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Relationship of 24-Hour Mean Arterial Pressure with Systolic and Diastolic Blood Pressure in Hypertension: Insights from Ambulatory Blood Pressure Monitoring

ABSTRACT

Background: Twenty-four-hour mean arterial pressure (MAP) is underutilized for the diagnosis and risk assessment of hypertension in clinical settings. The objective of this study is to assess the relation of MAP with systolic and diastolic blood pressure (BP) in diagnosing hypertension on 24-hour ambulatory blood pressure monitoring (ABPM), while also examining its diagnostic effectiveness.

Methods: This retrospective study analyzed 24-hour ABPM of 532 adults. Hypertension diagnosis was made based on 2 criteria: the standard 24-hour systolic/diastolic BP measurement criteria and the 24-hour MAP measurement criteria. The relation of the 24-hour MAP with systolic and diastolic measurements and the predictors affecting its accuracy were evaluated.

Results: A total of 532 patients were included, and 409 (76.9%) were diagnosed with hypertension based on 24-hour ambulatory systolic/diastolic BP criteria. Among hypertensive patients, 191 (46.7%) were overlooked by 24-hour MAP criteria. Multiple logistic regression analysis identified age ≥52.4 (OR = 3.23, 95% CI:2.02-5.16, *P* < .001), female gender (OR = 2.54, 95%CI:1.61-4.02, *P* < .001), and less variation in daytime/nighttime systolic/diastolic BP as significant independent predictors of overlooked hypertension by 24-hour MAP criteria.

Conclusion: Our study highlights a relation between 24-hour MAP and systolic/diastolic BP measurements in diagnosing hypertension via 24-hour ABPM, especially in older adults and women. Systolic/diastolic criteria offer greater sensitivity for hypertension detection compared to MAP alone. This underscores the need for refined diagnostic criteria and suggests that reliance on MAP alone may lead to underdiagnosis in these vulnerable populations, necessitating further investigation.

Keywords: Twenty-four-hour ambulatory blood pressure measurement, 24-hour mean arterial pressure, hypertension, diagnosis

ORIGINAL INVESTIGATION

INTRODUCTION

Hypertension is a widespread chronic disease that affects 40% of adults worldwide.[1] It is the most significant modifiable risk factor for cardiovascular disease and all-cause mortality.[2,3] The high prevalence of hypertension emphasizes the need for an accurate diagnosis to provide effective treatment and prevent cardiovascular complications.

Based on available evidence, 24-hour ambulatory blood pressure monitoring (ABPM) is superior to office blood pressure (BP) measurements in predicting total and cardiovascular mortality as well as overall and cause-specific cardiovascular complications in patients with hypertension and in population cohorts since it provides a more precise picture of BP status.[4-7] Relying solely on office BP may result in the misclassification of 50% of all analyzed patients by ignoring crucial data about the circadian BP pattern and nighttime BP. Current guidelines endorse 24-hour ABPM unanimously as the reference standard method for the diagnosis of hypertension.[7-10]

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In addition to systolic and diastolic BP measurements, 24-hour ABPM monitoring allows the evaluation of other parameters such as mean arterial pressure, dipping and non-dipping status, early morning surge pattern, pressure loads, and pulse pressure variability. Among them, mean arterial pressure (MAP) is a crucial indicator of the circulating pressure load during a cardiac cycle. MAP is related to both systolic and diastolic BP and records risk-related data associated with each.[11] In younger patients, MAP has been shown to be more important than pulse pressure in the prediction of stroke. However, in older patients, MAP has been found to be a weaker predictor of stroke and a better predictor of cardiovascular diseases.[12] Office MAP emerged as a greater predictor of vascular death than systolic or diastolic BP or pulse pressure in a meta-analysis of data from 1 million individuals.[13] Even though MAP has been shown to be an important parameter for sepsis, major trauma, intracranial bleeding, and stroke in intensive care units,[14] guidelines for managing hypertension neither define an optimal MAP as a target nor specify how risk stratification should be done using MAP.

In a recent population-based cohort of 11 596 adults, outcome-driven thresholds for 24-hour MAP and its associations with fatal and nonfatal cardiovascular endpoints were evaluated.[15] Using a composite cardiovascular endpoint as the primary outcome and the 10-year risks associated with 2017 American College of Cardiology/American Heart Association thresholds for office blood pressure as the reference, 24-hour MAP of <90, ≥90 to <92, ≥92 to <96, and ≥96 mmHg delineated normotension, elevated 24-hour MAP, stage 1 hypertension, and stage 2 combined with severe hypertension, respectively.[15]

Given the prognostic accuracy but underutilization of 24-hour MAP for the diagnosis of and risk assessment of hypertension in clinical practice, we designed a retrospective study to assess the relation of MAP with systolic and diastolic BP in diagnosing hypertension on 24-hour ABPM, while also examining its diagnostic effectiveness in conjunction with the 2017 ACC/AHA-driven thresholds for 24-hour ABPM and recently established thresholds for 24-hour MAP.

HIGHLIGHTS

- Underutilized MAP: Despite its potential, 24-hour MAP is underused in hypertension diagnosis.
- Diagnostic comparison: Study shows weak concordance between 24-hour MAP and systolic and diastolic BP in the diagnosis of hypertension using 24-hour ABPM
- High number of overlooked cases: Nearly half of hypertensive patients (46.7%) were missed by the MAP criteria.
- Predictors of missed cases: Age ≥52.4, female gender, and less BP variation predict missed cases.
- Clinical implications: Diagnosis using systolic/diastolic criteria may be more sensitive than using MAP criteria, warranting further research for optimal thresholds.

METHODS

Patients

This retrospective study analyzed 24-hour ABPM of 532 adult patients (≥18 years of age) who visited our outpatient clinic of the cardiology department with a history of high BP between the years 2015 and 2022. Demographic and clinical data were retrieved from patient records. The study protocol was approved by the Local Institutional Review Board, and the study was conducted in accordance with the Declaration of Helsinki. Artificial intelligence (AI)-assisted technologies (such as Large Language Models [LLM], chatbots, or image creators) were not used in the production of this study.

24-Hour Ambulatory Blood Pressure Measurements

ABPM was performed for 24 hours by means of an oscillometric device (Tracker 2 NIBP, Del Mar Reynolds Medical) using CardioNavigator V:2.414 (PDX) software. The device was set to measure BP every 30 minutes during the day (from 07:00 a.m. to 10:00 p.m.) and every 60 minutes during the night (from 10:00 p.m. to 07:00 a.m.). Devices were periodically calibrated with a mercury sphygmomanometer. The arm cuff was positioned on the non-dominant upper limb. In addition to 24-hour ambulatory systolic, diastolic, and MAP measurements, SDs of measurements during day and night, pulse pressure, and dipper/non-dipper pattern were evaluated.

Based on 24-hour systolic/diastolic BP measurements, stages of hypertension were defined with the following threshold values: elevated BP, 115/75 mm Hg; stage I hypertension, 125/75 mm Hg; stage II hypertension, 130/80 mm Hg; severe hypertension, 145/90 mm Hg.[8,16] In addition, stages were also defined based on 24-hour MAP measurements as follows: normotension; <90 mm Hg, elevated BP, 90-92 mm Hg; stage I hypertension, 92-95 mm Hg; stage II/severe hypertension, ≥96 mm Hg.[14] Dipper pattern was defined as at least a 10% decline in systolic nocturnal BP compared to awake BP. Pulse pressure was the difference between systolic and diastolic BP.

Statistical Analysis

For the analysis of data, IBM SPSS Statistics version 21.0 software was used. Descriptive data are presented in number (percentage) or mean ± SD. Normality of continuous variables was tested using Kolmogorov–Smirnov and Shapiro–Wilk tests. The chi-square test was used for between-group comparisons of categorical variables. For the between-group comparison of continuous variables, the Student's *t*-test for independent samples or Mann–Whitney *U* test was used, depending on the data distribution. Receiver operating characteristic (ROC) curves were generated and area under the curve (AUC) values were calculated with 95% confidence intervals to examine the predictive value of continuous variables for hypertension overlooked by 24-hour mean arterial pressure. The highest Youden index (sensitivity + specificity – 1) was used for the identification of optimal cutoff values. Multiple logistic regression analysis was used to identify the significant independent predictors of hypertension overlooked by 24-hour mean arterial blood pressure. A *P*-value <.05 was considered indication of statistical significance.

RESULTS

Patients

A total of 532 patients were included in this study. The median number of ambulatory readings recorded over 24 hours was 24 ± 2. Among all patients, 409 (76.9%) were diagnosed with hypertension based on 24-hour ambulatory systolic/diastolic BP criteria. None of the patients were diagnosed with hypertension based solely on hypertension criteria for 24-hour MAP. Thus, all patients diagnosed based on 24-hour MAP were also hypertensive based on 24-hour systolic/diastolic BP criteria. Demographical and clinical data of the patients are shown in Table 1.

Diagnosis with Different Criteria

Among patients diagnosed with hypertension based on 24-hour systolic/diastolic BP (n = 409), only 218 (53.3%) could meet diagnostic criteria based on 24-hour MAP; thus, 191 (46.7%) were overlooked by 24-hour MAP criteria. Table 2 shows the distribution of hypertension stages as diagnosed with 24-hour systolic/diastolic BP vs. 24-hour MAP criteria. Twenty-four-hour MAP identified the same stage with 24-hour systolic/diastolic BP in 221 (41.5%) patients; however, it underestimated the stage in the remaining 311 (58.5%) patients.

Predictors of Overlooked Hypertension by 24-Hour Mean Arterial Pressure

Table 3 shows the univariate analysis of factors that may affect overlooked hypertension by 24-hour MAP. Patients who meet systolic/diastolic BP criteria but not MAP criteria (i.e., missed cases) were significantly older and had lower BP variations during the day and night; in addition, missed cases were more common among female patients. Results of ROC analyses and cutoff points associated with a higher risk of overlooked hypertension are shown in Table 4. In addition, Figure 1A-E shows ROC curves. Multiple logistic regression analysis identified age ≥52.4 (OR = 3.23, 95% CI: 2.02-5.16, $P < .001$), female gender (OR = 2.54, 95% CI: 1.61-4.02, $P < .001$), ≤13.85 daytime SD of systolic BP (OR = 1.77, 95% CI: 1.05-3.00, $P = .033$), ≤8.95 daytime SD of diastolic BP (OR = 2.19, 95% CI: 1.35-3.53, $P = .001$), and ≤13.65 nighttime SD of systolic BP (OR = 2.03, 95% CI: 1.24-3.35, $P = .005$) as significant independent predictors of overlooked hypertension by 24-hour MAP criteria (Table 5). The 24-hour diastolic BP of the older patients (≥52.4 years) was significantly lower when

Table 1. Demographical and Clinical Data of the Subjects

Characteristics	All Patients, n = 532	Female Patients, n = 211 (39.7%)	Male Patients, n = 321 (60.3%)
Age, years	53.4 ± 13.3	54.7 ± 13.2	52.6 ± 13.4
Body mass index, kg/m^2	30.7 ± 5.7	31.4 ± 7.0	30.3 ± 4.7
Antihypertensive medication, n (%)	222 (42.0%)	87 (42.0%)	135 (42.1%)
24-hour systolic BP, mm Hg	133.0 ± 16.2	131.4 ± 17.2	134.1 ± 15.4
24-hour diastolic BP, mm Hg	78.2 ± 11.6	76.0 ± 11.3	79.6 ± 11.6
24-hour MAP, mm Hg	90.0 ± 11.6	88.0 ± 11.6	91.3 ± 11.5
Pulse pressure, mm Hg	54.9 ± 10.5	55.3 ± 11.3	54.5 ± 10.0
Daytime SD of systolic BP, mm Hg	13.1 ± 4.1	13.6 ± 4.2	12.8 ± 3.9
Daytime SD of diastolic BP, mm Hg	9.6 ± 3.5	9.8 ± 3.5	9.6 ± 3.5
Nighttime SD of systolic BP, mm Hg	12.7 ± 4.7	12.5 ± 4.9	12.9 ± 4.6
Nighttime SD of diastolic BP, mm Hg	9.5 ± 3.5	9.2 ± 3.3	9.7 ± 3.6
Nocturnal dipper, n (%)	165 (31.3%)	56 (26.7%)	109 (34.4%)
Diagnosed with hypertension†, n (%)	409 (76.9%)	154 (73.0%)	255 (79.4%)

Unless otherwise stated, data presented were as mean ± SD.

Table 2. Distribution of Hypertension Stages as Identified with 24-hour Systolic/Diastolic BP Versus 24-hour Mean Arterial Pressure Criteria (n = 532)

Stage	24-hour Systolic/Diastolic BP	24-hour MAP
No hypertension	58 (10.9%)	278 (52.3%)
Elevated BP	65 (12.2%)	36 (6.8%)
Stage I HT	85 (16.0%)	55 (10.3%)
Stage II/severe HT	334 (60.9%)	163 (30.6%)

Table 3. Univariate Analysis of Factors that May Affect Overlooked Hypertension by 24-hour Mean Arterial Pressure Among Patients Diagnosed with Hypertension Based on 24-Hour Systolic/Diastolic Blood Pressure (n = 409)

Characteristic	Hypertensive Based on 24-hour MAP: No (n = 191)	Hypertensive Based on 24-hour MAP: Yes (n = 218)	*P*
Age, years	56.3 ± 14.5	50.9 ± 11.6	<.001
Gender, n (%)			
Male	101 (39.6%)	154 (60.4%)	<.001
Female	90 (58.4%)	64 (41.6%)	
Body mass index, kg/m^2	30.9 ± 5.0	31.0 ± 5.9	.748
Antihypertensive medication, n (%)			
No	106 (44.9%)	130 (55.1%)	.436
Yes	83 (48.8%)	87 (51.2%)	
Pulse pressure, mm Hg	56.8 ± 10.7	57.2 ± 10.6	.838
Daytime SD of systolic BP, mm Hg	12.6 ± 3.4	14.0 ± 4.5	.004
Daytime SD of diastolic BP, mm Hg	8.9 ± 3.2	10.5 ± 3.9	<.001
Nighttime SD of systolic BP, mm Hg	12.0 ± 4.2	14.4 ± 5.2	<.001
Nighttime SD of diastolic BP, mm Hg	8.9 ± 3.1	10.7 ± 3.6	<.001
Nocturnal change, n (%)			
Non-dipper	138 (49.5%)	141 (50.5%)	.148
Dipper	53 (41.7%)	74 (58.3%)	

Unless otherwise stated, data presented in mean ± SD.

Table 4. Results of ROC Analysis for the Prediction of Overlooked Hypertension

Parameter	Optimal Cutoff	AUC	95% CI, AUC	*P*
Age	≥52.4 years	0.621	(0.566-0.676)	<.001
Daytime SD of systolic BP, mm Hg	≤13.85 mm Hg	0.583	(0.528-0.638)	.004
Daytime SD of diastolic BP, mm Hg	≤8.95 mm Hg	0.637	(0.583-0.691)	<.001
Nighttime SD of systolic BP, mm Hg	≤13.65 mm Hg	0.633	(0.579-0.686)	<.001
Nighttime SD of diastolic BP, mm Hg	≤8.15 mm Hg	0.640	(0.586-0.693)	<.001

compared to younger patients (74.9 vs. 81.1 mm Hg), although they do not differ in terms of 24-hour systolic BP.

DISCUSSION

This study has demonstrated that using the American College of Cardiology/American Heart Association thresholds for systolic/diastolic BP (<125/<75 mm Hg vs. ≥125/≥75 mm Hg), the diagnosis of HT with 24-hour ABPM is more sensitive when made in accordance with systolic/diastolic criteria than with 24-hour MAP criteria alone. To the best of our knowledge, this is the first study to evaluate the relation of MAP with systolic and diastolic BP in a 24-hour ambulatory setting in the diagnosis of adult hypertension, other than the study by Sulakova et al[17] conducted in pediatric patients.

The physiological relevance of MAP can be explained by several factors. Blood flow to the tissues seems to be more closely related to MAP rather than diastolic/systolic BP. For instance, the bloodstream only spends a brief period of time at the peak systolic pressure, making it an inadequate determinant of blood flow.[18] MAP is the pressure regulated by the constriction and dilation of arterioles. By the time blood reaches the distal arterioles where important vascular regulation occurs, it is no longer significantly pulsatile. Consequently, the systolic and diastolic pressures hold little meaning at the level of the arteriolar vascular bed.[18] Since MAP is consistent across the arterial tree and less affected by distal pulse amplification,[19] the question of whether central versus brachial BP increases cardiovascular risk is not a concern.[20] MAP's significance resides in the fact that it allows the blood in circulation to supply key organs with oxygen and crucial nutrients.[21] While lower MAP may be deleterious in unstable hemodynamics, higher levels of MAP are linked to target organ damage, cardiovascular, and cerebrovascular diseases.[22-24]

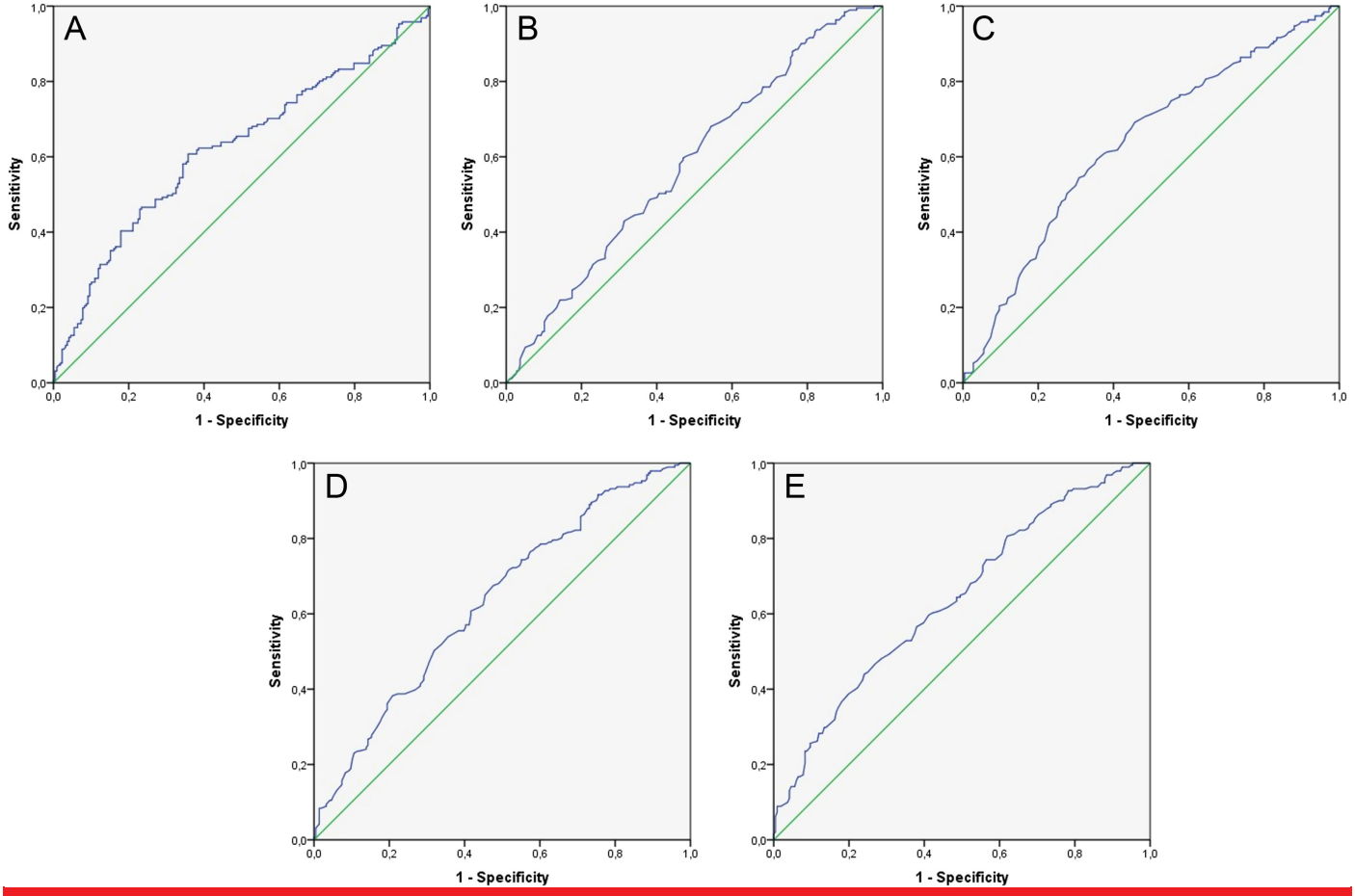

Figure 1. Receiver operating characteristic (ROC) curves for (A) age, (B) daytime SD of systolic BP, (C) daytime SD of diastolic BP, (D) nighttime SD of systolic BP, and (E) nighttime SD of diastolic BP to predict overlooked hypertension by 24-hour MAP criteria.

Table 5. Univariate and Multiple Logistic Regression Analysis of Selected Factors that May Affect Overlooked Hypertension by 24-Hour Mean Arterial Pressure Among Patients Diagnosed with Hypertension Based on 24-Hour Systolic/Diastolic Blood Pressure (n = 409)

Factor	Univariate Logistic Regression	Multiple Logistic Regression
Age ≥52.4 years	OR = 2.54, 95% CI: 1.70-3.79, *P* < .001	OR = 3.23, 95% CI: 2.02-5.16, *P* < .001
Female gender	OR = 2.14, 95% CI: 1.43-3.22, *P* < .001	OR = 2.54, 95% CI: 1.61-4.02, *P* < .001
Daytime SD of systolic BP ≤13.85 mm Hg	OR = 1.79, 95% CI: 1.19-2.68, *P* = .005	OR = 1.77, 95% CI: 1.05-3.00, *P* = .033
Daytime SD of diastolic BP ≤8.95 mm Hg	OR = 2.63, 95% CI: 1.76-3.93, *P* < .001	OR = 2.19, 95% CI: 1.35-3.53, *P* = .001
Nighttime SD of systolic BP ≤13.65 mm Hg	OR = 2.36, 95% CI: 1.56-3.56, *P* < .001	OR = 2.03, 95% CI: 1.24-3.35, *P* = .005
Nighttime SD of diastolic BP ≤8.15 mm Hg	OR = 2.48, 95% CI: 1.62-3.78, *P* < .001	OR = 1.54, 95% CI: 0.93-2.56, *P* = .096
Dipper pattern	OR = 0.73, 95% CI: 0.48-1.11, *P* = .149	OR = 1.00, 95% CI: 0.62-1.61, *P* = .098

The maximal oscillation of the cuff typically corresponds reasonably well to the invasively measured mean; therefore, the oscillating automated BP cuff monitor actually reports an accurate MAP.[24] A common technique for estimating MAP is the maximum amplitude algorithm, which considers the cuff pressure at the oscillometric waveform envelope's maximum amplitude, which corresponds to the arterial wall being unloaded and where the transmural pressure is zero. Using proprietary algorithms, the systolic and diastolic BPs are computed from the estimated MAP.[25] Maximum amplitude algorithm was used by the software implemented in automated ambulatory devices to compute MAP in our study.

Among patients diagnosed with hypertension based on 24-hour systolic/diastolic BP according to 2017 American College of Cardiology/American Heart Association thresholds, only 53.3% could meet the diagnostic criteria based on recently defined 24-hour MAP[15] in our study; thus, 46.7% were overlooked by 24-hour MAP criteria. In the study by Melgarejo et al[15] where the association of fatal and nonfatal cardiovascular outcomes with 24-hour MAP was evaluated, when systolic BP and MAP were considered, 54.2% of the patients were normotensive for both BP indexes, 7.0% had high systolic BP but normal MAP, 5.0% had normal systolic BP but elevated MAP, and 33.8% had both elevated systolic BP and MAP. For cross-classification with diastolic BP, these numbers were 55.4%, 5.7%, 4.5%, and 34.4%, respectively. The higher percentage of patients overlooked by 24-hour MAP thresholds compared with systolic/diastolic thresholds in our study might be related to ethnic differences and a higher percentage of patients under antihypertensive treatment (19.6% vs. 41.0%) in our study. On the other hand, Sulakova et al[17] showed that the inclusion of MAP in the definition of ambulatory hypertension significantly increased the number of hypertensive patients by 19%. None of the patients were diagnosed with hypertension based solely on hypertension criteria for 24-hour MAP in our study. Although the results of this study contradict our study, the patient groups in both studies are completely different. BP levels and BP normal upper limits change with growth and body size, making interpretation of 24-hour ABPM in children more difficult than in adults.[7] The normative pediatric ABPM results include systolic BP, diastolic BP, MAP, percentiles, and Z scores that are related to age and height;[26] however, these values do not precisely define ambulatory hypertension.

Patients who meet systolic/diastolic BP criteria for hypertension but not MAP criteria (i.e., missed cases) in our study were significantly older and had lower SDs of BP during day and night; additionally, missed cases were more common among female patients. According to a U.S. National Health and Nutrition Examination Survey, both men's and women's systolic BP rises with age, but it is higher in males than in females starting in early adulthood.[27] In addition, recent studies using 24-hour ABPM have shown that BP is higher in men than in women at similar ages. Among 352 Danish men and women, aged 20-79, who were considered normotensive for their age, Wiinberg et al[28] discovered that BP rose with age in both sexes, but males had 610 mm Hg higher 24-hour MAP than females until the age of 70-79 years, when BP was similar for men and women. This may provide an explanation for the higher percentage of missed cases in women. Diastolic BP increases progressively in both men and women due to increased peripheral resistance by the remodeling of the arterioles in the overall population until approximately the sixth decade of life, after which it decreases progressively with the reduction of arterial compliance. With increased arterial stiffness, the normal buffering capacity of the vessels during systole is impeded, leading to increased systolic blood pressure.[29] Physiologic changes associated with aging lead to an increase in systolic BP, MAP, and pulse pressure but a decrease in diastolic BP.[30] In our study, older patients (≥52.4 years) who were more likely to be missed by MAP had significantly lower 24-hour diastolic BP compared to younger patients (74.9 vs. 81.1 mm Hg), although they did not differ in terms of 24-hour systolic BP. However, as being older than 52 years of age can hardly be classified as 'elderly', according to any given standard, this does not necessarily bring about isolated systolic hypertension, which is generally encountered in much older patient populations. Among different potential causes, BP variability plays a crucial role in the diagnostic discrepancy between MAP and SBP/DBP findings on 24-hour ABPM. In older adults, BPV increases due to factors such as autonomic dysfunction, decreased baroreflex sensitivity, and medication effects.[31-33] This variability can lead to inconsistent readings, particularly in ambulatory settings. When BP is highly variable, brief periods of very high systolic BP may not significantly raise the average MAP if these spikes are counterbalanced by lower readings. This means that despite episodes of hypertension, the overall MAP might not cross the threshold needed for diagnosis, leading to underestimation. Decreased BPV, on the other hand, may lead to missed

hypertension diagnosis in a different way. When BP is more stable with less variability, the average MAP might be lower, and subtle but consistent elevations in systolic BP (often seen in older adults or those with arterial stiffness) might not be reflected in MAP readings. This can cause underdiagnosis, particularly if the MAP does not reach the diagnostic thresholds even though the systolic BP is consistently elevated, which is another finding in our study with missed hypertensive patients according to MAP with decreased BP variations independent of age. Both increased and decreased BPV can contribute to missed diagnoses, but through different mechanisms. These nuanced effects underscore the complexity of diagnosing hypertension using MAP alone, particularly in older patients with different BPV profiles.

Findings of this study need to be evaluated within the context of several limitations. A key and foremost limitation of this study is the inclusion of a substantial proportion of patients already diagnosed with hypertension under antihypertensive treatment. This status could have influenced the study outcomes, particularly the MAP-based hypertension diagnoses. As a result, the findings may not fully represent the characteristics of untreated hypertension. Future research should prioritize studying treatment-naive, newly diagnosed patients to provide a clearer understanding of the relation between MAP and SBP/DBP in hypertension diagnosis. Secondly, as this is a retrospective study, prospective studies could offer more robust data, overcoming the inherent constraints of retrospective designs. Finally, the lack of long-term follow-up prevents the evaluation of cardiovascular outcomes in the long term.

CONCLUSION

Our findings reveal a weak concordance between 24-hour MAP and systolic/diastolic BP measurements in diagnosing hypertension via 24-hour ABPM, particularly among older and female patients. The enhanced sensitivity of systolic/diastolic criteria over MAP highlights the potential for underdiagnosis when relying solely on MAP. This underscores the necessity of revising diagnostic criteria and prompts further prospective studies to elucidate the clinical utility and establish precise thresholds for 24-hour MAP, particularly in these vulnerable populations.

Ethics Committee Approval: The study protocol was approved by the institutional review board of the Anadolu Medical Center, Kocaeli, Türkiye (no. ASM-EK-23/197; date, January 10, 2023), and the study was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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