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Kronik Böbrek Hastalığında Ofis Kan Basıncı-Ambulatuvar Kan Basıncı Korelasyonu; Proteinüri-GFR Kaybıyla İlişkisi

Office Blood Pressure-Ambulatory Blood Pressure Correlation in Chronic Renal Disease; The Relationship Between Proteinuria- GFR Loss

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ÖZ

GİRİŞ ve AMAÇ: *Hipertansiyon, kronik böbrek hastalığı (KBH)'nın progresyonu ve ayrıca böbrek dışı morbidite ve mortalitede ciddi bir risk faktörüdür. Kan basıncının doğru ölçümü bu nedenle önemlidir. Bu çalışmada KBH olan ve olmayan hastalarda poliklinik kan basıncı ve ambulatuvar kan basıncı monitoziasyon (AKBM) ölçümlerinin, renal komplikasyonlar, kan basıncı paternleri ve diğer klinik ve labaratuvar verileri ile karşılaştırılarak incelenmesi amaçlanmıştır.*

YÖNTEM ve GEREÇLER: *Çalışmaya son 1 yıl içinde Selçuk Üniversitesi Tıp Fakültesi Nefroloji polikliniğinde takip edilen ve AKBM yapılan 163 hasta dahil edildi. Bu hastaların 61'i(%37,4) prediyaliz KBH, 102 (%62,6) 'i KBH tanısı olmayan hipertansif grupta idi. Hastaların AKBM sonuçları ve poliklinikte yapılan son 3 ölçümlerinin (ofis kan basıncı=OKBM) ortalaması tarandı. ABKM- OKBM arasındaki korelasyon, ayrıca bu iki ölçüm yöntemi ile klinik ve laboratuar verileri arasındaki korelasyon değerlendirildi. KBH olan ve olmayan grupta OKBM-AKBM ölçümleri, bu ölçümlerin demografik ve laboratuar verileri ile ilişkisi karşılaştırıldı.*

BULGULAR: *Ofis kan basıncı ölçümleri, ambulatuar kan basıncı ölçümlerinden anlamlı olarak yüksek bulundu. Sistolik ve diastolik KB ortalamaları OKBM'da 147/89 mmHg, AKBM'da ise 127/ 80 mmHg idi (p<0,01). OKBM'a göre 114 hasta hipertansif iken AKBM'a göre 65 hasta hipertansif idi (p<0,01). Ofis sistolik ve diastolik kan basıncı proteinüri ve GFR ile korele bulunmadı (p>0,05). Ancak AKBM ile ölçülen hem 24 saatlik hem gündüz hem gece ölçüm ortalamalarının proteinüri ile anlamlı şekilde pozitif korele, GFR ile anlamlı olarak negatif korele olduğu bulundu.*

TARTIŞMA ve SONUÇ: *Kronik böbrek hastalarında kan basıncı ambulatuar kan basıncı yöntemleri ile izlenmelidir. Renal hasarın önlenmesinde AKBM ofis kan basıncı ölçümüne göre daha etkili bir yol olabilir.*

Anahtar Kelimeler: *Kronik böbrek hastalığı, hipertansiyon, ambulatuvar kan basıncı monitorizasyonu*

ABSTRACT

INTRODUCTION: *Hypertension is a serious risk factor in the progression of chronic kidney disease(CKD), as well as in nonrenal morbidity and mortality. The correct measurement of blood pressure, therefore, is important. In this study, it was aimed to compare the office blood pressure(OBPM) and ambulatory blood pressure monitoring(ABPM) measurements in patients with and without CKD with renal complications and other data.*

METHODS: *163 patients who were followed up in the our outpatient clinic in the recent year, and who underwent ABPM were included in the study. 61 (37.4%) were in the pre-dialysis CKD group and 102(62.6%) were in the hypertensive group without CKD. Patients' ABPM results and the average of the last 3 measurements in the outpatient clinic(OBPM) were screened. Correlation between ABPM and OBPM, as well as the correlation between other data. OBPM-ABPM measurements in patients with and without CKD and their relation with demographic and laboratory data were compared.*

RESULTS: *OBPM measurements were found to be significantly higher than ABPM measurements. The mean systolic and diastolic BP values were 147/89 mmHg in OBPM and 127/80 mmHg in ABPM(p<0.01). While 114 patients were hypertensive according to OBPM, 65 patients were hypertensive according to ABPM(p<0.01). OBPM measurements were'nt correlated with proteinuria and GFR(p>0.05). However it was found that the 24-hour measurement averages measured with ABPM significantly correlated with proteinuria in positive direction while correlating significantly with GFR in negative direction.*

DISCUSSION and CONCLUSION: *In patients with CKD, blood pressure should be monitored by ABPM. ABPM can be more effective way to prevent renal damage than OBPM.*

Keywords: *chronic kidney disease, hypertension, ambulatory blood pressure monitoring*

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INTRODUCTION

Hypertension is one of the most important risk factors that can be modified in patients with chronic kidney disease. Therefore, control of blood pressure is one of the main goals in slowing the progression to end stage renal failure in this patient group. Office blood pressure monitoring (OBPM) are the most commonly used method for monitoring blood pressure. However, the gold standard in blood pressure monitoring is ambulatory blood pressure monitoring (ABPM). It is more valuable both in progression of disease and in diagnosis, as well as in predicting complications (1). It is also necessary to perform ABPM for the diagnosis of White coat hypertension (WCH) and masked hypertension (MHT). It has been known for a long time that OBPM is higher than the methods measured outside the hospital (2). Therefore we aimed to investigate this difference and the related tables in our pre-dialysis CKD patient group.

METHODS

After the approval of the Local Ethics Committee of the Selçuk University Faculty of Medicine was obtained, the study was started. (2019/71) Files of patients who were admitted to the nephrology outpatient clinic of our hospital, and who underwent ABPM during 1 year were screened retrospectively, starting from February 2019. Patients' demographic data, height, weight, body mass index (BMI), other systemic diseases, antihypertensives they used were recorded from their files. From laboratory data, urea, creatinine, glomerular filtration rate, sodium, potassium, calcium, phosphorus, uric acid, albumin, lipid profile and hemogram results were screened.

CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula was used to calculate eGFR of the patients (3). Chronic kidney disease was identified according to the KDIGO 2012 clinical practice guideline (4). The study included patients with normal renal function, and patients in all pre-dialysis stages between 1 and 5. Hemodialysis, peritoneal dialysis and renal transplant patients were excluded from the study.

OBPM (Office blood pressure monitoring):

Blood pressure of all patients was measured in the sitting position manually by the oscillatory method with the same aneroid device (Maxima Perfect aneroid, Turkey), which was regularly calibrated, from the non-dominant arm after patients rested for at least 5 minutes. Systolic blood pressure (SBP)≥140 mmHG and/or diastolic blood pressure (DBP)≥90 mmHg, or the patient's being previously diagnosed with hypertension, or the patient's using antihypertensive, was defined as hypertension. Patients' average of the last 3 OBPMs prior to ABPM were calculated (5)

ABPM (Ambulatory blood pressure monitoring):

ABPM measurements were made with 7 same-brand (Mobil-O-Graph, Germany) holter devices. Measurements were made using appropriate cuffs for the patients. Patients were advised to continue their daily activities but not to exercise heavily. Daytime (07.00-23.00) and nighttime (23.00-07.00) measurements were performed every 30 minutes. In the ABPM results, 24-hour mean blood pressure ≥130/80 mmHg, or daytime mean blood pressure ≥135/85 mmHg, or nighttime mean blood pressure ≥120/70 mmHg was defined as hypertension.

White coat hypertension: While the blood pressure was ≥140/90 mmHg in OBPM, the mean daytime blood pressure being <130/80 mmHg in ABPM and the mean daytime blood pressure being <135/85mmHg, and the mean nighttime blood pressure being <120/70mmHg was defined as WCH.

Masked hypertension: While the blood pressure was <140/90 mmHg in OBPM, the mean 24-hour blood pressure being ≥130 and/or 80 mmHg in ABPM and/or the mean daytime blood pressure being ≥135 and/or 85 mmHg and/or the mean nighttime blood pressure being ≥120 and/or ≥70 mmHg was defined as MHT.

Chronic hypertension: Office blood pressure being ≥140 mmHg and/or ≥90 mmHg, and 24-hour mean blood pressure being ≥130 and/or 80 mmHg in ABPM, and/or the mean daytime blood pressure being ≥135 and/or 85 mmHg, and/or the mean nighttime blood pressure being ≥120 and/or ≥70 mmHg was defined as CH (5).

RESULTS

The study was completed with a total of 163 patients. The mean age of the patients was 50.3±14.3 years. Of 163 patients, 92 (56.4%) were female. Of the patients, 61 (37.4%) were pre-dialysis CKD and 102 (62.6%) were non-CKD

hypertensive patients. The mean BMI of the patients was 29.7±5.8 and the mean GFR was 92.4±34.4 mL/ min. Other demographic, blood pressure and laboratory data of the patients are shown in Table 1. 85.2% of patients with CKD and 63.7% of patients without CKD were using at least one antihypertensive drug. Demographic, blood pressure, laboratory data, and antihypertensive drugs used by patients with and without CKD are shown in Table 2.

Table 1. Clinical and laboratory data of all patients in the study

Patients	Results
Age (years)	50.3±14.3
Gender (F/M)	92/71
Group CKD, n Non-CKD Hypertension, n	61 102
BMI (kg/m^2)	29.7±5.8
DM	53/163
Hypertension	132/163
Coronary artery disease	11/152
Office SBP (mmHG) Office DBP (mmHG)	147±26.4 89±15.7
24-hour mean aeteral pressure (MAP) (mmHg)	100±14.3
ABPM 24-hour mean SBP (mmHg) ABPM 24-hour mean DBP (mmHg)	127±15.5 78±11.6
ABPM mean daytime SBP (mmHg) ABPM mean daytime DBP (mmHg)	128±15.7 80±15.7
ABPM mean nighttime SBP (mmHg) ABPM mean nighttime DBP (mmHg)	122±17.3 74±12.6
WCH	47 (28.8%)
MHT	14 (8.6%)
CH	45(27,6%)
Creatinine (mg/dl)	1+0.8
GFR (ml/min)	92±34.4
Albumin(g/dl)	4.1±0.5
Uric acid (mg/dl)	5.8±1.5
LDL cholesterol (mg/dl)	133±43.5
Spot pro/cre(mg/g kre)	138 (18-18531)
Spot ma/cre (mg/g kre)	147 (1-9258)
Hemoglobin(g/dl)	13.6±1.9

Table 2. Demographic dataof patients with and without CKD

	CKD (+)	CKD (-)	p value
Age (Years)	52.7±14.9	48.8±13.8	0.09
Gender (F/M)	21/40	71/31	<0.01*
Body Weight (kg)	81.5±17.1	83±16,1	0.58
BMI (kg/m2)	28.5±5.6	30.3±5.8	0.06
DM	25/61	28/74	0.08
Coronary Artery Disease	11/50	0/102	<0.01*
WCH	12/61	34/102	0.06
MHT	6/61	9/102	0.82
CH	33/61	33/102	<0.01*
Creatinine (mg/dl)	1.7±1.1	0.7±0.14	<0.01*
GFR (ml/min)	62.7±37.3	110±14.5	<0.01*
Albumin(g/dl)	3.9±0.6	4.2±0.3	<0.01*
Uric Acid(mg/dl)	6.6±1.5	5.2±1.2	<0.01*
LDL (mg/dl)	136±53	131±35	0.56
Spot pro/cre(mg/gr cre)	1290 (40-18531)	85 (18-205)	<0.01*
Spot ma/cre(mg/gr cre)	466 (2,4-9258)	9.7 (1-29)	<0.01*
Hemoglobin (g/dl)	13.4±2.3	13.6±1.6	0.55
Antihypertensive drugs			
ACEI	14	19	
ARB	28	33	
CCB	25	35	
Beta blocker	11	4	
Alpha blocker	10	6	
Diuretics	18	19	
Number of medications	1.6	1	

ABPM and OBPM averages of all patients were compared. The mean SBP was 147±26.4 mmHg and the mean DBP was 89±15.7 mmHg in OBPM. In ABPM, the mean SBP was 127±15.5 mmHg and the mean DBP was 80±15.7 mmHg. OBPM measurements were significantly higher than ABPM measurements (p<0.01 for SBP and DBP measurements) (Tablo 3).

Table 3. Comparison of OBPM-ABPM averages in all patients

	Office BP	ABPM	ABPM daytime	p value
Systolic blood pressure (mmHg)	147±26.8	127±15.5*	128±15.7*	<0.01
Diastolic blood pressure (mmHg)	89+15.7	78±11.6*	80±11.7*	<0.01

p value <0.01 compared with office BP

Hypertensive patients were compared according to OBPM and ABPM. According to the OBPM and

ABPM results, the number of hypertensive and non-hypertensive patients was significantly different in all groups (p<0.01). While 114 (69.9%) patients were hypertensive according to OBPM, 98 (60.1%) patients were hypertensive according to ABPM.

Whether there was any difference between the measurements of OBPM and ABPM in patients with and without CKD were evaluated. There was no significant difference between the values of OBPM SBP and DBP in patients with and without CKD. OBPM SBP was 150±28.8 mmHg in patients with CKD and 146±24.8 mmHg in non-CKD patients (p=0.3). OBPM DBP was 92±17 mmHg in patients with CKD and 87±14.7mmHg in non-CKD patients (p=0.08). ABPM measurements were significantly different in patients with and without CKD, and the ABPM measurements were significantly higher in patients with CKD (Table 4).

Table 4. Comparison of OBPM and ABPM measurements in patients with and without CKD

	Patients with CKD	Patients without CKD	p value
Office SBP (mmHg)	150±28.8	146±24.8	0.3
Office SBP (mmHg)	92±17	87±14.7	0.08
ABPM 24-hour SBP (mmHg)	132±15.7	123±14.5	<0.01*
ABPM 24-hour DBP (mmHg)	82,8±11.6	76±11	<0.01*
ABPM daytime SBP (mmHg)	133±15.9	125±14.9	<0.01*
ABPM daytime DBP (mmHg)	84±11.6	78±11.3	<0.01*
ABPM nighttime SBP (mmHg)	128±18.2	118±15.6	<0.01*
ABPM nighttime DBP (mmHg)	78±13.1	71±11.6	<0.01*
MAP 24-hour (mmHg)	103±17	98±12	<0.01*
MAP daytime (mmHg)	106±12.1	99±12.2	<0.01*
MAP nighttime (mmHg)	101±14.1	93±13.1	<0.01*

Correlation of office blood pressure measurements and ABPM measurements with laboratory and demographic data of patients was also evaluated. There was no significant correlation between Office SBP and DBP and GFR, spot urine protein/creatinine, spot urine microalbumin/creatinine and albumin values. When ABPM measurements were compared with these data, there was a significant positive correlation between spot urine pro/creatinine ratio and ABPM 24-hour SBP and DBP, daytime SBP and DBP, nighttime SBP and DBP, 24-hour daytime and nighttime ABP measurements. There was a significant positive correlation between spot urine microalbumin/creatinine ratio and ABPM 24-hour DBP, daytime DBP, nighttime SBP and DBP and MAP night measurements. There was a significant negative correlation between GFR and ABPM 24-hour SBP and DBP, daytime SBP and DBP, nighttime SBP and DBP, 24-hour total MAP, nighttime and daytime MAP measurements. There was a significant negative correlation between albumin values and nighttime SBP and DBP (Table 5). When the groups were separated as pre-dialysis CKD and non-CKD patients, there was a significant positive correlation between ABPM nighttime DBP (r=0.32, p=0.02) and spot microalbumin/creatinine in CKD group. There was a significant correlation between spot urine pro/creatinine and ABPM DBP total (r=0.29, p=0.02), ABPM daytime DBP (r=0.30, p=0.02) and ABPM nighttime DBP (r=0.30, p=0.02). In this patient group, negative correlation (r=-0.31, p=0.01) between GFR and the mean nighttime SBP and nighttime MBP continued. There was no significant correlation between these parameters and OBPM measurements in CKD group. In the non-CKD group, a significant negative correlation was found only between GFR and ABPM nighttime SBP (r=-0.24, p=0.01).

Statistical analysis

Data analysis was performed using SPSS 21.0 version. The parametric data were presented as mean ±standard deviation, and nonparametric data as median (min-max) values. In dependent groups, paired Simples T test was used for normally distributed variables, and Wilcoxon test was used for variables that did not conform to normal distribution. In comparison of two independent groups, Student's T test was used for normally distributed variables, and Mann-Whitney U test was

used for variables that did not conform to normal distribution. Pearson and Spearman correlation analysis were used to evaluate the correlation between the groups. The level of significance was accepted as p=0.05.

Table 5. Correlation of blood pressure measurements with renal parameters in all patients

		Office SBP	Office DBP	OAB Total	OAB day	OAB night	24h avg SBP	24h avg DBP	Day SBP	Day DBP	Night SBP	Night DBP
Spot urine ma/cre	r value	0.1	0.07	-0.007	0.21*	0.22*	0.18	0.22*	0.16	0.21*	0.23*	0.28*
	p value	0.26	0.41	0.94	0.01	0.01	0.05	0.01	0.07	0.02	0.01	<0.01
Spot urine pro/cre	r value	0.08	0.04	-0.06	0.22*	-0.08	0.25*	0.27*	0.24*	0.28*	0.24*	0.28*
	p value	0.31	0.57	0.46	0.01	0.77	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
GFR	r value	-0.1	-0.07	-0.13	-0.2	-0.24	-0.31*	-0.23*	-0.29*	-0.20*	-0.38*	-0.29*
	p value	0.2	0.31	0.31	0.31	0.22	<0.01	<0.01	<0.01	0.01	<0.01	<0.01
Albumin	r value	0.06	0.11	0.02	0.06	0.15	-0.16*	-0.06	-0.13	-0.04	-0.23*	-0.13
	p value	0.41	0.14	0.8	0.42	0.05	0.04	0.44	0.09	0.59	<0.01	0.1

DISCUSSION

OBPM has been used for almost a century for blood pressure monitoring and is the most common method of monitoring blood pressure. However, in many studies, OBPM measurements have been shown to be higher than they should be in reality. For this reason, ABPM is the gold standard in hypertension diagnosis and MHT-WCH diagnosis, because of its superiority in non-dipper pattern detection (2). Hypertension prevalence in the CKD patient group varies between 60-100% and its prevalence increases with the progression of CKD (6). The correct diagnosis and treatment of hypertension, which is an important contributor to progression in CKD patients, is therefore important. In a compilation study reviewing ABPM in patients with CKD by Cohen et al., in the pre-dialysis CKD group, there was a significant correlation between ABPM measurements and SBP progression and cardiovascular mortality (1).

We also evaluated the relationship between OBPM and ABPM measurements in pre-dialysis patients with and without CKD, as well as evaluating the correlation between renal parameters such as creatinine, GFR, albumin, spot urine albumin/creatinine, spot urine protein/creatinine.

Our OBPM measurements were significantly higher than ABPM measurements (p<0,01 for each 2 measurements). This is a long-known situation (2). When we divided the groups as those with and without CKD, we found that in both groups, OBPM was still significantly higher. In a study by Jahromi et al., in patients with CKD, patients' measurements in the office were found to be significantly higher than ABPM measurements (7). In SPRINT ABPM Study, ABPM measurements were found to be lower than office measurements in a study involving 275 CKD patients comparing blood pressure measurement techniques (8).

One of the important findings of our study is that although OBPM is not associated with renal damage

findings such as GFR and proteinuria, there was a significant correlation between ABPM measurements and renal damage findings. Consistent with our results, in a study by Agarwal et al., on patients with CKD, there was a stronger relationship between ambulatory blood pressure and proteinuria compared to home and clinical blood pressure measurements (9). Similarly, while ABPM was independently associated with progression of albuminuria in diabetic patients, it was not associated with office blood pressure (10).

A recent study in patients over 60 years of age in China investigated the relationship between clinical and 24 h blood pressure and chronic kidney damage. They described chronic kidney injury as eGFR 60 mL/ min and/or microalbuminuria. In multiple logistic regression analysis, while clinical, 24-hour mean, daytime and nighttime SBP were significantly correlated with low eGFR, 24-hour mean, daytime and nighttime SBP were found to be significant risk factors for microalbuminuria. The strongest correlation was found between 24-hour mean SBP and chronic kidney damage (11).

In a study investigating hypertension-associated target organ damage (ECG, echocardiography and microalbuminuria were investigated for target organ damage findings.), ABPM measurements were reported to correlate better with organ damage than OBPM (12). A similar condition has also been shown in CKD patients. In an Italian study involving stage 2-4 pre-dialysis CKD patients, patients after ABPM were followed for 4.2 years. Primary endpoints were determined as the time of renal death time (end-stage renal disease or death) and fatal or nonfatal CV events. During the follow-up, 155 patients reached the renal endpoint and 103 patients reached cardiovascular end point. At the end of the study, it was shown that office blood pressure measurements did not predict renal and cardiovascular end point. As a result, in chronic renal disease, ambulatory BP measurement and, in particular, night BP measurement were concluded to provide more accurate prediction of renal and cardiovascular risk (13). Agarwal et al. also investigated whether office BP and ABPM predicts end-stage renal failure and death in 217 patients with CKD. After 3.5 years of follow-up, in patients with CKD, ABPM was found to be a stronger predictor of ESRD or death compared to clinical blood pressure (14).

The blood pressure measurement of ABPM allow us to obtain real-life data, during the night sleep and during the patient's daily routine activity. The ESH/ESC 2018 guideline recommends the use of out-of-office blood pressure measurements (ABPM and/or HBPM) as an alternative to repeated office blood pressure measurements to confirm HT diagnosis. Among the specific indications in which use of ABPM is recommended, CKD patients are also included. Other indications in which use of ABPM is recommended include patients with suspected nocturnal HT, such as sleep apnea, DM, endocrine HT or autonomic dysfunction (15).

In the Turkish Hypertension Consensus Report, it was stated that ABPM was the ideal method in the diagnosis and follow-up of HT, and it was suggested to be used in all possible cases. If the possibilities are limited, ABPM is recommended to be used for the following cases: Office and home blood pressure discrepancy, investigation of dipping status, suspicion of nocturnal HT, determination of blood pressure variability (16).

In 2018, a striking data was published in our country. How many of the 1650 hypertensive patients included in the PatenT-2 study had a sphygmomanometer and validation of devices were evaluated. As a result, 332 (20.1%) patients were reported to have sphygmomanometer, although wrist device use and non-validated device use were widespread, and the appropriate cuff size selection was neglected (17).

All of this shows that the importance of ABPM in HT evaluation has been increasing gradually. The fact that the use rates of correct device for home blood pressure measurements in our country is very low, that it has been shown that office blood pressure measurements can be misleading in the diagnosis of HT in our study, and that ABPM is associated with signs of renal damage, but not office BP, has once again supported the importance of ABPM.

Our study has some limitations. We could not evaluate the prognostic effect of different blood pressure measurement methods or findings on cardiac damage due to the retrospective design of our study. The number of CKD patients in our study was relatively low.

Conclusion

In patients with chronic kidney disease, ABPM is

more closely associated with findings of renal organ damage compared to the office blood pressure. Office blood pressure measurement does not seem to be an optimal technique. This group of patients with high-risk should be monitored with ABPM measurements, as office blood pressure measurements may lead to misdiagnosis and unnecessary treatment in the CKD patient population.

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