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Research Article

The effect of intermittent fasting on blood pressure variability in patients with newly diagnosed hypertension or prehypertension

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Abstract

Intermittent fasting is a phenomenon which can be observed in most humans. The effect of intermittent fasting on blood pressure variability (BPV) has not previously been investigated. The purpose of this study was to assess the effect of fasting on blood pressure (BP) (with office, home, central, and ambulatory blood pressure monitoring [ABPM]) and on BPV. Sixty individuals were included in the study. Office, home, ABPM, and central BP measurements were performed before and during intermittent fasting. Standard deviation and coefficient variation were used for office and home BPV measurement, while the smoothness index was used to calculate ABPM variability. Patients' BP and BPV values before and during intermittent fasting were then compared. Intermittent fasting resulted in a significant decrease in office BP values and ABPM measurements but caused no significant change in home and central BP measurements. Twenty-four hour urinary sodium excretion decreased. Smoothness values obtained from ABPM measurements were low; in other words, BPV was greater. BPV was higher in patients who woke up to eat before sunrise, but BPV was low in patients with high body mass index. Intermittent fasting produced a significant decrease in BP values in terms of office and ABPM measurements in this study but caused no significant change in central BP and home measurements. We also identified an increase in BPV during intermittent fasting, particularly in patients who rose before sunrise. J Am Soc Hypertens 2018;12(1):42–49.

Keywords: BPV; central blood pressure; fasting.

Introduction

Various types of fasting have been performed since ancient times, for reasons of both health benefits and religious belief. Intermittent fasting is a religious obligation performed by many believers worldwide. It generally involves consuming no food or drink, broadly from before sunrise to sunset. In addition, in order to prepare themselves for hunger and thirst throughout the day, people who fast often wake up before sunrise, have an early meal (sahur), and then go back to sleep. Other individuals who fast may forego the sahur. Intermittent fasting therefore results in temporary changes to the individual's familiar patterns of sleep and eating.

While the effect on human health of intermittent fasting is uncertain, previous studies have shown that it may have potentially beneficial effects in the prevention and treatment of diseases such as obesity, type 2 diabetes mellitus,

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and cardiovascular diseases.[1,2] Previous animal studies have shown that blood pressure (BP) falls during the fasting period and then increases again after eating.[3] Very few clinical studies have investigated the effects of intermittent fasting on BP control and course in hypertensive patients. One such study was performed by Perk et al,[4] who determined no change before and after intermittent fasting in ambulatory blood pressure monitoring (ABPM) of hypertensive patients under treatment. Ural et al investigated the course of BP before and after intermittent fasting in Stage 2–3 hypertensive patients receiving combination treatment and also determined no difference.[5] However, apart from a very few studies of hypertensive patients, no studies have investigated the effects of intermittent fasting on blood pressure variability (BPV) and urinary sodium excretion in prehypertensive and/or newly diagnosed hypertensive patients.

The purpose of this study was to assess the effects of intermittent fasting on BPV, central BP, and urinary sodium excretion in prehypertensive and/or newly diagnosed hypertensive patients.

Materials and Methods

Cappadocia Cohort

This is a prospective cohort study conducted by Turkish Society of Internal Medicine.[6] The observational part of the study began in March 2013. Once informed written consent had been obtained, participants were administered a questionnaire to collect baseline data. Study personnel collected the following information from participants while administering a 167-question electronic questionnaire: demographic characteristics, place of residence, level of education, employment status, lifestyle information, and medical history, including diagnosed illnesses and medication use. Physical examinations were performed on all subjects, including the measurement of BP (at least twice), body weight, height, and waist and neck circumferences. The study participants survey every year in terms of changes in these factors, the development of new illnesses, changes in weight, waist size, and medication use, level of physical activity, smoking status, alcohol consumption, and nutritional factors.

Patient Selection

Individuals followed up due to prehypertension and hypertension in the Cappadocia cohort and living in Gülşehir, aged 18 years or over, who had been informed about the study and gave verbal agreement to participate, with a sufficient intellectual level to provide a medical history, to measure BP at home and to perform 24-hour ABPM, and who fasted intermittently were included in the study. Pregnant subjects; patients with known heart failure, kidney failure, or chronic liver disease; subjects using antihypertensive drugs; who had fasted in the previous 24 hours before their visit; and subjects who were unwilling to provide contact details were excluded. Ethical committee approval for the study was obtained from the Hacettepe University Medical Faculty, and the study began once informed written consent had been received from patients.

Study Protocol

Individuals from the Cappadocia cohort diagnosed with prehypertension and hypertension (systolic blood pressure [SBP] 120–139 and $\geq$140; diastolic blood pressure [DBP] 80–89 and $\geq$90 mm Hg) according to the JNC 8 guideline,[7] under monitoring and wishing to be included in the study, underwent a detailed physical examination. Those subjects who did not use antihypertensive agents were included in the study. Office BP, central BP, and home BP measurement and 24-hour ABPM and 24-hour urine collection procedures were then repeated before and during the intermittent fasting period, after subjects had fasted for at least 1 week, using the protocol and equipment described below.

Office BP Measurement

Office BP measurements were performed with a UA-651SL monitor (Kitamoto-shi, Saitama 364-8585 Japan). Before office BP measurement, the patient was left for at least 5 minutes in a relaxed position in a silent room at a suitable temperature. Patients were asked whether they had used caffeine, alcohol, or cigarettes in the previous 1–2 hours. BP was measured from both arms using an appropriately sized cuff on the forearm, with the forearm at heart level, with the back and the forearm supported, and the patient in a seated position. Care was taken during BP measurement to ensure that patients did not cross their legs or speak. BP was measured five times at 1-minute intervals. The first measurement was not included in the analysis. The mean of the subsequent four values was taken and recorded as office BP. Office measurements were performed twice, before and during the intermittent fasting period, after subjects had fasted for at least 1 week.

Home BP Measurement

Home BP was measured with a UA-651SL (Kitamoto-shi, Saitama 364-8585 Japan) device. Home BP measurements were performed by patients following appropriate training in the technique. BP was measured five times at 1-minute intervals in the morning and evening for 1 week. At the end of 1 week, mean morning and evening values were taken and recorded as home BP values. Home BP was measured twice, once before and once during the intermittent fasting period, after subjects had fasted for at least 1 week.

Ambulatory Blood Pressure Measurement

Twenty-four hour BP (24-hour ABPM) was measured twice, once before and once during the intermittent fasting period, after subjects had fasted for at least 1 week, using a Mobil-O-Graph NG 24h ABPM Classic (I.E.M. GmbH, Stolberg, Germany) device. Both monitoring periods began at approximately the same time. Monitoring was performed from the nondominant arm. Patients were asked to record their hours of sleeping, waking, and eating and their daily activities. Sleeping-waking periods were evaluated accordingly. Patients were instructed to keep the relevant arm immobile during BP measurement. Daytime BP measurement was performed once every 15 minutes and nighttime measurement once every half hour. Measurements with at least 70% validity from day and nighttime measurements in 24-hour ABPM records were included for analysis.

Central BP Measurement

Central BP was measured using the ARCSolver method. The ARCSolver method is commercially available in the oscillometric Mobil-O-Graph NGW 24-hour ambulatory BP and pulse wave analysis monitor (IEM; Stolberg, Germany). The device is approved by the Food and Drug Administration and by Conformité Européenne, and its BP detection unit has been validated according to British Hypertension Society[8] and European Society of Hypertension[9] recommendations. The algorithms for the generation of central SBP and aortic BP curves, using the oscillometric method, have been reported previously[10] but are briefly explained here. Following conventional oscillometric BP assessment, peripheral pressure waves are recorded, using the brachial cuff, at the DBP level for 10 seconds. Following digitization, a three-step algorithm is applied. First, the single pressure waves are verified for their plausibility by testing minima position and corresponding wavelengths. Minima are detected by means of an iterative procedure evaluating higher order time derivatives of the pressure signal. The second stage involves comparison of all single pressure waves with one another to recognize artifacts. Aortic pulse waves are then generated via a general transfer function. Modulus and phase characteristics of the ARCSolver transfer function are available.[10] Finally, the coherence of the measured parameters is verified and displayed within the Mobil-O-Graph NG software package which also allows visual inspection to reveal consistently recorded intrinsic waveform distortion manually. The entire process takes between 2 and 3 minutes.

24-Hour Urine Collection

Patients were asked to collect 24-hour urine; they were instructed not to save the urine from their first urination on the morning when collection began but to urinate into a collection container every time thereafter, including the first urination the following morning, and then to bring all collected urine to the laboratory. Urine sodium was measured in patients' 24-hour urine via the enzymatic colorimetric method using a Hitachi Modular P800 (Roche Diagnostic Corp. Indianapolis, IN) autoanalyzer. The 24-hour sodium excretion value (mmol/d) for each individual was calculated as the concentration of sodium in the urine (mmol/L) $\times$ urinary volume (L/d). Twenty-four hour urine was collected twice, once before and once during the intermittent fasting period, after subjects had fasted for at least 1 week.

BPV Analyses

Standard deviation (SD) and coefficient variation (CV) (SD/mean) for SBP, DBP, and heart rate in the calculation of BPV of office and home BP measurements were calculated separately. SBP, DBP, and heart rate were also calculated separately using the smoothness index formula (SI) for BPV from ABPM records. Hourly average BP measurements over 24 hours (at 15-minute intervals by day and 30 minutes at night) and SD were recorded for each patient. ΔH was obtained based on mean BP at the time interval when ABPM was started, with the difference between mean BP at every subsequent time interval and mean BP at the initial hour being taken, and total BP differences at each time interval being divided by the total number of hours over which measurement was performed. Similarly, SD was obtained based on mean SD at the time interval when ABPM was started, with the difference between mean SD at every subsequent time interval and mean SD at the initial hour being taken, and total SD differences at each time interval being divided by the total number of hours over which measurement was performed.

Statistical Analysis

PASW 18.0 for Windows software was used for statistical analysis. Compatibility with normal distribution of variables was examined using the Kolmogorov–Smirnov and Shapiro–Wilks tests. Normally distributed data were analyzed using the paired t test or using the Wilcoxon Signed Rank test if normality was not established. Correlation analyses were performed using Pearson and Spearman analyses. Type-1 error levels below 0.05 were interpreted as statistically significant.

Results

Sixty patients were included in the study. The median age of the subjects was 46.77 years, and 61.7% were female. Of these patients, 51.7% rose for sahur. Mean body mass index (BMI) of the patient group was 30.35 $\pm$ 5.87. Mean BMI of the patients who rose for sahur was

30.73 ± 5.01, compared to 29.94 ± 6.78 for those who did not perform sahur. The difference was not significant. A significant decrease occurred during intermittent fasting, compared to pre–intermittent fasting values, in office SBP, DBP, and heart rate ($P < .001$, .039, and .003, respectively). No significant difference was observed in home BP before and during intermittent fasting. When ABPM measurements before and during intermittent fasting were compared, no significant difference was observed in all-day and daytime SBP, DBP, mean arterial pressure (MAP), or heart rate values, while DBP, MAP, and heart rate values among nighttime ABPM data were significantly lower compared to pre–intermittent fasting values ($P < .003$, .025, and .012, respectively). Urinary sodium excretion and urinary volume in the intermittent fasting period were significantly lower compared to pre–intermittent fasting values ($P < .004$ and .016, respectively) (Table 1). Central SBP and DBP in the pre–intermittent fasting period were 112.5 (85–151) and 76.5 (60–109) mm Hg, respectively, compared to 112 (85–161) and 79.5 (61–112) mm Hg in the intermittent fasting period, the difference being statistically non-significant.

Examination of BPV parameter values before and during intermittent fasting revealed no significant difference in CV and SD, with which we assessed office BP and home measurements. ABPM data for 41 of the 60 patients in the study were included in the analysis (the others were excluded for reasons such as insufficient measurement or no second ABPM measurement being performed). We used SI to determine the variability of ABPM measurements before and during intermittent fasting. Briefly, a numerically large SI calculated using the formula ΔH/SD indicates low variability. SI SBP, SI DBP, and SI heart rate were significantly lower during intermittent fasting than before ($P < .012$, .005, and 0.002, respectively) (Figure 1A–C).

We assessed parameters affecting BPV individually both before and during intermittent fasting. Age, sex, urinary sodium excretion, and BMI before intermittent fasting had no effect on variability obtained with office, home, and ABPM measurements. There was no significant relation between age, sex, urinary sodium excretion, or BMI and office BPV during the intermittent fasting period. While no home measurement parameters significantly affected BPV, SI SBP obtained from ABPM measurements was positively correlated with BMI (r: 0.597, $P = .003$). In other words, the BPVs of patient with greater BMI were lower in the intermittent fasting period. Sahur caused no change in home BPV, although office CV SBP and SD SBP among individuals who did rise for sahur were significantly higher compared to those who did not ($P < .047$ and .0.29, significantly). SI SBP obtained from ABPM data for individuals who rose for sahur was lower than in those who did not ($P = .027$). In other words, BPV was higher in those individuals who performed the sahur (Table 2).

Table 1
Patients demographic parameters and a comparison of the blood pressure measurements before and during intermittent fasting

n = 60	Before Intermittant Fasting Median (Min.–Max.)	During Intermittant Fasting Median (Min.–Max.)	*P*
Office			
SBP (mm Hg)	122.75 (88.25–184.5)	116.88 (99–163.25)	<.001
DBP (mm Hg)	77.38 (57.50–113.50)	77.38 (46.00–98.00)	.039
Heart rate (bpm)	80.63 (55.25–97.50)	75.63 (55.00–90.75)	.003
Home (all day)			
SBP (mm Hg)	116.01 (91.47–151.74)	115.49 (89.51–155.76)	.219
DBP (mm Hg)	72.78 (57.54–101.34)	73.96 (56.74–99.16)	.750
ABPM (all day) (n = 41)			
SBP (mm Hg)	119.00 (100.00–176.00)	120.00 (95.00–151.00)	.713
DBP (mm Hg)	74.00 (56.00–110.00)	75.00 (60.00–94.00)	.936
MAP (mm Hg)	92.00 (78.00–140.00)	93.00 (80.00–120.00)	.844
Daytime			
SBP (mm Hg)	120.00 (99.00–171.00)	120.00 (102.00–156.00)	.489
DBP (mm Hg)	75.00 (55.00–110.00)	78.00 (60.00–98.00)	.134
MAP (mm Hg)	94.00 (77.00–138.00)	97.00 (81.00–125.00)	.213
Nighttime			
SBP (mm Hg)	117.00 (93.00–183.00)	111.50 (88.00–142.00)	.094
DBP (mm Hg)	73.00 (56.00–110.00)	69.00 (54.00–85.00)	.003
MAP (mm Hg)	92.00 (75.00–143.00)	88.00 (72.00–111.00)	.025
Urine			
Sodium (mEq/d)	234.50 (129.00–465.00)	213.00 (50.00–390.00)	.004
Volume (L)	2.3 (0.9–4.7)	2.0 (0.5–2.5)	.016

ABPM, ambulatory blood pressure monitoring; DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

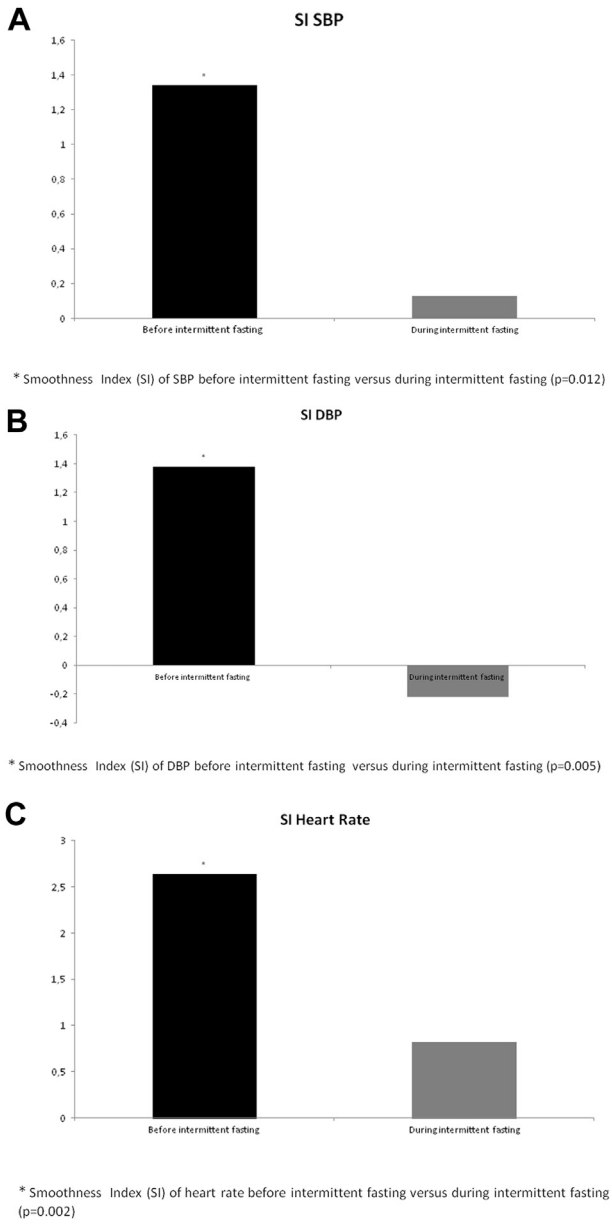

Figure 1. (A) Comparison of SBP SI values before and during intermittent fasting ($P = .012$). (B) Comparison of DBP SI values before and during intermittent fasting ($P = .005$). (C) Comparison of heart rate SI values before and during intermittent fasting ($P = .002$). DBP, diastolic blood pressure; SBP, systolic blood pressure; SI, smoothness index.

Discussion

Fasting involves avoiding food and/or drink for specific periods of time in order to obtain spiritual benefits in various faith systems or else for health benefits. Fasting in humans involves abstaining from food and/or drink for periods between 12 hours and 3 weeks. Fasting every alternate day or twice weekly is defined as intermittent fasting, while abstaining from food and/or drink for several days every 2 or more weeks is defined as periodic fasting.[11] The fasting undertaken over a specific number of hours for a specific number of days in various faith systems is defined as intermittent fasting. In the Judaic faith, believers fast for 26 days over Yom Kippur. Some Orthodox Christians fast by abstaining from animal products for 49 days during Easter, while Muslims fast for 1 month during Ramadan every year. Hypertensive patients frequently seek medical advice to inquire whether there are any objections in terms of health to intermittent fasting. Few studies have investigated the effect of intermittent fasting on course of BP in hypertensive patients, and none have assessed its impact on BPV. We therefore think that there is a need for scientific studies showing how these patient groups are affected by intermittent fasting.

The positive effects of long-term fasting were best shown by Muller et al[12] in patients with rheumatoid arthritis, the authors reporting a decrease in inflammation and pain with long-term fasting in this patient group. Previous studies have also shown that intermittent fasting may have potentially beneficial effects in the prevention and treatment of diseases such as obesity, type 2 diabetes mellitus, and cardiovascular diseases.[1,2] A few studies have considered the effect on BP of intermittent fasting as a religious observance recommended at different times and for different periods of time in various faiths. The few previous studies involving hypertensive patients have shown a significant decrease in BP values during intermittent fasting compared to pre–intermittent fasting levels.[13–15] However, a few studies have also observed no change in BP during intermittent fasting.[3,4] In a study of normotensive individuals, Samad et al[16] determined a significant decrease in SBP and DBP levels during intermittent fasting compared to prefasting values. In our study, we observed a significant decrease in office SBP, DBP, and heart rate among fasting subjects. No significant change was observed in home measurements and central BP values. Among the ABPM data, while there was no change in SBP, we determined a significant decrease in DBP, MAP, and heart rate values. When we analyzed office, home, ABPM, and central BP data together, we observed a general decrease in BP values in individuals fasting intermittently. We think that low BP values being observed in some studies while there was no change in others may be due to variations among BP measurement techniques (office, home, and ABPM). This study differs from previous research in that it was performed among prehypertensive and newly diagnosed hypertensive individuals and used four methods of measurement.

We also investigated how 24-hour urinary sodium excretion was affected by intermittent fasting and observed that both urinary volume and sodium excretion were lower during the intermittent fasting period compared to pre–intermittent fasting levels. Very few previous studies have analyzed the effect of fasting on urinary sodium excretion. These studies have also shown that fasting reduces urinary volume and sodium excretion.[17] High salt consumption has

Table 2
The effect of eating before sunrise on blood pressure variability

	Do Not Eat Before Sunrise	Eat Before Sunrise	*P*
Office BPV			
CV SBP	0.03 (0 to 0.59)	0.04 (0.02 to 0.11)	.047
CV DBP	0.04 (0.01 to 0.13)	0.04 (0.01 to 0.13)	.762
CV heart rate	0.04 (0.01 to 0.14)	0.03 (0.01 to 0.12)	.459
SD SBP	3.32 (0 to 51,6)	5.62 (1.83 to 14.45)	.029
SD DBP	2.87 (0.5 to 9.47)	3.32 (0.96 to 9.98)	.554
SD heart rate	2.63 (0.82 to 10.02)	2.38 (1 to 9.11)	.442
Home BPV			
CV SBP	0.07 (0.04 to 0.14)	0.08 (0.03 to 0.23)	.283
CV DBP	0.08 (0.05 to 0.17)	0.09 (0.05 to 0.13)	.344
CV heart rate	0.08 (0.03 to 0.2)	0.08 (0.05 to 0.18)	.633
SD SBP	8.1 (3.81 to 15.83)	8.88 (4.61 to 22.83)	.359
SD DBP	5.85 (3.24 to 12.12)	6.57 (2.89 to 11.35)	.287
SD heart rate	6.33 (3.06 to 15.44)	6.57 (3.71 to 11.9)	.883
ABPM BPV			
SI SBP	0.32 (−0.87 to 5.73)	−0.53 (−14.49 to 4.13)	.027
SI DBP	0.37 (−3.34 to 8.65)	−0.75 (−28.29 to 3.53)	.145
SI heart rate	0.97 (−3 to 4.31)	0.8 (−6.8 to 2.57)	.429

ABPM, ambulatory blood pressure monitoring; BPV, blood pressure variability; CV, coefficient variation; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; SI, smoothness index.

long been known to be closely associated with high BP and hypertension-related organ damage. A reduction in salt intake is therefore recommended as a lifestyle change in hypertensive patients.[18–21] A significant decrease in patients' salt excretion was determined during intermittent fasting in this study. We similarly determined a significant decrease in BP values at office and ABPM BP measurements. We think that decreased salt consumption may have contributed to the fall in BP in the intermittent fasting period. Few studies have investigated the relation between salt consumption and BPV. Özkayar et al[22] reported a positive association between salt intake in diet and BPV in 136 primary hypertensive patients. However, we determined no relation between salt intake in diet and BPV in our study. The relationship between salt consumption and BPV remains unclear. The inconsistency between the results by Özkayar et al and ours may derive from our study involving more prehypertensive and newly diagnosed Stage 1 hypertensive patients and from their not using antihypertensive medication.

Several studies have shown that the 24-hour course of BP is affected by routine activities such as sleep, wakefulness, physical activity, nutrition, and emotional stimuli, while 24-hour BPV is affected by various humoral and vasomotor factors, particularly sympathetic activity.[23,24] Experimental and clinical studies have shown that a low-calorie diet leads to a fall in BP, and there are studies showing increases in BP during refeeding. These studies have shown an increase in sympathetic tonus in the refeeding stage.[3,25] We hypothesized that repletion following a prolonged period of fasting and an alteration in sleep periods (rising before sun-up) might lead to an increase in BPV. We observed an increase in BPV in the intermittent fasting period at calculation of BPV from ABPM data. Our scan of the literature revealed no previous studies investigating the relation between BPV and fasting. Analysis of the parameters affecting BPV revealed that BMI and rising before sun-up both affected BPV. BPV was higher among individuals rising for sahur. We attributed this to waking and returning to sleep and the consumption of an extra meal between the two. Variability was low during the intermittent fasting period among individuals with high BMI, but there was no relation between BMI and BPV before the intermittent fasting period. Recent studies have shown greater mean BP and BPV in overweight or obese patients.[26,27] BPV being low in patients with high BMI during fasting in our study may be attributed to patients with high BMI tolerating hunger better than thinner patients and to lower hormonal variation.

The main objective for many years in the treatment of hypertension has been to lower BP.[7] However, in recent years, in addition to BP, high BPV has also been shown in numerous studies to be important in the occurrence and progression of cardiac, renal, and cerebral events.[28,29] Studies have shown that an increase in BPV is associated with a decrease in microalbuminuria and/or glomerular filtration rate, left ventricular hypertrophy, and stroke.[28–30] We determined an increase in BPV during intermittent fasting, particularly in patients with patients with impaired sleep and wakefulness periods and rising to consume an extra meal. We think that our findings should be further investigated with studies of BPV and renal, cardiac, and cerebrovascular outcomes.

The low patient number represents one limitation of our study of the effect of intermittent fasting on BPV. However, we think that the absence of any previous studies evaluating the effect of intermittent fasting on BPV and that our use of four methods for determining BP nevertheless make our study particularly valuable. Another limitation of this study is that we were unable to measure the amount and variety of foods consumed by our patients. However, we think that our measurement of 24-hour urine and salt excretion make it possible to draw conclusions concerning salt consumption at least.

In conclusion, there are increasing questions concerning whether intermittent fasting leads to health problems in hypertensive and prehypertensive patients. In this study, we investigated the effects of intermittent fasting on BP with office, home, ABPM, and central BP measurements. These four methods have not been used together in any previous study. The effect of intermittent fasting on BPV has also not been investigated previously. Our results show that intermittent fasting produces a significant decrease in office and ABPM BP values but causes no significant change in central BP and home measurements. At the same time, we determined that BPV increases during intermittent fasting, particularly in patients who rise to eat before sun-up. We think that the long-term cardiovascular effects of intermittent fasting should now be analyzed by wider, prospective studies.

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