The effect of blood pressure variability on the prognosis of hypertensive patients

Ziad A. Taher, Waleed W. Khayyat[1], Marwan M. Balubaid[1], Mohamed Y. Tashkandi[1], Haifaa A. Khayyat[2], Abdulhalim Jamal Kinsara

Department of Cardiology, Ministry of National Guard Health Affair, King Saud Bin Abdulaziz University for Health Sciences, COM-WR, King Abdullah International Medical Research Center; Jeddah-*Saudi Arabia*
[1]King Saud Bin Abdulaziz University for Health Sciences, COM-WR; Jeddah-*Saudi Arabia*
[2]Department of Cardiology, King Fahad Hospital; Jeddah-*Saudi Arabia*

Abstract

Objective: Our study aims to compare the effects of blood pressure variability (BPV) during ambulatory blood pressure measurement (ABPM) and visit-to-visit measurements to predict future cardiovascular complications among hypertensive patients.
Methods: This is a retrospective case-control study of patients with hypertension over 10 years. All adult patients with at least one recorded ABPM, and at least three recorded visit measurements were included. Patients with incomplete ABPM readings, a history of a tested outcome, or the occurrence of any of the tested outcomes within the measurement period were excluded. The outcome was the development of any of the following: acute coronary syndrome (ACS), chronic ischemic heart disease (IHD), heart failure (HF), or stroke.
Results: Of the 305 cases reviewed, 152 were included. The mean follow-up was 6.6±2.3 years. The mean age was 53.5±14.3 years. Eighty-two (53.9%) patients were male, while 70 (46.1%) were female. Risk factors included diabetes mellitus (53.9%), dyslipidemia (39.5%), obesity (16.4%), and smoking (8.6%). Comorbidities included stroke (2%), ACS (8.6%), IHD (20.4%), HF (2.6%), and renal failure (1.3%). One or more complications were seen in 22.4 % of the included patients. The variation of the daytime systolic ABP had been found to predict the future risk of developing IHD (OR=1.94; 95% CI=1.09–3.45; p=0.025). Moreover, IHD was associated with night-time systolic standard deviation (SD) in ABPM (OR=1.23; 95% CI=1.00–1.51; p=0.048). On the other side, ACS was found to be associated with systolic SD in visit-to-visit measurement (OR=1.10; 95% CI=1.01–1.21; p=0.04).
Conclusion: Hypertensive patients with high variability of daytime and night-time SD in ABPM are more likely to have IHD. Whereas, having high variability in systolic SD in visit-to-visit measurements is associated with developing ACS. *(Anatol J Cardiol 2019; 22: 112-6)*
Keywords: hypertension, prognosis, ambulatory blood pressure monitoring, variability, visit-to-visit

Introduction

Hypertension (HTN) is the most prevalent treatable risk factor for cardiovascular diseases (1, 2). Measurement of the mean blood pressure has been relied upon to predict HTN prognosis (3, 4). However, it has been suggested that blood pressure variability (BPV) may be as important as the mean blood pressure in predicting future risk of cardiovascular diseases (5, 6). BPV is defined as either the standard deviation (SD) or the coefficient of variation of different blood pressure measurements, or the mean absolute difference between successive readings (5, 6). Despite evidence supporting the clinical significance of BPV, it continues to be dismissed in evaluating HTN patients, being considered as normal fluctuations in BP (7, 8).

Some studies have tested the significance of BPV from visit-to-visit or within 24 hours via ABPM (9). Results have shown that BPV is consistent in individuals over time and is able to predict future organ damage and cardiovascular mortality independent of the mean blood pressure (10-12). BPV has also been suggested to account for the different effects of antihypertensive treatments on cardiovascular disease risk (13, 14). There is a growing body of evidence that BPV is important and should be implemented in the clinical assessment of HTN patients. Our study aimed to compare the effects of BPV during ABPM and

Address for correspondence: Abdulhalim Jamal Kinsara, MD, Department of Cardiology, Ministry of National Guard Health Affair, King Saud Bin Abdulaziz University for Health Sciences, COM-WR, King Abdullah International Medical Research Center; Jeddah-*Saudi Arabia*
Phone: 966 569 968 182 E-mail: akinsara@yahoo.com
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visit-to-visit measurements in predicting future complications in the same population of HTN patients in the largest public hospital in Jeddah. Our hypothesis is that a high fluctuation of BP negatively affects the prognosis of HTN patients. Therefore, we attempted to find which between the two methods is better to predict HTN prognosis: variability during ABPM or visit-to-visit measurements.

Methods

This study is a retrospective case-control study performed at King Fahad Hospital, a public hospital in Jeddah, Saudi Arabia. Charts of HTN patients who visited the cardiology clinics over a period of five years were recruited and tested for inclusion and exclusion criteria. The eligible charts were reviewed, and data were collected over a period of 9 months.

BP data were collected from the clinic visit and from the report of the 24-hour ABPM. All included patients were older than 18 years at the time of HTN diagnosis, with at least one recorded ABPM report and at least three recorded BP measurements. Patients with follow-up time less than three years were excluded. We used non-probability sampling technique, which is a consecutive sampling technique.

The independent variables were the SD of systolic and diastolic BP that were measured in the daytime, nighttime, and after 24 hours by ABPM device. Also, SD of systolic and diastolic BP of visit-to-visit measurements were independent variables. From the other side, the dependent variables were the complications of interest in this study, which are: stroke, acute coronary syndrome (ACS), ischemic heart disease (IHD), heart failure (HF), and overall complications.

The diagnostic criteria used in this study were as follows: patients were considered HTN when the mean daytime ABPM of systolic BP was ≥135 mm Hg or diastolic BP was ≥85 mm Hg. Obesity was identified when BMI > 30 kg/m^2. Hyperlipidemia was diagnosed by any of the following (in mg/dL): total cholesterol >200, LDL >100, HDL <40 (for men) or <50 (for women), and triglycerides >140. The patients were labeled as diabetics if they used antidiabetic medications and had a fasting blood glucose level of ≥7.0 mmol/L or random blood glucose of ≥11.1 mmol/L. The diagnosis of stroke had to be confirmed by neurological imaging (brain CT or MRI) or neurology consultation. ACS was diagnosed based on ECG changes (ST depression/transient elevation and/or T-wave changes; persistent ST elevation) along with troponin and confirmed by coronary angiogram. Diagnosis of IHD was established by ECG exercise stress test. HF cases were diagnosed when the clinical signs and symptoms indicated HF, supported by B-type Natriuretic Peptide levels of more than 100 pg/mL.

We classified data based on ABPM (24-hour, daytime, and nighttime) and visit-to-visit BP readings into systolic and diastolic measurements. We assessed each of these parameters for the risk of developing one of the assessed outcomes to find out which of them could be more predictive for developing complications in the same patient.

To describe the data, we used proportions for qualitative variables and mean with SD for quantitative variables. Data on the developed complications and their association with the variability of the BP readings of both visit-to-visit or ABPM were analyzed using binary logistic regression. Univariate analysis for each variable was made to either rule a variable in or out in the binary logistic regression equation. All variables that were significant in univariate analysis were considered in binary logistic regression.

Ethical approval was granted by the Ministry of Health in Saudi Arabia, Medical Research and Studies Department. There was no need for informed consent as the study is a retrospective chart review and no patients' identifiers were collected. All statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) version 20.

Results

Of the 305 patients diagnosed with HTN based on 24-hour ABPM, 152 (49.83%) were included. Out of these 152 patients, 34 (22.4%) patients developed at least one or more of HTN complications (Fig. 1).

The mean age of the study group was 53.5 (±14.3) years. Of all included cases, 82 (53.9%) were males, 82 (53.9%) had diabetes mellitus, 60 (39.5%) had dyslipidemia, 25 (16.4%) had obesity, and 13 (8.6%) were smokers. Mean follow-up time was 6.6±2.3 years starting from the diagnosis of HTN. Forty-one (26.9 %) designated cardiovascular (CV) outcomes were noted in the above 34 patients during the follow-up period: 6 (3.9%) had stroke, 13 (8.6%) had ACS, 14 (9.2%) had IHD, 7 (4.6%) developed HF and 1 patient (0.7%) developed renal failure (Table 1).

The fluctuation of both visit-to-visit and ABPM measurements were analyzed. Some outcomes were statistically correlated with fluctuations of ABPM while others were correlated with visit-to-visit variability. IHD was associated with the fluctuation of two parameters in ABPM. The SD of daytime systolic blood pressure (SBP) measurements were associated with developing IHD (OR=1.94; 95% CI=1.09–3.45; p=0.025). The SD of the nighttime SBP measurements was also associated with developing IHD (OR=1.23; 95% CI=1.00–1.51; p=0.048). SD of daytime SBP was the only parameter associated with the risk of developing any of the tested complications (OR=1.50; 95% CI=1.00–2.25; p=0.049). In comparison, visit-to-visit measurements showed

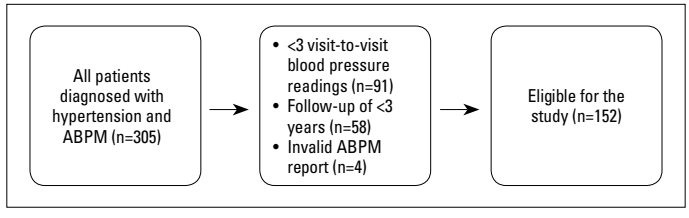

Figure 1. Formula to determine the included patients

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Table 1. Baseline characteristics of included patients (n=152)

Age (years, means±SD)	53.5 (±14.3)
Male sex	82 (53.9%)
Obese	25 (16.4%)
Smoking	13 (8.6%)
Dyslipidemia	60 (39.5%)
Diabetes	82 (53.9%)
History of stroke	3 (2%)
History of ACS	13 (8.6%)
History of IHD	31 (20.4%)
History of HF	4 (2.6%)
History of RF	2 (1.3%)
Follow-up duration (years, mean±SD)	6.6 (±2.3)
Developed Stroke	6 (3.9%)
Developed ACS	13 (8.6%)
Developed IHD	14 (9.2%)
Developed HF	7 (4.6%)
Developed RF	1 (0.7%)

ACS - acute coronary syndrome; IHD - ischemic heart disease; HF - heart failure; RF - renal failure

only one association of SBP variability with the development of ACS (OR =1.10; 95% CI=1.01–1.21; p=0.04). Logistic regression analysis for all investigated parameters is summarized in Table 2.

Discussion

Data in this study found that some complications were associated with ABPM variability while others were associated with visit-to-visit variability. This indicates that ABPM variability is more predictive for some specific complications such as IHD, while visit-to-visit variability is a better predictor for some other complications such as ACS. There was no clear cut-off value where the complication occurrence increases, but rather, as the variation between BP readings increased, the risk of developing a complication increased similarly.

There have not been many studies comparing ambulatory and visit-to-visit BP. However, the few studies that compared the predictability of these two methods for developing complications reported different results. Three studies support the effectiveness of ABPM over visit-to-visit variability in predicting future complications (15-17). A fourth study concluded that ABPM variation was associated only with hard CV disease (stroke, fatal or non-fatal myocardial infarction and sudden cardiac death) while visit-to-visit BP was associated with both hard and soft CV disease (angina, congestive HF, end-stage renal disease requiring hemodialysis, peripheral artery disease, and transient ischemic attacks). Therefore, they assumed that because visit-to-visit measurements were spread throughout the year, it would better to represent seasonal variation resulting in better predictability (18).

Among different investigated parameters reported in ABPM, the daytime and nighttime SBP measurements were the only variables associated with developing a complication. On the other hand, the analysis of visit-to-visit BP showed that SBP was statistically associated with the development of ACS. Other studies concluded that variability in total SBP is the best predictor of developing end-organ damage (15, 19, 20). However, larger sample size studies had different results where variable SBP measured in visit-to-visit was associated with high mortality (9, 21). A similar effect of ABPM readings variation was also noted in type 2 diabetes mellitus with fluctuating night BP measured by ABPM, leading to additional cardiovascular complications (22).

Table 2. Prognostic value of blood pressure variability parameters in predicting hypertension complications

	Dependent variables [Odds ratio (95% CI)]				
Independent	**ACS**	**IHD**	**Stroke**	**HF**	**Any complications**
SD.Sys.Total	1.57 (0.74-3.31) *P*=0.24	1.81 (0.98-3.32) *P*=0.06	1.32 (0.51-3.40) *P*=0.57	1.08 (0.45-2.59) *P*=0.87	1.48 (0.95- 2.31) *P*=0.08
SD.Sys.Daytime	1.53 (0.78-3.01) *P*=0.21	1.94 (1.09-3.45) *P*=0.025	1.06 (0.45-2.53) *P*=0.89	1.60 (0.69-3.72) *P*=0.27	1.50 (1.00-2.25) *P*=0.049
SD.Sys.Night	1.01 (0.82-1.23) *P*=0.97	1.23 (1.00-1.51) *P*=0.048	1.09 (0.82-1.45) *P*=0.55	1.16 (0.90-1.50) *P*=0.25	1.00 (0.88-1.14) *P*=0.98
SD.Dia.Total	1.14 (0.62-2.08) *P*=0.68	1.39 (0.69-2.78) *P*=0.35	1.58 (0.45-5.49) *P*=0.47	1.61 (0.52-4.93) *P*=0.41	1.59 (0.90-2.80) *P*=0.11
SD.Dia.Daytime	1.13 (0.67-1.90) *P*=0.64	1.46 (0.78-2.71) *P*=0.24	1.20 (0.37-3.38) *P*=0.83	1.85 (0.68-5.02) *P*=0.23	1.48 (0.90-2.45) *P*=0.12
SD.Dia.Night	1.07 (0.84-1.37) *P*=0.58	1.06 (0.81-1.38) *P*=0.68	1.00 (0.66-1.52) *P*=0.998	1.15 (0.79-1.67) *P*=0.46	1.02 (0.85-1.23) *P*=0.82
SD.Sys	1.10 (1.01-1.21) *P*=0.04	1.01 (0.94-1.09) *P*=0.74	1.01 (0.92-1.10) *P*=0.91	1.04 (0.94-1.14) *P*=0.46	1.00 (0.95-1.06) *P*=0.88
SD.Dia	1.01 (0.91-1.12) *P*=0.92	1.08 (0.94-1.24) *P*=0.26	1.05 (0.94-1.17) *P*=0.41	1.03 (0.89-1.19) *P*=0.70	1.01 (0.94-1.09) *P*=0.72

SD.Sys.Total - standard deviation of systolic blood pressure over 24 hours; SD.Sys.Daytime - standard deviation of systolic blood pressure over daytime; SD.Sys.Night - standard deviation of systolic blood pressure over night; SD.Dia.Total - standard deviation of diastolic blood pressure over 24 hours; SD.Dia.Daytime - standard deviation of diastolic blood pressure over daytime; SD.Dia.Night - standard deviation of diastolic blood pressure over night; SD.Sys - standard deviation of systolic blood pressure for visit-to-visit; SD.Dia - standard deviation of diastolic blood pressure for visit-to-visit; ACS - acute coronary syndrome; IHD - ischemic heart disease; HF - heart failure

In our study, all the predictive parameters were systolic measurements. This correlates with some reports that found systolic measurements to be of more predictive value for morbidity and mortality than diastolic measurements (23, 24). However, our findings contrast with other studies that found that diastolic measurements might be as predictive or even more predictive than systolic measurements (15, 19, 25-27).

SBP measured in ABPM was a strong cardiovascular risk predictor in studies that compared ABPM and visit-to-visit values (27, 28). ABPM variability was shown to have good predictability of some of its parameters to detect CV events, even in a small sample size. On the contrary, visit-to-visit variability predictability was more likely to be detected in larger sample size studies which might suggest a weak association (17, 28).

Our study was limited by a relatively small sample size which might have underestimated the effect of some parameters. It is a retrospective study dependent on chart review, resulting in a potential deficiency of documentation of risk factors. A potential source of bias in this study was inevitable as ABPM is usually ordered by the cardiology clinic. Atherosclerosis is a highly complex process. The paper solely focuses on BPV. Several confounding variables i.e., inflammation, gender, age, and population-specific factors can affect the aforementioned findings.

Conclusion

The fluctuation measured in ABPM, specifically daytime and nighttime SBP, is more predictive of developing IHD while variability in visit-to-visit SBP measurements is more predictive of ACS. This can be applied clinically to predict the risk of developing complications in hypertensive patients.

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