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Blood Pressure Variability as an Independent Predictor of Early Cardiac, Renal, and Retinal Target Organ Damage in Adults with Essential Hypertension

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ABSTRACT

Background: during the day may impose additional haemodynamic stress and contribute to subclinical organ injury. Evidence linking short-term blood pressure variability with simultaneous cardiac, renal, and retinal involvement remains limited.

Objective: To determine whether increased 24-hour systolic blood pressure variability is independently associated with early cardiac, renal, and retinal target-organ damage among adults with essential hypertension.

Methods: This analytical cross-sectional study enrolled 70 adults with essential hypertension at Frontier Medical College, Abbottabad, between February 2025 and January 2026. Participants underwent 24-hour ambulatory blood pressure monitoring, transthoracic echocardiography, urinary albumin-to-creatinine ratio measurement, estimated glomerular filtration rate calculation, and dilated fundus examination. Twenty-four-hour systolic average real variability was used as the principal variability measure. Multivariable logistic regression accounted for age, sex, hypertension duration, mean 24-hour systolic pressure, and nocturnal dipping pattern.

Results: Participants had a mean age of 51.5 ± 8.9 years, and 38 (54.3%) were men. Early target-organ damage was identified in 35 (50.0%) participants. Cardiac, renal, and retinal involvement occurred in 25 (35.7%), 20 (28.6%), and 16 (22.9%) individuals, respectively. Any organ damage was more frequent in the high-variability group than in the low-variability group (68.6% vs 31.4%; p=0.002). Higher systolic variability independently predicted cardiac, renal, retinal, composite, and multiorgan involvement. Its discriminatory performance for composite damage yielded an area under the curve of 0.76.

Conclusion: Greater short-term systolic blood pressure variability was independently related to early multiorgan injury. Incorporating variability indices into ambulatory monitoring may provide additional risk information beyond mean blood pressure alone.

Keywords: hypertensive retinopathy, albuminuria, ambulatory blood pressure monitoring; blood pressure variability; essential hypertension; target organ damage

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INTRODUCTION

Hypertension is a significant modifiable risk factor for cardiovascular disease, chronic renal disease, cerebrovascular incidents, and early death [1]. The average office or ambulatory blood pressure is a crucial tool for evaluating and making treatment decisions since blood pressure varies throughout the day [2]. It fluctuates with exercise, stress, sleep, wakefulness, and the activity of the autonomic nervous system, influenced by the timing of medication and environmental circumstances. These swings are collectively referred to as blood pressure variability and may provide greater insight into

cardiovascular risk than average blood pressure alone [3]. Blood pressure variability can be evaluated throughout many timeframes, encompassing beat-to-beat alterations, short-term variances during 24-hour ambulatory monitoring, daily variations recorded at home, and long-term visit-to-visit discrepancies [4]. The short-term variability assessed with ambulatory blood pressure monitoring is more pertinent, as it captures fluctuations that transpire during routine everyday activities, including sleep. Common indicators encompass standard deviation, coefficient of variation, weighted standard deviation, and average actual variability. The average actual variability is defined as the absolute difference between consecutive blood pressure readings and may offer a more accurate assessment of dynamic blood pressure variability than the conventional standard deviation [5-8].

Fluctuating blood pressure can induce recurrent mechanical stress, endothelial injury, oxidative stress, sympathetic system activation, and insufficient tissue perfusion within the vascular system [6]. These impacts may result in structural and functional alterations in highly vascular organs, even before the clinical onset of cardiovascular or renal illness. Frequent modifications of left ventricular afterload may result in myocardial hypertrophy and impaired diastolic relaxation. Similarly, changes in renal perfusion pressure may damage the microcirculation within the glomerulus, leading to increased urinary excretion of albumin. Alterations in retinal arteriolar pressure can result in narrowing, arteriovenous crossing defects, and other initial indicators of hypertensive retinopathy [2-5].

Early target organ damage from hypertension is therapeutically significant since it aids in identifying individuals at elevated risk for future cardiovascular events, even in the absence of symptoms [7]. Left ventricular hypertrophy and diastolic dysfunction are the first cardiac consequences of prolonged hemodynamic stress. Moderately high albuminuria serves as an early sign of glomerular and systemic endothelial impairment, while hypertensive retinal alterations are direct manifestations of microvascular injury. These anomalies may coexist, indicating generalised vascular involvement and a more advanced hypertension syndrome [8].

Previous investigations have indicated that blood pressure variability (BPV) is associated with cardiac, renal, cerebral, and retinal disorders [9]. However, several investigations have focused on a specific organ system, raising concerns about the independence of these correlations from mean ambulatory blood pressure [10]. Nonetheless, disparate outcomes are attributable to a range of research populations, monitoring techniques, variability indices, treatment conditions, and definitions of target organ damage. The concurrent assessment of cardiac, renal, and retinal damage data is notably limited in South Asian hypertensive populations, where delayed diagnosis, variable treatment adherence, and a high prevalence of cardiovascular risk factors may amplify the clinical significance of blood pressure fluctuations [11]. This study aimed to assess the correlation between 24-hour blood pressure fluctuation and target organ damage in the cardiovascular, renal, and retinal systems in adults with essential hypertension. The objective was to ascertain if the amplitude of blood pressure variability is independently correlated with target organ involvement, considering mean ambulatory blood pressure and other conventional cardiovascular risk factors [12].

MATERIALS AND METHODS

The research was an analytical cross-sectional study carried out at the Department of Medicine at Frontier Medical College, Abbottabad, from February 2025 to January 2026. The study focused on adult patients with essential hypertension from the medical outpatient department, recruited by a non-probability sequential selection procedure, totalling 70 participants. The Institutional Research and Ethics Committee of Frontier Medical College, Abbottabad, accepted the study (FMC/IREC/2025/021). All participants executed informed consent forms before recruitment, and the confidentiality of personal and clinical information was upheld throughout the study.

Men and women aged 30–65 years who had been diagnosed with essential hypertension for at least six months were eligible. Hypertension was defined as an office pressure > 140mmHg and/or a diastolic pressure > 90mmHg or taking prescribed antihypertensive medication. Patients with new diagnosis and those who have been treated were both taken into account. If any participants were already on antihypertensive medications, they needed to be at an unchanged regimen for at least 4 weeks.

People were excluded if they had secondary hypertension, diabetes mellitus, ischaemic heart disease, previous myocardial infarction, heart failure, cardiomyopathy, clinically significant valvular disease, persistent arrhythmia or a history of stroke. Other exclusion criteria included chronic renal disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2), overt proteinuria, preexisting retinal disorders, glaucoma, retinal vascular occlusion, acute infection, chronic inflammatory disease, malignancy, pregnancy, and incomplete ambulatory blood pressure (BP) recording. To minimise the confounding effects of diabetic nephropathy and retinopathy, diabetes was specifically excluded when examining renal and retinal outcomes.

Demographic and clinical data were recorded on a structured data-collection form. These variables were added to the list: age, sex, smoking habit, years after the onset of hypertension, family history of cardiovascular disease, antihypertensive therapy, number of antihypertensive drugs, and self-reported adherence to antihypertensive drugs. Body weight was measured using a

calibrated digital scale, without shoes and light clothing. A wall mounted stadiometer was used to obtain height. BMI was defined as weight in kg / height in metres squared.

Office blood pressure measurements were made using a calibrated automated monitor following at least five minutes of quiet sitting. Smoking, caffeine and high intensity exercise were abstained from for 30 minutes preceding measurement. A cuff of an appropriate size was fitted to a supported upper arm at heart level. Three readings for the one-minute periods were taken and the average of the second and third readings was used for analysis.

All participants then had their blood pressure monitored for 24 hours using a validated oscillometric monitor placed on the non-dominant arm. Measurements were programmed at 30-minute intervals while awake and at 60-minute intervals during sleep. It was advised that participants should do their normal routine for the day but nothing out of the ordinary for exercise. They were also asked to maintain the monitored arm at rest during cuff inflation and to document waking and sleeping times, medication use, activity levels, symptoms and other events in a diary.

An ambulatory recording was considered valid if at least 70% of the measurements were technically valid, with at least 20 daytime and 7 nighttime measurements. A failed recording was re-monitored if it did not meet these criteria.

Mean 24-hour, daytime and nighttime systolic and diastolic pressure were calculated. The prespecified primary measure of short-term variability was the 24-hours average real variability of the systolic pressure. As supplementary indices standard deviation of both systolic and weighted values and coefficient of variation was also calculated. Average real variability was the average of the absolute difference between each pair of sequential valid systolic measurements. Standard deviation of the systolic blood pressure divided by the mean systolic blood pressure multiplied by 100 yielded the coefficient of variation.

The participants were then divided into high average real variability (ARV) and low ARV groups using the median of the ARV of the study population. Median value was used as cutoff point: values equal to or greater than the median was assigned to the high-variability group and values less than the median were assigned to the low-variability group. A nocturnal decrease in SBP of less than 10% from the daytime SBP was considered as a non-dipping pattern.

Fasting blood samples were taken for the estimation of plasma glucose, serum creatinine, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, sodium and potassium. The estimated glomerular filtration rate was calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equation. All biochemical analyses were performed in the institutional laboratory according to standard operating procedures.

Cardiac target-organ involvement was evaluated through transthoracic echocardiography. The examination was conducted by an experienced cardiologist who was blinded to the participant's ambulatory blood pressure findings. Recorded measurements included interventricular septal thickness, left ventricular posterior wall thickness, left ventricular internal dimensions, left atrial volume, transmitral inflow velocities, and tissue Doppler velocities.

Left ventricular mass was calculated using the Devereux formula and indexed to body surface area. Left ventricular hypertrophy was defined as a left ventricular mass index greater than 115 g/m² in men or greater than 95 g/m² in women. Diastolic function was assessed through an integrated evaluation of early and late transmitral filling velocities, the E/A ratio, septal and lateral early diastolic myocardial velocities, the mean E/e′ ratio, and left atrial volume index. Cardiac target-organ damage was considered present when left ventricular hypertrophy, left ventricular diastolic dysfunction, or both were identified.

Renal involvement was investigated using serum creatinine, estimated glomerular filtration rate, and urinary albumin-to-creatinine ratio. A first-morning midstream urine specimen was collected from each participant. When the initial albumin-to-creatinine ratio was elevated, a second sample was obtained within two weeks. Early renal target-organ damage was defined as persistent moderately increased albuminuria, represented by an albumin-to-creatinine ratio from 30 to less than 300 mg/g in two consecutive samples, together with an estimated glomerular filtration rate of at least 60 mL/min/1.73 m².

Retinal involvement was assessed through bilateral dilated fundus examination by an ophthalmologist who was unaware of the ambulatory blood pressure results. Both eyes were examined for diffuse or focal arteriolar narrowing, arteriovenous crossing changes, retinal haemorrhage, cotton-wool spots, hard exudates, and optic-disc swelling. Hypertensive retinal abnormalities were graded according to the Keith–Wagener–Barker system. Grade I or II hypertensive retinopathy in either eye was regarded as early retinal target-organ damage.

The primary outcome was the presence of early damage in at least one of the three evaluated organ systems. Secondary outcomes comprised cardiac, renal, and retinal involvement considered separately, as well as multiorgan damage affecting two or more systems. To reduce assessment bias, both the cardiologist and ophthalmologist remained blinded to blood pressure variability classification. Elevated urinary albumin excretion was verified with repeat testing to minimise the misclassification of temporary albuminuria.

Statistical analyses were performed using IBM SPSS Statistics, version 27.0. Continuous data were summarized as mean ± standard deviation or median (interquartile range) depending on the distribution of the data.

Categorical data were presented as frequency and percentage. Independent-samples t test or Mann–Whitney U test was used for continuous variables and chi-square test or Fisher exact test for categorical variables for comparing the different groups.

Pearson or Spearman correlation coefficients were computed as appropriate to evaluate the associations between average real variability of systolic blood pressure and retinopathy grade, urinary albumin-to-creatinine ratio and left ventricular mass index. Finally, multivariable logistic regression models were used to assess the independent association of elevated SBPV with cardiac, renal, retinal, composite and multiorgan damage. Covariates were age, sex, body mass index, smoking status, mean 24-hour systolic pressure, hypertension duration, antihypertensive medication use and nocturnal dipping status. Association was reported as adjusted odds ratio (OR) and 95% confidence interval (CI). Statistically significant results were those with a p-value< 0.05.

RESULTS

A total of 70 adult subjects having essential hypertension were analyzed. Their mean age was 51.5 ± 8.9 years; 38 participants (54.3%) were men and 32 (45.7%) were women. The median 24-hour real variability was used to classify participants into 2 groups of equal size (35 participants each).

There were no great differences in sex distribution, age, body mass index, smoking status, length of duration of hypertension, office blood pressure, or use of multiple antihypertensive agents. In contrast, mean 24-hour systolic pressure was higher among participants with high variability than among those with low variability (141.8 ± 10.3 vs 136.4 ± 9.6 mmHg; p=0.026). Mean 24-hour diastolic pressure did not differ significantly.

As anticipated from the grouping method, systolic average real variability, weighted standard deviation, and coefficient of variation were substantially greater in the high-variability category. A non-dipping nocturnal profile was also more common in this group, occurring in 20 of 35 participants (57.1%), compared with 10 of 35 participants (28.6%) in the low-variability group (p=0.016), as presented in Table 1.

Early target-organ involvement in at least one of the assessed systems was identified in 35 participants (50.0%). Cardiac abnormalities were present in 25 (35.7%), renal involvement in 20 (28.6%), and retinal changes in 16 (22.9%). Damage affecting two or more organ systems was observed in 12 participants (17.1%).

Cardiac structural and functional abnormalities were more frequent among participants with greater blood pressure variability. Mean left ventricular mass index was significantly higher in the high-variability group than in the low-variability group (109.6 ± 24.8 vs 94.8 ± 20.3 g/m²; p=0.008). Left ventricular hypertrophy was detected in 14 participants (40.0%) with high variability and six (17.1%) with low variability. Similarly, left ventricular diastolic dysfunction occurred in 16 (45.7%) and eight (22.9%) participants, respectively. Overall cardiac target-organ damage was therefore more common in the high-variability group (17 [48.6%] vs 8 [22.9%]; p=0.025).

Renal markers showed a comparable pattern. The mean urinary albumin-to-creatinine ratio was greater in participants with high variability than in those with low variability (38.6 ± 28.4 vs 21.7 ± 16.5 mg/g; p=0.004). Persistent moderately increased albuminuria was documented in 14 participants (40.0%) in the high-variability group and six (17.1%) in the low-variability group (p=0.034). Mean estimated glomerular filtration rate was also lower in the high-variability group, although no participant had a value below 60 mL/min/1.73 m².

Early hypertensive retinopathy was identified in 12 participants (34.3%) with high blood pressure variability compared with four (11.4%) with low variability (p=0.023). The prevalence of damage in any evaluated organ system was 68.6% in the high-variability group and 31.4% in the low-variability group. Involvement of multiple organ systems was likewise substantially more frequent among participants with greater systolic blood pressure variability, as summarised in Table 2.

Twenty-four-hour systolic average real variability showed moderate positive correlations with left ventricular mass index (r=0.38; p=0.001) and urinary albumin-to-creatinine ratio (r=0.41; p<0.001). A significant relationship was also observed between systolic average real variability and increasing severity of hypertensive retinopathy (Spearman's ρ=0.32; p=0.007). By comparison, mean 24-hour systolic blood pressure demonstrated weaker correlations with left ventricular mass index (r=0.27; p=0.024) and urinary albumin-to-creatinine ratio (r=0.25; p=0.036).

Multivariable logistic regression was performed to determine whether elevated systolic blood pressure variability independently predicted early target-organ damage. Given the number of outcome events, parsimonious models were adjusted for age, sex, duration of hypertension, mean 24-hour systolic pressure, and nocturnal dipping status. After adjustment, high systolic variability remained independently associated with cardiac, renal, retinal, composite, and multiorgan involvement.

Participants in the high-variability group had 2.84-fold greater adjusted odds of cardiac target-organ damage and 3.12-fold greater odds of renal involvement. The adjusted odds of early hypertensive retinopathy were 3.76 times higher in those with marked systolic variability. High variability was also strongly related to the composite outcome, with an adjusted odds ratio of 4.21 for damage in at least one organ system. Furthermore, it independently predicted involvement of two or more organ systems, with an adjusted odds ratio of 5.62, as presented in Table 3.

The receiver operating characteristic curve study indicated that the 24-hour systolic average real variability has enough discriminating capacity for identifying individuals with any target organ impairment. The area beneath the curve was 0.76, accompanied with a 95% confidence range of 0.65–0.87 and a p-value less than 0.001. The average true variability threshold of SBP for detecting composite target organ damage, with a sensitivity of 71.4% and specificity of 68.6%, was 10.8 mmHg.

Table 1: Demographic, clinical, and ambulatory blood pressure attributes of the participants

Variable	High variability, n=35	Low variability, n=35	p-value
Age, years	52.8 ± 8.7	50.1 ± 9.0	0.206
Male sex	20 (57.1%)	18 (51.4%)	0.631
Female sex	15 (42.9%)	17 (48.6%)	0.631
Body mass index, kg/m²	28.5 ± 3.4	27.9 ± 3.2	0.450
Current smoking	8 (22.9%)	6 (17.1%)	0.550
Duration of hypertension, years	8.1 ± 4.3	6.9 ± 4.0	0.231
Office systolic blood pressure, mmHg	150.2 ± 14.3	146.8 ± 13.6	0.312
Office diastolic blood pressure, mmHg	92.3 ± 8.4	90.7 ± 8.0	0.417
Mean 24-hour systolic blood pressure, mmHg	141.8 ± 10.3	136.4 ± 9.6	0.026
Mean 24-hour diastolic blood pressure, mmHg	84.4 ± 7.0	82.7 ± 6.8	0.306
Systolic average real variability, mmHg	13.9 ± 2.0	8.4 ± 1.4	<0.001
Systolic weighted standard deviation, mmHg	14.8 ± 2.7	10.1 ± 2.1	<0.001
Systolic coefficient of variation, %	11.3 ± 1.9	7.9 ± 1.5	<0.001
Non-dipping pattern	20 (57.1%)	10 (28.6%)	0.016
Use of at least two antihypertensive drugs	21 (60.0%)	18 (51.4%)	0.470

Table 2: Cardiac, renal, and retinal target organ findings according to blood pressure variability

Target organ finding	High variability, n=35	Low variability, n=35	p-value
Left ventricular mass index, g/m²	109.6 ± 24.8	94.8 ± 20.3	0.008
Left ventricular hypertrophy	14 (40.0%)	6 (17.1%)	0.034
Left ventricular diastolic dysfunction	16 (45.7%)	8 (22.9%)	0.044
Any cardiac target organ damage	17 (48.6%)	8 (22.9%)	0.025
Urinary albumin-to-creatinine ratio, mg/g	38.6 ± 28.4	21.7 ± 16.5	0.004
Estimated glomerular filtration rate, mL/min/1.73 m²	83.4 ± 13.1	89.6 ± 12.7	0.048
Persistent moderately increased albuminuria	14 (40.0%)	6 (17.1%)	0.034
Early hypertensive retinopathy	12 (34.3%)	4 (11.4%)	0.023
Any target organ damage	24 (68.6%)	11 (31.4%)	0.002
Damage involving at least two systems	10 (28.6%)	2 (5.7%)	0.011

Table 3: Multivariable association between high systolic blood pressure variability and early target organ damage

Outcome	Adjusted odds ratio	95% confidence interval	p-value
Cardiac target organ damage	2.84	1.01–7.98	0.048
Renal target organ damage	3.12	1.02–9.52	0.046
Retinal target organ damage	3.76	1.08–13.06	0.037
Any target organ damage	4.21	1.54–11.50	0.005
Damage involving at least two systems	5.62	1.11–28.40	0.037

DISCUSSION

This investigation revealed a strong correlation between heightened short-term systolic blood pressure fluctuation and early impairment of cardiac, renal, and retinal target organs in persons with essential hypertension [1]. The high-variability group had increased left ventricular mass, elevated urine albumin excretion, reduced eGFR, and a greater frequency of early hypertensive retinopathy in comparison to the low-variability group. The correlation between elevated SBP variability and organ damage was unaffected by age, sex, hypertension duration, average 24-hour SBP, and nocturnal dipping status. The findings suggest that the variability of ambulatory blood pressure may provide clinically relevant information beyond the mean ambulatory blood pressure [2].

Fifty percent of the study sample had early target organ damage in at least one system. The predominant abnormality seen was cardiac involvement, followed by renal and retinal damage [3]. The anomalies identified across several organs indicate that hypertension impacts haemodynamics and microvasculature in a generalised manner, rather than only causing structural alterations in specific organs. Moreover, both composite and multiorgan damage were much more common among those exhibiting high blood pressure fluctuation, indicating that this group may represent a higher risk subset of hypertensives [4].

The correlation between systolic blood pressure variability and cardiac damage aligns with existing results, which suggest that elevated ambulatory blood pressure variability is linked to left ventricular hypertrophy and further subclinical cardiac injury [5]. Subjects in the high variability group had a significant elevation in left ventricular mass indices and a greater incidence of left ventricular hypertrophy and diastolic dysfunction. Persistent fluctuations in systolic pressure can result in

sporadic changes in left ventricular (LV) afterload, inducing cardiomyocyte hypertrophy, LV wall remodelling, interstitial fibrosis, and compromised relaxation. Prior studies have demonstrated a correlation between blood pressure variability and subclinical cardiac injury, which may differ based on the measurement method of blood pressure variability, treatment status, and adjustments for mean ambulatory blood pressure [6].

Elevated blood pressure fluctuation was substantially correlated with renal target organ damage [7]. The urine albumin-to-creatinine ratio and the probability of sustained moderately elevated albuminuria were greater in those exhibiting considerable variability. Renal microcirculation depends on autoregulatory mechanisms to sustain glomerular perfusion at a generally stable level [8-10]. Nevertheless, frequent or abrupt fluctuations in pressure might surpass the capacity for autoregulation, resulting in excessive pressure inside the glomerular capillaries and heightened endothelial permeability [11]. Albuminuria may occur before a clinically substantial decline in filtration performance and can serve as an indicator of renal and systemic vascular injury. Short-term blood pressure variability and visit-to-visit blood pressure variability have been associated with diminished renal function, albuminuria, and an increased risk of chronic kidney disease.

The incidence of early hypertensive retinopathy was about three times greater in the high variability group compared to the low [12]. The retinal circulation facilitates the clinical assessment of tiny vessels and may provide insight into analogous microvascular alterations in other organs. Frequent fluctuations in pressure may contribute to arteriolar vasoconstriction, endothelial dysfunction, vascular wall thickening, and anomalies in arteriovenous crossing. Additional evidence for a graded correlation between blood pressure variability and retinal vascular damage is the positive link between systolic average real variability and the severity of retinopathy. The retinal observations further substantiate the overall outcomes, indicating that the association with blood pressure variability extended beyond echocardiographic or laboratory data [13,14].

The high variability group exhibited an elevated 24-hour mean systolic blood pressure, which correlated with certain indicators of target organ damage. However, the associations of high variability with cardiac, renal, retinal, or composite outcomes remained significant even after including the mean ambulatory systolic blood pressure into the regression models. This suggests that BPV and MBP may be interrelated yet represent distinct facets of hemodynamic strain [9-11]. The mean blood pressure reflects chronic exposure, but the variability signifies the frequency and magnitude of fluctuations around the mean. The average actual variability, considering the sequence of measurements, may be beneficial, as may the computation of the standard deviation of the readings; however, the latter is contingent upon the disparity between the mean daytime pressure and the mean nocturnal pressure [1,6].

Significant association was seen between high blood pressure variability and a non-dipping pattern [10]. A reduced decline in nocturnal values may result from an autonomic nervous system imbalance, sleep disruptions, heightened sympathetic activity, arterial stiffness, or inadequate adherence to nighttime medicines [5]. Irregular nocturnal blood pressure and heightened blood pressure variability may be linked to prolonged and/or intermittent organ exposure to haemodynamic stress. Nonetheless, the correlation with target organ damage persisted despite the existence of nocturnal dipping status, indicating that the relationship between high variability and target organ damage was not entirely elucidated by anomalous nocturnal blood pressure patterns [11].

Receiver operating characteristic study indicated that the discrimination of average actual variability of systolic blood pressure for identifying any target organ damage was satisfactory [12]. The found threshold may assist in recognising hypertensive individuals requiring further study; nevertheless, it should not be regarded as a definitive clinical standard. Blood pressure variability is influenced by the variability of the ambulatory device, the time between readings, sleep and wake cycles, physical activity levels, emotional stress, the timing of medication administration, and the mathematical index employed. Consequently, there is a necessity for externally verified thresholds and standardised monitoring protocols before employing variability as an independent treatment objective. Recent studies emphasise the clinical significance of blood pressure variability and the absence of comprehensive standardisation in its measurement and interpretation for therapeutic interventions [13].

The findings have clinical significance for essential hypertension. Patients with comparable office or mean ambulatory blood pressure (MAP) may have differing levels of short-term blood pressure fluctuation, resulting in diverse degrees of subclinical organ involvement [14]. Average actual variability, weighted standard deviation, nocturnal blood pressure, and dipping status may therefore be regularly employed in the analysis of ambulatory recordings, alongside mean data. A meticulous assessment of treatment adherence, drug duration of action, salt consumption, sleep quality, autonomic system impacts, and indicators of early organ damage may be necessary in individuals exhibiting heightened variability. However, the present findings do not demonstrate that only reducing variability through pharmacological means can rectify organ damage [15].

This study had several strengths. All three indices of cardiac, renal, and retinal damage were assessed concurrently, hence achieving a more thorough evaluation of hypertension-induced organ damage. Numerous variability indices were calculated from the ambulatory monitoring, and cardiac and retinal assessments were

conducted by observers unaware of the variability categorisation. The probability of erroneously categorising transient albuminuria as renal impairment was reduced by doing several urine albumin tests [16].

The results should be interpreted within the framework of some restrictions, however. The cross-sectional approach does not establish the temporal sequence between blood pressure fluctuation and target organ damage, hence failing to demonstrate causation [8-12]. The sample size was rather limited, derived consecutively from a single centre, hence constraining generalizability. A single 24-hour blood pressure measurement was utilised to evaluate blood pressure variability, perhaps influenced by activity or sleep on the day of the assessment [13,15,17]. Treatment adherence, dietary salt consumption, sleep apnea, psychosocial stress, and vascular stiffness were not assessed objectively. The outcomes were constrained, and parsimonious regression models were employed for the retinal and multiorgan damage outcomes, as indicated by the broad confidence interval. Larger prospective, multicenter trials with regular ambulatory monitoring are necessary to determine if increased variability correlates with organ damage and if blood pressure stabilisation leads to a reduction in eventual cardiovascular and renal risk [18-20].

CONCLUSION

Elevated 24-hour systolic blood pressure fluctuation was independently linked to early impairment in cardiac, renal, and retinal target organs in persons with essential hypertension. Even after adjusting for average ambulatory systolic blood pressure and nocturnal dipping status, individuals exhibiting significant variability were more prone to composite and multiorgan involvement, increased instances of albuminuria, a higher prevalence of hypertensive retinopathy, and elevated left ventricular mass. An assessment of blood pressure variability during ambulatory monitoring may complement traditional average blood pressure measurements and assist in identifying hypertensive individuals with early subclinical organ damage. Subsequent studies should validate clinically significant thresholds and ascertain if a decrease in blood pressure variability halts the progression of hypertension-related organ damage.

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Authors' Contributions: R.M. conceived and designed the study, recruited participants, and prepared the manuscript. F.T. contributed to ambulatory blood pressure monitoring, cardiovascular assessment, data interpretation, and manuscript revision. N.U.K. contributed to biochemical analysis, data compilation, statistical interpretation, and supervision. All authors reviewed and approved the final manuscript.

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Data Availability: The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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