaro P ²⁴	81	44.2	135/86	119/77	/	12/10	/	81 ^a	47.3	142/88	125/79	/	12/10	/
Tadic M ²⁵	174	49.8	140/88	125/78	137/86	11/11	40.8 [†]	144 ^a	51.1	144/92	130/82	140/89	10/11	52.8 [†]
Rhee MY ²⁶	332	45.4	/	/	115/75	/	/	131 ^c	49.0	/	/	126/85	/	/
Yan B ²⁷	388	60.2	135/80	128/74	133/79	5/8	/	121 ^a	59.8	139/81	133/76	138/80	4/6	/
Colantonio LD ²⁸	298	54.1	124/78	114/67	120/73	8/14	/	61 ^b	56.0	128/77	119/68	125/73	7/12	/

Abbreviations: BP, Blood pressure; MetS, Metabolic syndrome; RefN, Reference number.

Definition of MetS applied:

^aAdult Treatment Panel (ATP) III;

^bThe 2009 harmonized definition;

^cAdult Treatment Panel (ATP) III and central obesity criteria for Korean.

*Studies published after the year of 2010 are listed.

[†]Non-dippers plus reverse dippers

[‡]48-h BP.

2.3 | Non-dipping BP pattern and morning BP surge in MetS

BP follows a circadian variation, being lower at night than during the day, and surging upon awakening and getting up in the morning. Four BP patterns consisting of dipping, non-dipping, reverse dipping, and extreme dipping are usually defined according to a night-to-day BP ratio of 0.8-0.9, 0.9-1.0, >1.0, and <0.8, respectively. Abnormal circadian BP variations, including non-dipping, reverse dipping, exaggerated morning BP surge, and morning hypertension, have been demonstrated to be associated with worse target organ damage and adverse cardiovascular outcome.^{30,31}

Most previous studies found that non-dipping was more common among subjects with MetS than those without, and the prevalence of non-dipping increased with the number of the MetS components.^{12,22,25} Table 2 lists the studies published after 2010.²²⁻²⁸ In a meta-analysis which was published in 2010 and included 7 studies,¹² the overall relative ratio for non-dipping in patients with MetS ($n = 352$), in comparison with those without MetS ($n = 326$), was 1.19 (95% CI 1.03-1.374, $p = .018$). Among the 509 hypertensive patients (254 men and 255 women, 45 to 75 years old) enrolled from September 2013 to March 2014 in China,²⁷ 121 (23.8%) were defined as having MetS according to the NCEP ATP III definition. MetS was found in 42.9% and 24.6%, respectively, in patients with reverse dipping ($n = 124$) or without ($n = 385$). After multivariate adjustment for age, smoking, and other BP indices, only the reverse dipping (OR 2.298; $p = .006$) and 24-hour systolic BP (OR, 1.063; $p = .021$) were significantly associated with MetS in men. No BP indices were found to be associated with MetS in women.²⁷

Few studies addressed the association between ambulatory morning BP surge and MetS. In 352 Portuguese with newly diagnosed hypertension but without diabetes,³² MetS was defined based on the International Diabetes Federation 2005 criteria. The 140 patients with MetS, compared to the 212 controls matched for age and casual BP, had significantly higher ambulatory morning BP surge (28 vs 25 mmHg, $p < .03$). Among the 1087 South Korean hypertensive patients,³³ Bastos et al found that MetS was more common ($p = .019$) in patients with morning hypertension (97/173, 59.5%) defined as a self-measured home morning BP of $\geq 135/85$ mmHg as compared to those without (415/914, 49.5%). Similar findings were observed in 181 Japanese with hypertension.³⁴

2.4 | 24-hour ambulatory BP control in MetS

Since MetS is characterized by a high prevalence of masked hypertension, blunted nocturnal BP dipping, and exaggerated morning BP surge, it is important for patients with MetS to control 24-hour BP level and circadian BP variations. On the basis of lifestyle modifications (exercise and diet), long-acting antihypertensive drugs with long half-life are recommended in order to achieve perfect control of 24-hour BP.^{11,31}

Current guidelines^{35,36} recommend that renin-angiotensin system blockers, including angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), are the first choice of antihypertensive drugs in patients with MetS. ACEIs and

ARBs were more useful than other drugs in the prevention of new-onset diabetes mellitus which might be related to the alleviation of insulin resistance as suggested by several clinical trials, for instance Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) and the Valsartan Antihypertensive Long-term Use Evaluation (VALUE).³⁶ Calcium channel blockers and alpha-blockers can be added on if patients had an uncontrolled BP treated with a single drug. Asian patients with MetS are more salt-sensitive than non-MetS ones,^{37,38} thereby reducing salt intake and a judicious use of diuretics in patients with MetS are preferred. As adverse metabolic effect associated with short-term exposure of atenolol and hydrochlorothiazide was common,³⁹ especially in those with abdominal obesity, vasodilating beta-blockers are recommended to counteract increased sympathetic tone in hypertensive MetS patients.⁴⁰ New hypoglycemic drugs, such as sodium-glucose cotransporter-2 inhibitors (SGLT2i), not only reduces blood glucose, but also improves 24-hour BP control, especially for patients with uncontrolled nocturnal hypertension,⁴¹ which might also be desirable for patients with MetS. Many studies have shown that 50%-70% of hypertensive patients need two or more drugs to achieve the goal of BP reduction, initiation of antihypertensive treatment with a single-pill combination is therefore highly recommended by international guidelines.⁴²

Between ACEIs and ARBs, no significant difference was found in their antihypertensive effect among patients with MetS in several small-sized clinical trials that used office BP measurement.^{43,44} The Zofenopril in Advanced MEtabolic Syndrome (ZAMES) study is a multicenter, randomized, double-blind clinical trial conducted in Italy and Romania.⁴³ Totally 466 patients with MetS and hypertension (mean age 59 years, male 53%) were randomly assigned to the treatment with a fixed-dose combination of zofenopril 30 mg plus hydrochlorothiazide 12.5 mg (231 patients) or irbesartan 150 mg plus hydrochlorothiazide 12.5 mg (235 patients) once daily for 24 weeks. After 8 and 16 weeks, drug dosages were doubled if office BP was uncontrolled. In 20% of patients, an ambulatory BP monitoring was performed. There was no significant difference in the office and 24-hour ambulatory BP reduction (mean systolic/diastolic BP difference, 0.1/-0.9 mmHg, $p \geq .54$) between the two groups, as well as the incidence of adverse events (both $\sim 5\%$). In the MEtabolic parameters, Diabetes mellitus, and NephropAthy (MEDINA) study,⁴⁴ a total of 439 hypertensive patients with MetS and/or diabetes mellitus were randomized to 2 groups: group 1 receiving ramipril or perindopril (217 patients) or group 2 losartan (222 patients). Hydrochlorothiazide or amlodipine, and then a statin were added if BP was uncontrolled. Office BP decreased by 24.1/13.3 mmHg in the ACEIs group and 25.9/13.5 mmHg in the losartan group. There was also no significant difference in changes of the MetS components between the two arms.⁴⁴

To improve BP control at night and in the morning, some researchers proposed to prescribe at least one antihypertensive drug at bedtime. However, for long-acting antihypertensive drugs with long half-life, such as amlodipine,⁴⁵ or for ACEIs or ARBs in high-dose or full-dose,⁴⁶ the 24-hour BP reduction was comparable between different strategies of dosing time. For patients on therapy of ≥ 1 antihypertensive agent, a

recent trial by Poulter et al also demonstrated that the 24-hour systolic and diastolic BPs, daytime, nighttime, and clinic BPs did not differ between the daytime (6 AM to 11 AM) and evening (6 PM to 11 PM) dosing.⁴⁷ The Hygia Chronotherapy Trial online-published in 2020 reported that bedtime dosing of antihypertensive drugs significantly reduced the incidence of cardiovascular events and mortality by ~40% to 50% along with a greater reduction in ambulatory nighttime systolic/diastolic BP by 3/2 mmHg. However, it is rather difficult to explain the observed huge benefit by the small BP difference between the groups. Therefore, whether chronotherapy of antihypertensive medication will be beneficial for hypertensive patients, especially for those having MetS, still needs to be explored in future trials.⁴⁸

3 | CONCLUSION

Asian countries are facing an increasing prevalence of MetS, which may aggravate the burden of cardiovascular diseases in this region. MetS was closely associated with ambulatory BP. High-risk masked hypertension and blunted nighttime BP dipping were common in patients with MetS. A perfect 24-hour BP control by using long-acting antihypertensive drugs and early initiation of combination therapy might be especially important for patients with MetS.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the expert clerical assistance of Ayako Okura from the Jichi Medical University School of Medicine, Tochigi, Japan.

CONFLICT OF INTEREST

Y Li reports having received research grants from A&D, Bayer, Omron, Salubris, and Shyndec and lecture fees from A&D, Daiichi Sankyo, Omron, and Takeda. J Shin has received lecture honoraria from Pfizer Inc, Hanmi Pharm. Co. Ltd., Yuhan Co. Ltd., and Boryung Pharmaceutical Co. Ltd.; consulting fees from Hanmi Pharm. Co. Ltd. And Menarini.; and research grants from Sanofi Pharm. and Hanmi Pharm. Co. Ltd. YC Chia has received honorarium and sponsorship at attend conferences and seminars from Pfizer, Omron, Servier and Xepa-Sol and an investigator research grant from Pfizer. CH Chen reports personal fees from Novartis, Sanofi, Daiichi Sankyo, SERVIER, Bayer, and Boehringer Ingelheim Pharmaceuticals, Inc HM Cheng received speakers honorarium and sponsorship to attend conferences and CME seminars from Eli Lilly and AstraZeneca; Pfizer Inc; Bayer AG; Boehringer Ingelheim Pharmaceuticals, Inc; Daiichi Sankyo, Novartis Pharmaceuticals, Inc; SERVIER; Co., Pharmaceuticals Corporation; Sanofi; TAKEDA Pharmaceuticals International and served as an advisor or consultant for ApoDx Technology, Inc K Kario reports research grants from Omron Healthcare, Fukuda Denshi, A&D, Pfizer Japan, and honoraria from Omron Healthcare. JG Wang reports having received research grants from Chengdu Di-Ao and Omron, and lecture and consulting fees from Astra-Zeneca, Novartis, Omron, Servier, and Takeda. All other authors report no potential conflicts of interest in relation to this article.

AUTHOR CONTRIBUTIONS

Yan Li conceptualized the topic of this manuscript. Jian-Feng Huang and Yan Li performed literature search, independently reviewed and extracted data from the articles, and wrote the first draft of manuscript. All other authors read, edited, and approved the manuscript.

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REFERENCES

1. Reaven GM. Role of insulin resistance in human disease. *Diabetes*. 1988;37(12):1595-1607.
2. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care*. 1991;14(3):173-194.
3. Eckel RH, Alberti KG, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet*. 2010;375(9710):181-183.
4. Mancia G, Bombelli M, Facchetti R, et al. Impact of different definitions of the metabolic syndrome on the prevalence of organ damage, cardiometabolic risk and cardiovascular events. *J Hypertens*. 2010;28(5):999-1006.
5. Sheng CS, Hu BC, Fan WX, Zou J, Li Y, Wang JG. Microalbuminuria in relation to the metabolic syndrome and its components in a Chinese population. *Diabetol Metab Syndr*. 2011;3(1):6.
6. Gong J, Xie Q, Han Y, et al. Relationship between components of metabolic syndrome and arterial stiffness in Chinese hypertensives. *Clin Exp Hypertens*. 2020;42(2):146-152.
7. Ranasinghe P, Mathangasinghe Y, Jayawardena R, Hills AP, Misra A. Prevalence and trends of metabolic syndrome among adults in the asia-pacific region: a systematic review. *BMC Public Health*. 2017;17(1):101.
8. Staessen JA, Li Y, Hara A, Asayama K, Dolan E, O'Brien E. Blood pressure measurement anno 2016. *Am J Hypertens*. 2017;30(5):453-463.
9. Mancia G, Bombelli M, Facchetti R, et al. Long-term risk of diabetes, hypertension and left ventricular hypertrophy associated with the metabolic syndrome in a general population. *J Hypertens*. 2008;26(8):1602-1611.
10. Cuspidi C, Facchetti R, Bombelli M, et al. Risk of new-onset metabolic syndrome associated with white-coat and masked hypertension: data from a general population. *J Hypertens*. 2018;36(9):1833-1839.
11. Kario K, Park S, Chia YC, et al. 2020 Consensus summary on the management of hypertension in Asia from the HOPE Asia Network. *J Clin Hypertens (Greenwich)*. 2020;22(3):351-362.
12. Pierdomenico SD, Cuccurullo F. Ambulatory blood pressure monitoring in type 2 diabetes and metabolic syndrome: a review. *Blood Press Monit*. 2010;15(1):1-7.
13. Baguet JP, Lévy P, Barone-Rochette G, et al. Masked hypertension in obstructive sleep apnea syndrome. *J Hypertens*. 2008;26(5):885-892.

14. Konstantopoulou AS, Konstantopoulou PS, Papargyriou IK, Liatis ST, Stergiou GS, Papadogiannis DE. Masked, white coat and sustained hypertension: comparison of target organ damage and psychometric parameters. *J Hum Hypertens*. 2010;24(3):151-157.
15. Thomopoulos C, Daskalaki M, Papazachou O, et al. Association of resistin and adiponectin with different clinical blood pressure phenotypes. *J Hum Hypertens*. 2011;25(1):38-46.
16. Hermida RC, Ayala DE, Mojón A, Fernández JR. Sleep-time blood pressure and the prognostic value of isolated-office and masked hypertension. *Am J Hypertens*. 2012;25(3):297-305.
17. Afsar B. Comparison of demographic, clinical, and laboratory parameters between patients with sustained normotension, white coat hypertension, masked hypertension, and sustained hypertension. *J Cardiol*. 2013;61(3):222-226.
18. Mancia G, Facchetti R, Parati G, Zanchetti A. Effect of long-term antihypertensive treatment on white-coat hypertension. *Hypertension*. 2014;64(6):1388-1398.
19. Mancia G, Facchetti R, Grassi G, Bombelli M. Adverse prognostic value of persistent office blood pressure elevation in white coat hypertension. *Hypertension*. 2015;66(2):437-444.
20. Saeed S, Waje-Andreassen U, Fromm A, Øyegarden H, Naess H, Gerdtts E. Prevalence and covariates of masked hypertension in ischemic stroke survivors: the Norwegian Stroke in the Young Study. *Blood Press Monit*. 2016;21(4):244-250.
21. Kenny IE, Saeed S, Gerdtts E, Midtbø H, Halland H, Lønnebakken MT. Masked hypertension in obesity: potential predictors and arterial damage. *Blood Press Monit*. 2017;22(1):12-17.
22. Hermida RC, Chayán L, Ayala DE, Mojón A, Fontao MJ, Fernández JR. Relationship between metabolic syndrome, circadian treatment time, and blood pressure non-dipping profile in essential hypertension. *Chronobiol Int*. 2011;28(6):509-519.
23. Shivpuri S, Allison MA, Macera CA, Lindsay S, Gallo LC. Associations between nocturnal blood pressure dipping and the metabolic syndrome in high- vs. low-acclimated Mexican American women. *Am J Hypertens*. 2013;26(8):1030-1036.
24. Nazzaro P, Schirosi G, Mezzapesa D, et al. Effect of clustering of metabolic syndrome factors on capillary and cerebrovascular impairment. *Eur J Intern Med*. 2013;24(2):183-188.
25. Tadic M, Ivanovic B, Celic V, Cuspidi C. Are the metabolic syndrome, blood pressure pattern, and their interaction responsible for the right ventricular remodeling? *Blood Press Monit*. 2013;18(4):195-202.
26. Rhee MY, Kim JH, Kim YS, et al. High sodium intake in women with metabolic syndrome. *Korean Circ J*. 2014;44(1):30-36.
27. Yan B, Yan H, Sun L, et al. Novel association between the reverse-dipper pattern of ambulatory blood pressure monitoring and metabolic syndrome in men but not in women. *Medicine (Baltimore)*. 2015;94(47):e2115.
28. Colantonio LD, Anstey DE, Carson AP, et al. Metabolic syndrome and masked hypertension among African Americans: The Jackson Heart Study. *J Clin Hypertens (Greenwich)*. 2017;19(6):592-600.
29. Asayama K, Sato A, Ohkubo T, et al. The association between masked hypertension and waist circumference as an obesity-related anthropometric index for metabolic syndrome: the Ohasama study. *Hypertens Res*. 2009;32(6):438-443.
30. Yang WY, Melgarejo JD, Thijs L, et al. International database on ambulatory blood pressure in relation to cardiovascular outcomes (IDACO) investigators. Association of office and ambulatory blood pressure with mortality and cardiovascular outcomes. *JAMA*. 2019;322(5):409-420.
31. Wang JG, Kario K, Chen CH, et al. Management of morning hypertension: a consensus statement of an Asian expert panel. *J Clin Hypertens (Greenwich)*. 2018;20(1):39-44.
32. Bastos JM, Bertoquini S, Polónia J. Relationship of circadian blood pressure and morning blood pressure surge with the severity of metabolic syndrome in newly diagnosed hypertensives. *Rev Port Cardiol*. 2007;26(7-8):731-741.
33. Lee JH, Bae JW, Park JB, et al. Morning hypertension in treated hypertensives: baseline characteristics and clinical implications. *Korean Circ J*. 2011;41(12):733-743.
34. Tamaki S, Nakamura Y, Yoshino T, et al. The association between morning hypertension and metabolic syndrome in hypertensive patients. *Hypertens Res*. 2006;29(10):783-788.
35. Joint Committee for Guideline Revision. 2018 Chinese guidelines for prevention and treatment of hypertension-A report of the Revision Committee of Chinese Guidelines for Prevention and Treatment of Hypertension. *J Geriatr Cardiol*. 2019;16(3):182-241.
36. Umemura S, Arima H, Arima S, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2019). *Hypertens Res*. 2019;42(9):1235-1481.
37. Chen J, Gu D, Huang J, et al. GenSalt Collaborative Research Group. Metabolic syndrome and salt sensitivity of blood pressure in non-diabetic people in China: a dietary intervention study. *Lancet*. 2009;373(9666):829-835.
38. Kim BK, Lim YH, Kim SG, Kim YM, Shin J. Relationship between sodium intake and blood pressure according to metabolic syndrome status in the Korean National Health and Nutrition Examination Survey. *Blood Press Monit*. 2012;17(3):120-127.
39. Cooper-DeHoff RM, Wen S, Beitelshes AL, et al. Impact of abdominal obesity on incidence of adverse metabolic effects associated with antihypertensive medications. *Hypertension*. 2010;55(1):61-68.
40. Lee HY, Shin J, Kim GH, et al. 2018 Korean Society of Hypertension Guidelines for the management of hypertension: part II-diagnosis and treatment of hypertension. *Clin Hypertens*. 2019;25:20.
41. Kario K, Okada K, Kato M, et al. 24-Hour blood pressure-lowering effect of an SGLT-2 inhibitor in patients with diabetes and uncontrolled nocturnal hypertension: results from the randomized, placebo-controlled SACRA Study. *Circulation*. 2018;139(18):2089-2097.
42. Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension global hypertension practice guidelines. *Hypertension*. 2020;75(6):1334-1357.
43. Napoli C, Omboni S, Borghi C. ZAMES (Zofenopril in Advanced METabolic Syndrome) Study Group. Fixed-dose combination of zofenopril plus hydrochlorothiazide vs. irbesartan plus hydrochlorothiazide in hypertensive patients with established metabolic syndrome uncontrolled by previous monotherapy. The ZAMES study (Zofenopril in Advanced METabolic Syndrome). *J Hypertens*. 2016;34(11):2287-2297.
44. Spinar J, Vitovec J, Soucek M. Anti-hypertensive strategies in patients with METabolic parameters, diabetes mellitus and/or Nephropathy (the MEDINA study). *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2014;158(3):412-421.
45. Nold G, Strobel G, Lemmer B. Morning versus evening amlodipine treatment: effect on circadian blood pressure profile in essential hypertensive patients. *Blood Press Monit*. 1998;3(1):17-25.
46. Zappe DH, Crikelair N, Kandra A, Palatini P. Time of administration important? Morning versus evening dosing of valsartan. *J Hypertens*. 2015;33(2):385-392.
47. Poulter NR, Savopoulos C, Anjum A, et al. Randomized crossover trial of the impact of morning or evening dosing of antihypertensive agents on 24-hour ambulatory blood pressure. *Hypertension*. 2018;72(4):870-873.
48. Burnier M, Kreutz R, Narkiewicz K, Kjeldsen S, Oparil S, Mancia G. Circadian variations in blood pressure and their implications for the administration of antihypertensive drugs: is dosing in the evening better than in the morning? *J Hypertens*. 2020;38(8):1396-1406.

How to cite this article: Huang J-F, Li Y, Shin J, et al; Characteristics and control of the 24-hour ambulatory blood pressure in patients with metabolic syndrome. *J Clin Hypertens*. 2021;23:450-456. <https://doi.org/10.1111/jch.14229>