Short term blood pressure variability and target organ damage—an observational study of ambulatory blood pressure monitoring in a clinic setting in South India

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Article

Keywords: Hypertension, Blood pressure variability, Ambulatory blood pressure monitoring, Target Organ Damage

DOI: https://doi.org/10.21203/rs.3.rs-191830/v1

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Abstract

High blood pressure (BP) is an important risk factor for Cardiovascular diseases. The association of short term BP Variability (BPV) with target organ damage (TOD) is not clearly established. We conducted this observational study to evaluate the degree of concordance between Office Blood Pressure monitoring (OBPM) and Ambulatory Blood Pressure Monitoring (ABPM) and to study the effect of short term BPV on TOD. Patients attending clinics of the authors between January 2018 and August 2019 were enrolled. Their BP status was determined by OBPM and ABPM and the degree of concordance analysed. ABPM parameters between those with TOD and without TOD were compared using appropriate statistical measures. Data from 968 subjects (males 61.5%, mean age 59.39 ± 14.86 years) were analysed. Masked hypertension and white coat hypertension were seen in 138 (14.3%) and 50 participants (5.2%) respectively. There was moderate Concordance between ABPM and OBPM readings (Cohen's kappa = 0.692). There were 530 (54.8%) non dippers and 189 (19.5%) reverse dippers. High morning surge (MS) was seen in 193 (19.9%) and TOD in 225 (23.2%). Percent time elevation (PTE) of systolic BP (P = 0.004, OR 1.009, 95% CI 1.003, 1.016) and diastolic BP in active period (p = 0.034, OR 1.009, CI 1.001, 1.017) and PTE of diastolic BP in passive period (p = 0.006, OR 1.011, 95% CI 1.003, 1.018), as assessed by ABPM were significantly associated with TOD. Dipping status, diurnal index and MS were not associated with TOD. ABPM is a useful tool for diagnosis and accurate categorisation of hypertension. Analysis of ABPM parameters helps to identify the patients with significant BP load who are at risk of developing TOD.

Introduction

High blood pressure (BP) is an important modifiable risk factor for Cardiovascular diseases (CVD) and accounts for more than 12.8% of deaths globally. An estimated 1.39 billion adult population worldwide have high BP and the prevalence is increasing in low and middle income countries. High systolic BP (SBP) is found to be the leading risk factor for Disability adjusted life years (DALY) in adults aged 50 years and above. In India CVD is a major cause of mortality accounting for nearly one fourth of all deaths and Hypertension (HTN) contributes significantly to both cardiovascular and cerebrovascular deaths. The effects of high BP levels on target organ damage (TOD) and the beneficial effects of antihypertensive therapy has been well established. Blood pressure in an individual is not constant and varies significantly in the same individual at different times of the day and between days. These BP variability (BPV) may be occurring over short term like minutes to days or long term over days to months. Though the most common method of monitoring BP in an individual is office BP measurement (OBPM), the use of ambulatory blood pressure monitoring (ABPM) which measures BP over 24 hours or more is gaining importance in recognition and management of HTN. Evidence from many preclinical and clinical studies have clearly shown the role of long term BPV in cardiovascular complications of HTN. ABPM can help in detecting HTN in individuals with normal OBPM as in masked hypertension (MH) and also to exclude people who have higher BP only in OBPM but normal BP during outside clinic settings as in White Coat hypertension (WCH). Studies have recognised that TOD is associated with some circadian changes of BP or BP load during the day rather than isolated BP elevation. ABPM has been shown to be a strong predictor of all-cause and CV mortality than OBPM and many clinical practice guidelines like National Institute for Health and Care (NICE), Joint National Council (JNC) and European Society of Cardiology (ESC) have recommended the use of ABPM in clinical practice. In this background we aimed to analyse the BP patterns by ABPM and study its association with TOD.

Aims and Objectives of the study:
This observational study was undertaken to evaluate the degree of concordance between ABPM and OBPM and to study the short term BP variability in the hypertensive and normotensive participants. We also aimed to determine the association between BPV and target organ damage (TOD) status of the participants.

**Materials And Methods**

**Study setting and participants:**

This observational study was conducted in Shivamogga city, Karnataka state, India. Patients visiting clinics of the authors (SBH, AS) for the regular medical management between the period of January 2018 to August 2019 were enrolled as study participants.

**Inclusion and exclusion criteria:**

Participants aged 18 years and above were included in the study after written informed consent. Patients with any hemodynamic instability and those who did not tolerate ABPM were excluded from the study.

**Data Collection:**

Patient details such as age, gender, habits like smoking, tobacco or alcohol consumption were collected. History of diabetes, hypertension and their duration, presence of other co morbid conditions such as cardiovascular disease and stroke were elicited. BP, height and weight were recorded and Body mass index (BMI) was calculated. Electrocardiography (ECG) and Echocardiography were done in all participants while Carotid Doppler, CT scan or MRI brain were done in selected cases based on clinical requirements.

**Measurement of BP by OBPM and ABPM:**

Office BP was recorded using a calibrated mercury sphygmomanometer (Diamond™, Pune, India) with the patient in sitting position. Average of three readings taken five minutes apart was considered to be the office BP (OBPM). ABPM was done using the ABPM 05 machine (Meditech™, Hungary) which measures BP by oscillometry method and analysed using Easy ABPM software. During their visit to the clinic, the routine assessments along with OBPM, were performed by their treating physician. ABPM was recorded on all subjects enrolled in the study. Their medications were not modified during this period of the study.

The ABPM included BP monitoring for a 24 hour period, which was divided into active (day/awake time) and passive (night/sleep time) period. The measurement interval times were programmed to every 15 minutes at day time (active period) and every 30 minutes at night time (passive period). The ABPM report provided the BP data recorded during 24 hrs, active and passive period. The report also provided the details of percent time elevation (PTE), hyperbaric impact (HBI), diurnal index and morning surge.

**Definition of relevant terms:**

All subjects with either history of HTN or on antihypertensive medications or systolic BP > 140 mmHg and or diastolic BP > 90 mm Hg on office BP measurements were considered as hypertensives. Based on the presence or absence of high BP recordings on OBPM, subjects were divided into two groups-Group 1 with HTN and Group 2- without HTN.

Study subjects were classified into four categories based on their OBPM and ABPM values as per European Society Hypertension Guidelines. The threshold values for OBPM and ABPM are as follows; SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg on OBPM, 24-h SBP ≥ 130 and/or DBP ≥ 80 mmHg on ABPM recording.
(1) Normotension: normal OBPM and normal ABPM. This could indicate either a nonhypertensive person or a hypertensive whose BP is well controlled.

(2) Persistent Hypertension (PH): elevated OBPM and elevated ABPM

(3) White-coat hypertension (WCH): elevated OBPM and normal ABPM,

(4) Masked hypertension (MH): normal OBPM and elevated ABPM.

The short-term BPV refers to the BP changes that occur within a day (24 hours), and is characterized by normal circadian variations, such as nocturnal BP dipping, nocturnal hypertension and morning BP surge.

- Morning Surge (MS): defined as the morning BP (BP 2-hour after rising) minus the sleep BP (the average BP during sleep).
- Nocturnal Dipping: is defined as the difference between the mean systolic pressure in the day and mean systolic pressure during the night, expressed as a percentage of the day time mean.

These were further categorised into the following category based on their dipping patterns:

- Dippers: individuals whose BP falls in the range of 10% – 20%.
- Extreme Dippers: those who dip > 20%.
- Non-Dippers: those who exhibit < 10% dip in BP.
- Reverse Dippers: on the other hand, those who have an increase in nocturnal BP, instead of a fall.
- Diurnal index defined as ratio of the difference between daytime SBP and night time SBP to daytime SBP expressed as percentage
- Percent time elevation (PTE) is the percentage of time of 24 hours during which BP values are considered to be higher than normal.
- Hyperbaric index (HBI) is a measure of the total load exerted on the arterial wall and is calculated as the total area (within one cycle) of any given patient's BP above the threshold.

Obese subjects were classified according to obesity grading - Grade I having BMI of 25-29.9 kg/m2, Grade II having a BMI of 30-39.9 kg/m2 and Grade III having BMI greater than or equal to 40 kg/m2 while those with BMI 18–25 kg/m2 were considered as normal BMI

**Target organ damage (TOD)** was defined as presence of any of these organ damages: cardiovascular disease or cerebrovascular disease or renal diseases. Cardiovascular diseases could be left ventricular hypertrophy (LVH) or ischemic heart diseases such as angina, or myocardial infarction (MI) as determined by ECG/echocardiography. Cerebrovascular diseases were defined as transient ischemic attacks (TIA) or stroke as determined by clinical examination and radiologic abnormalities. CKD was defined as estimated glomerular filtration rate < 60ml / min/1.73 sqm.

**Human rights protection:**

Study protocol was approved by an independent accredited ethics committee. The subjects were enrolled after written informed consent. They were given sufficient time and information regarding the study protocol. Their apprehensions were suitably addressed and they participated voluntarily without any force by the investigators. They were also given the option to withdraw themselves anytime during the study.
**Statistical Analysis:**
Main demographic and clinical data were summarized by calculating the mean (± SD) in case of continuous variables and the absolute (n) and relative (%) frequency in case of categorical variables. Association of BPV parameters with TOD was assessed by One-way ANOVA in case of continuous variables and chi square test in case of categorical variables. P value < 0.05 was considered as statistically significant. Parameters which were found to be associated with TOD having P value < 0.1 were used as independent variables in a multiple logistic regression to determine significant associations with TOD as the dependent variable. All statistical analysis was done using SPSS statistical software (SPSS version 16, SPSS Inc., Chicago, IL, USA).

**Results**
A total of 1064 subjects were enrolled in the study. Data of 968 (90.9%) subjects was considered as evaluable with successful readings (readings having >70% of 24 hour ABPM recordings) and was included in the study analysis and 96 subjects were excluded because of incomplete recordings. This cohort of 968 subjects included 656 patients with known hypertension on treatment and 312 (32.2%) subjects without history of HTN. On evaluation by OBPM 735 (75.9%) subjects had HTN (Group 1) Group I comprised of with HTN on OBPM and the remaining 233 (24.1%) subjects (Group 2), who had no HTN.

**Subject Characteristics:** Baseline characteristics of the study participants is shown in Table 1. The mean age of the subjects was 59.39 ± 14.86 years with an age range of 18-96 years. There were 595 (61.5%) males and 373 (38.5%) females. More than 80 percent of the subjects were in the age group of 40-79 years with nearly half of the participants in the age group of 60-79 years. There were 528 (54.54%) subjects with BMI more than 25.

**BP measurements and Hypertension categories:** Mean SBP and DBP by OBPM was 142.5 (±26.7) and 83.1 (±16.2) mm Hg respectively. The highest BP (reading was 290/190 mm Hg) and the least was 90/60 mm Hg. Mean 24 hr SBP and DBP on ABPM was 135.9 (±21.6) and 78.2 (±12.8) mm Hg respectively. 24-hr mean SBP ranged between 89 and 218 mmHg while mean DBP ranged between 45 and 130 mm Hg respectively (Table 2). Based on OBPM and ABPM values patients were classified into four categories-persistent hypertension (PH), normotension, MH and WCH as described earlier (Figure 1). MH was seen in 138 (14.3%) and WCH was seen in 50 (5.2%) subjects. With OBPM 503 (52%) subjects were classified as hypertensives, after ABPM additional 91 subjects were diagnosed to have HTN taking the total number of hypertensives to 594 (61.1%) (Figure 2).

**Circadian variations and BP variability:** The means of ABPM parameters and proportion of circadian variations were analysed. In all, 232 (24.0%) were dippers while 530 (54.8%) were non dippers, 17 (1.8%) were extreme dippers and reverse dipping was seen in 189 (19.5%) patients. High morning surge (MS) was seen in 20% of patients. Mean diurnal index was 5.2 (SD 7.21) with the value being highest in WCH and lowest in MH.

**Target organ damage (TOD) and ABPM parameters:**
There were 225 (23.2%) patients with TOD, cardiovascular diseases were seen in 69 (7.1%) patients, Cerebrovascular diseases in 185 (19.11%) and CKD in 18 (1.9%) patients. TOD was found in a higher proportion of patients with MH and PH than with normotension or WCH (Figure 3). When compared to normotension, MH was associated with TOD (OR 2.41, 95% CI 1.51, 4.07, P < 0.001). Similarly PH was also associated with increased risk of TOD (OR 2.98, 95% CI 2.04, 4.36, P < 0.001). WCH was not significantly associated with TOD (OR 1.10, 95% CI 0.46, 2.61, P = 0.827). The means of all ABPM parameters namely BPV, HBI and PTE were significantly higher in subjects with TOD. The association of BPV, dipping status and MS with presence of TOD was examined (Table 3). Dipping status was not associated with TOD. MS, BPV, PTE SBP and DBP in active phase, HBI SBP and HBI DBP in active phase were significantly associated
with TOD on multivariate analysis. However when logistic regression was performed the only significant predictors of TOD were PTE SBP in active phase and PTE DBP in passive phase (table 4).

**Discussion**

In this clinic-based study of ABPM, we demonstrated that after ABPM at least 10% more people were identified as hypertensives when compared to OBPM measurements. We found MH in 14.3% and WCH in 5.2% participants. The detection of MH and WCH is an important diagnostic utility of ABPM. If only OBPM was considered for diagnosis as is routine in most clinic settings in India these 19% individuals would have been wrongly diagnosed as normotensives or hypertensives. ABPM parameters were found to be significantly different in patients with TOD than those without.

Prevalence of MH is estimated to be 10–15% of the general population. MH is a clinical entity that is gaining importance in recent times. It is associated with adverse CV outcomes similar to that of persistent HTN. In a recent metaanalysis with pooled population of 7961 subjects the overall adjusted HR was 2.09 (1.55,2.8, P = 0.001) for MH versus normotension and 2.59 (2.0,2.35, P = 0.001) for sustained HTN versus normotension. In our study too, we found MH to be a predictor of TOD with all ABPM parameters elevated when compared to normotension group.

Prevalence of WCH is estimated to be 9–16% in population-based studies. Our study recorded WCH in 5% subjects and the low prevalence could be because this was not a population-based study and the number of sustained HTN patients were higher. In India-ABPM study, a large clinic-based study involving 27472 subjects, MH and WCH were found in 19.3% and 12% respectively. Though our study population was comparable to India-ABPM, the differences in prevalence may be due to the smaller sample size in our study. CV morbidity was found to be lower in WCH than sustained HTN and is said to be on par with that in normotensives in many previous studies. Several newer studies have however contradicted this view and found greater risk of organ damage even in WCH. In present study though OR for TOD was higher than in normotensives it was not statistically significant.

ABPM is a useful tool to detect short term variability of BP and diurnal variability which are known to be responsible for several long term effects of HTN. Blunted nocturnal dipping is more common and more severe in patients with left ventricular hypertrophy (LVH) and ventricular arrhythmia. In the PAMELA study a 10 mm Hg increase in night time SBP was associated with much higher increase in CV mortality than a 10 mm Hg increase in daytime SBP. Non dipper status is also found to be associated with reduced brain matter volume, steeper decline in cognitive function and silent cerebrovascular disease. Similar association with non-dipping has been found in patients with renal dysfunction too. However, we did not find any significant association of dipping status with the presence of TOD. However, when sub analysis of BP categories was done, we noted that the blunted nocturnal dipping and reverse dipping was more prominent in PH and MH categories. We included only severe forms of TOD and the milder and subclinical forms of TOD were not assessed. This may probably explain the lack of association between dipping status and TOD in the present study. In ABODH study which evaluated the association of subclinical and clinical parameters of TOD with dipping/non-dipping status in a hypertensive population showed no relationship was found between the markers of organ damage and nocturnal BP fall. There are pointers to suggest that the absolute value of nocturnal BP (< 120/70 mm Hg) may be more organ protective than the dipping itself. In addition to non-dipping, another important circadian variation in BP is MS. High MS is attributed to neurohumoral alterations including activation of sympathetic nervous system and catecholamines on waking. Several studies have shown the association of MS with cardiovascular events and increased risk of cerebral haemorrhage. Incidences of coronary events and ischemic stroke are higher in the early morning period probably due to morning rise in BP.
In our study too we observed significant MS in PH and MH in comparison to normotensives. However, we did not find significant association of MS with TOD after adjusting for all other variables.

We also looked at several ABPM parameters which are not routinely applied in clinical settings like PTE and HBI. HBI is an indicator of BP load and is defined as the area encircled by polygonal line of ambulatory BP and the boundary line of HTN. HBI judges HTN by combined multiple BP measurements and time based on BP variability. HBI has been examined in few studies in hypertension and diabetes complications and also as a predictor of pregnancy induced hypertension. CKD-JAC, a Japanese study which examined the effect of HBI on kidney function suggested that HBI might be a sensitive indicator of BP load on kidney. We found that mean PTE and mean HBI in both active and passive period were significantly higher in PH and MH than in normotensives. However, in our study PTE in the active period, both in systolic and diastolic phase and PTE in the passive period in diastolic phase was associated with TOD after adjusting for all other variables. Similar correlation has been noted by Cui et al where there was negative correlation between PTE and ejection fraction.

The study has several strengths. Nearly a thousand patients were enrolled in this study from a single centre. Around 300 non HTN subjects were also included and this allowed us to document the range of circadian BP variations in these subjects and note the magnitude of difference in ABPM parameters between hypertensives and non hypertensives. Several ABPM parameters not routinely evaluated in other studies such as HBI and PTE were also examined in our study. However, there are a few limitations to this study. We defined TOD based on only a few major markers of organ involvement which would have underestimated the presence of TOD in the study population. Microalbuminuria and urinary albumin excretion rate were not done and hence CKD may have been underdiagnosed. We also did not look for peripheral vascular disease and retinopathy in all participants. The preponderance of cardiac and neurological patients in this study centre could have resulted in selection bias while enrolling study participants.

Conclusions

In this observational study on the utility of ABPM in a clinic setting we could demonstrate that diagnosis of MH and WCH is missed in routine office measurements of BP and that ABPM is a useful tool to identify patients at higher risk of TOD. The study showed that non dipping status was common in PH and MH than normotensives. The dipping status was not associated with TOD in this study, but PTE was significantly associated with TOD in hypertensive population. Controlled HTN as detected by normal OBPM in routine clinic visits may not always indicate adequate control as these patients may have significant BPV on ABPM which puts them at higher risk for TOD. It is important to perform ABPM on all hypertensive patients to identify these patients which could help in educating them about the need for better control and to modify therapy to suit their needs and to detect MH in people at risk of hypertension.
Summary

What is already known about this topic:
- ABPM is a useful tool in evaluation of hypertensive patients
- ABPM is useful in detecting Masked Hypertension and White Coat Hypertension
- It helps in knowing dipping status of hypertensive patients and non-dipping is associated with higher CV mortality

What this study adds
- Demonstration of substantial differences in HBI and BPV between hypertensives and non-hypertensives individuals which may predispose to higher risk of TOD
- Masked hypertension is significantly associated with TOD
- HBI and PTE can be useful additional parameters to assess the burden of HTN and risk of TOD

Declarations

Source of funding:
Nil

Conflict of interests:
The authors declare that they have no conflict of interest

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Tables
| Characteristics          | Total cohort number(%) | Group 1 HTN by OBPM number (%) | Group 2 Non HTN by OBPM number (%) | P value |
|--------------------------|------------------------|-------------------------------|----------------------------------|---------|
|                         | n=968                  |                               |                                  |         |
| Number of HTN by OBPM    |                        |                               |                                  |         |
|                         | 735 (75.90%)           | 233 (24.1%)                   |                                  |         |
| Age Mean (SD) years     | 59.39(14.69)           | 61.37(13.08)                  | 53.12 (17.52)                   | < 0.001 |
| <39 years               | 97(10.02)              | 43(5.9)                       | 54(23.2)                        | <0.001  |
| 40-59 years             | 339(35.02)             | 259(35.2)                     | 80(34.3)                        |         |
| 60-79 years             | 467(48.2)              | 379(51.6)                     | 88(37.8)                        |         |
| >80 years               | 65(6.7)                | 54(7.3)                       | 11(4.7)                         |         |
| Gender                  |                        |                               |                                  | 0.204   |
| Male                    | 595(61.5)              | 460(62.6)                     | 135(57.9)                       |         |
| Female                  | 373(38.5)              | 275(37.4)                     | 98(42.1)                        |         |
| Smokers                 | 77(8.0)                | 58(7.9)                       | 19(8.2)                         | 0.897   |
| Alcohol users           | 46(4.8)                | 39(5.3)                       | 7(3.0)                          | 0.15    |
| Tobacco users           | 15(1.5)                | 10(1.4)                       | 5(2.1)                          | 0.398   |
| Co morbidities          |                        |                               |                                  |         |
| Diabetes                | 397(41.0)              | 339(46.1)                     | 58(24.9)                        | <0.001  |
| IHD                     | 70 (7.23)              | 60(8.16)                      | 10(4.29)                        | <0.001  |
| Stroke                  | 222(22.9)              | 203(27.6)                     | 19(8.2)                         | <0.001  |
| Hypercholesterolemia    | 237(24.5)              | 207(28.2)                     | 30 (12.9)                       | <0.001  |
| CKD                     | 18(1.9)                | 15(2.0)                       | 3(1.3)                          | 0.458   |
| Obesity                 | 528(54.54)             |                               |                                  |         |
| Grade I                 | 350(36.15)             | 284(38.6)                     | 66(28.20)                       |         |
| Grade II                | 163(16.8)              | 137(18.6)                     | 26(11.2)                        | <0.001  |
| Grade III               | 15(1.55)               | 11(1.5)                       | 4(1.7)                          |         |
Abbreviations
OBPM-Office blood pressure measurements; SD-standard deviation
HTN- Hypertension ;IHD- Ischemic heart disease ;CKD- Chronic kidney disease

P <0.05 significant ,values highlighted in bold

Table 2 Showing ABPM Parameters

| Parameter       | 24 hr Mean | 24 hr Mean SD | Active Phase Mean | Active Phase SD | Passive Phase Mean | Passive Phase SD |
|-----------------|------------|---------------|------------------|-----------------|--------------------|------------------|
| 24 hr Mean SBP  | 135.93     | 21.6          | 138.37           | 21.86           | 131.11             | 22.75            |
| 24 hr Mean DBP  | 78.23      | 12.83         | 80.83            | 25.43           | 74.53              | 13.25            |
| PTE SBP         | 53.86      | 35.28         | 50.24            | 36.64           | 61.29              | 36.38            |
| PTE DBP         | 37.28      | 32.17         | 34.09            | 32.91           | 43.74              | 35.15            |
| HBI SBP         | 316.81     | 359.18        | 286.38           | 352.5           | 386.85             | 421.21           |
| HBI DBP         | 117.8      | 169.71        | 107.39           | 170.71          | 143.58             | 196.53           |
| Morning surge   | 15.14      | 12.26         |                  |                 |                    |                  |
| Diurnal Index   | 5.21       | 7.11          |                  |                 |                    |                  |

SD Standard deviation

SBP- Systolic blood pressure

DBP- Diastolic blood pressure

PTE SBP- Percent time elevation Systolic Blood pressure
PTE DBP- Percent time elevation diastolic blood pressure
HBI SBP - Hyperbaric index Systolic blood pressure
HBI DBP- Hyperbaric index Diastolic blood pressure
ABPM- Ambulatory blood pressure monitoring

Table 3 Association of ABPM parameters with TOD
| Parameter | TOD Present N(%) | TODAbsent N(%) | P value | OR | 95% CI | Parameter | Mean Value TOD Present | Mean Value No TOD | P value |
|-----------|------------------|---------------|---------|----|--------|-----------|-----------------------|-----------------|--------|
| BPV       | 225 (23.2)       | 743 (76.8)    | Univariate analysis - categorical variables |
|          |                  |               |         |    |        | BPV       | 15.1                 | 13.8           | .615   |
| Surge     | 61 (27.1)        | 132 (17.8)    | < .002  | 1.72 | 1.21, 2.44 | BPV       | 15.1                 | 13.8           | .615   |
| P TPE     | 51 (22.7)        | 181 (24.4)    | .636    |    |        | Active    | 63.1                 | 46.3           | .003   |
|          |                  |               |         |    |        | PTE       |                      |                 |        |
|          |                  |               |         |    |        | SBP       |                      |                 |        |
| P SBP     | 63.1             | 46.3          | .003    |    |        |           |                      |                 |        |
|          |                  |               |         |    |        |           |                      |                 |        |
| Dippers   | 2 (0.9)          | 15 (2.0)      | .331    | 0.47 | .10,    | Active    | 41.6                 | 31.7           | .458   |
|          |                  |               |         |    | 2.14   | PTE       |                      |                 |        |
|          |                  |               |         |    |        | DBP       |                      |                 |        |
| P SBP     | 41.6             | 31.7          | .458    |    |        |           |                      |                 |        |
|          |                  |               |         |    |        |           |                      |                 |        |
| 1 dipper  | 125 (55.6)       | 405 (54.5)    | .629    | 1.09 | .57, 1.59 | Active    | 395.2                | 253.4          | .002   |
|          |                  |               |         |    |        | HBI       |                      |                 |        |
|          |                  |               |         |    |        | SBP       |                      |                 |        |
| P SBP     | 395.2            | 253.4         | .002    |    |        |           |                      |                 |        |
| Passive   | 47 (20.9)        | 142 (19.1)    | .486    | 1.17 | .74, 1.85 | Active    | 146.3                | 95.6           | <.001  |
| HBPV      | 170 (75.5)       | 447 (60.2)    | < .001  | 2.04 | 1.46, 2.86 | Passive   | 73.2                 | 57.6           | <.001  |
|                | SBP         | DBP         | PTE         | HBI         |
|----------------|-------------|-------------|-------------|-------------|
| SBP active     | 151(67.1)   | 378(50.9)   | <0.001      | 1.97        |
| SBPV           | 1.44,2.69   | Passive     | 53.9        | 40.6        |
|                |             | PTE DBP     |             |             |
| SBP active     | 39(17.3)    | 70(9.4)     | 0.001       | 2.01        |
| DBPV           | 1.32,3.08   | Passive     | 525.4       | 344.8       |
|                |             | HBI SBP     |             |             |
| h              | 38(16.9)    | 94(12.7)    | 0.105       | 1.40        |
| Passive SBPV   | 0.93,2.11   | Passive     | 191.4       | 121.1       |
|                |             | HBI DBP     |             | .002        |
| h              | 209(92.9)   | 610(82.1)   | <0.001      | 2.84        |
| Passive PV     | 1.65,4.89   | -           | -           | -           |

**Abbreviations**
- **TOD**: Target organ damage
- **PTE SBP**: Percent time elevation Systolic Blood pressure
- **PTE DBP**: Percent time elevation diastolic blood pressure
- **HBI SBP**: Hyperbaric index Systolic blood pressure
- **HBI DBP**: Hyperbaric index Diastolic blood pressure
- **BPV**: Blood pressure variability
- **SBPV**: Systolic Blood pressure variability
- **DBPV**: Diastolic blood pressure variability
- **OR**: Odds ratio
- **CI**: Confidence interval
- **P value <0.05**: Significant value, highlighted in bold

**Table 4**: Results of multiple logistic regression of ABPM parameters with TOD
| ABPM parameters     | P value | OR     | 95% CI   |
|---------------------|---------|--------|----------|
| High BPV            | 0.069   | 1.433  | 0.97, 2.11 |
| High active SBPV    | 0.612   | 1.143  | 0.68, 1.91 |
| High active DBPV    | 0.213   | 1.353  | 0.841, 2.176 |
| High Passive SBPV   | 0.594   | 0.881  | 0.553, 1.484 |
| High Passive DBPV   | 0.377   | 1.385  | 0.672, 2.852 |
| Morning surge       | 0.054   | 1.45   | 0.99, 2.11 |
| Active PTE SBP      | 0.004   | 1.009  | 1.003, 1.016 |
| Active PTE DBP      | 0.034   | 0.991  | 0.983, 0.999 |
| Active HBI SBP      | 0.598   | 1.000  | 0.998, 1.001 |
| Active HBI DBP      | 0.571   | 1.00   | 0.999, 1.002 |
| Passive PTE SBP     | 0.664   | 0.997  | 0.985, 1.010 |
| Passive PTE DBP     | 0.006   | 1.01   | 1.003, 1.018 |
| Passive HBI SBP     | 0.771   | 1.00   | 0.99, 1.001 |
| Passive HBI DBP     | 0.482   | 0.999  | 0.997, 1.002 |

Abbreviations:

TOD- Target organ damage  ABPM - ambulatory blood pressure monitoring
PTE SBP- Percent time elevation Systolic Blood pressure
PTE DBP- Percent time elevation diastolic blood pressure
HBI SBP - Hyperbaric index Systolic blood pressure
HBI DBP- Hyperbaric index Diastolic blood pressure
BPV- Blood pressure variability
SBPV- Systolic Blood pressure variability
DBPV- Diastolic blood pressure variability
OR - Odds ratio
CI - confidence interval
P<0.05 significant values highlighted in bold