



Comparisons between different blood pressure measurement techniques in patients with chronic kidney disease

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Background: Automated office blood pressure (AOBP) machines measure blood pressure (BP) multiple times over a brief period. We aimed to compare the results of manual office blood pressure (MOBP) and AOBP methods with ambulatory BP monitoring (ABPM) in patients with chronic kidney disease (CKD).

Methods: This study was performed on 64 patients with CKD (stages 3–4). A nurse manually measured the BP on both arms using a mercury sphygmomanometer, followed by AOBP of the arm with the higher BP and then ABPM. Mean BP readings were compared by paired *t* test and Bland–Altman graphs.

Results: The mean \pm standard deviation (SD) age of participants was 59.3 ± 13.6 . The mean \pm SD awake systolic BP obtained by ABPM was 140.2 ± 19.0 mmHg, which was lower than the MOBP and AOBP methods (156.6 ± 17.8 and 148.8 ± 18.6 mmHg, respectively; $P < 0.001$). The mean \pm SD awake diastolic BP was 78.6 ± 13.2 mmHg by ABPM which was lower than the MOBP and AOBP methods (88.9 ± 13.2 and 84.1 ± 14.0 mmHg, respectively; $P < 0.001$). Using Bland–Altman graphs, MOBP systolic BP readings showed a bias of 16.4 mmHg, while AOBP measurements indicated a bias of 8.6 mmHg compared with ABPM.

Conclusion: AOBP methods may be more reliable than MOBP methods for determining BP in patients with CKD. However, the significantly higher mean BPs recorded by AOBP method suggested that AOBPs may not be as accurate as ABPM in patients with CKD.

Keywords: Ambulatory blood pressure monitoring, Chronic renal insufficiency, Hypertension, Sphygmomanometers

Received September 12, 2018; Revised February 7, 2019;

Accepted February 23, 2019

Edited by Gheun-Ho Kim, Hanyang University College of Medicine, Seoul, Korea

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Introduction

Chronic kidney disease (CKD) is a worldwide health problem with an age-standardized prevalence of 15% and an estimated incidence of 173.5 per 100,000 populations in Iran [1]. CKD ultimately leads to end-stage renal disease requiring renal replacement therapy, and is also associated with numerous complications including cardiovascular disease (CVD) [2], infection, and death [3].

Various risk factors are associated with CKD, including age, female sex, high body mass index (BMI), hypertension (HTN), diabetes mellitus, and dyslipidemia [4,5]. In

addition, CKD exhibits a graded relationship with HTN, with a higher relative risk of CKD associated with higher stages of HTN [6]. The pathogenic mechanisms of nephropathy at the molecular level in hypertensive patients with CKD have been the subject of numerous investigations [7]. In addition, patients with CKD are at increased risk for developing resistant HTN [8], often requiring multiple medications for blood pressure (BP) control. Various guidelines have been proposed for controlling BP in such patients [9].

In some patients, BP measurements obtained in the office can lead to a diagnosis of HTN even though 24-hour ambulatory BP monitoring (ABPM) recordings would be normal. This phenomenon is referred to as white-coat HTN (WCHT) [10], and is frequently observed in patients with CKD [11,12]. The prevalence of WCHT and masked HTN (MHT) (normal BP in clinic but high BP in ABPM) in patients with CKD varies among studies [11,13]. Whereas both WCHT and MHT share a close relationship with target organ damage in patients with CKD, MHT is associated with a level of risk similar to that of persistent HTN [13,14]. Accordingly, ABPM is the best method for monitoring BP in patients with CKD [15–17], and contributes to better renal outcomes [18] and decreased CVD risk [19].

Among ABPM recording indices, mean awake BPs are of a greater clinical significance than mean 24-hour readings, and will more accurately predict target organ damage, CVD risk, and facilitate individualized HTN chronotherapy [10]. On the other hand, recent findings indicate that BPs obtained during sleep are predictive of cardiovascular and cerebrovascular risk in patients independent of CKD status [16]. Although international guidelines have documented the clinical and cost-effective superiority of ABPM compared to home and office measurements, long-term ABPM is not practical [20]. Therefore, office and home measurements are routinely used for the measurement of BP [21], which can be performed by various devices both manually and in an automated manner.

Manual and automated methods for measuring BP have been compared in several studies [22–24]. In automated office BP (AOBP) methods, BP is measured several times over a short period of time in the office without the need for the presence of a nurse or physician, and the mean of the measurements is reported by the device. In hyper-

tensive patients without CKD, BP measurements have a stronger relationship with ABPM than conventional manual office BP (MOBP) methods [24,25].

Despite the importance of BP measurement in patients with CKD, the validity of AOBP monitoring has not been widely evaluated in such patients. Therefore, the present study aimed to compare MOBP and AOBP measurements with ABPM.

Methods

Study design

In this cross-sectional study, we enrolled patients with CKD stages 3 and 4 who were referred to Motahari Nephrology Clinic, Shiraz, southern Iran, during 2016. Sixty-four patients were enrolled in the study by convenience sampling after fulfilment of inclusion/exclusion criteria. The inclusion criteria were glomerular filtration rate (GFR) between 15 to 59 mL/min/1.73 m² (calculated by CKD-EPI formula), office systolic BP of at least 130 mmHg, and diastolic BP of 80 mmHg. We excluded patients with atrial fibrillation and patients whose anti-hypertensive medication had been adjusted in the previous month.

Blood pressure measurements

Blood pressures were initially measured by manual mercury sphygmomanometer of both arms with the patient in a seated position after 5 minutes of rest in a moderate-temperature room. Specifically, each patient was positioned such that he or she had their back pressed against the chair, feet on the ground, and arms at the level of the heart. BP cuffs were selected based on arm size, with the cuff bladder covering at least 80% of the arm circumference. The midline of the cuff bladder was placed over the brachial artery in the antecubital fossa, with approximately 2 cm of space left between the lower end of the cuff and the antecubital fossa for position of a stethoscope.

For automated BP measurements, patients were positioned in the same manner and measurements were obtained with Microlife automated equipment (Watch BP O3; Widnau, Switzerland) three times in one-minute intervals from the arm with the higher reading on MOBP

measurement. The Watch BP O3 device is validated for use in the adult population [26].

All measurements were performed by a single nurse throughout the study. The nurse left the room during AOBP measurements. After a maximum of 48 hours, ABPM was performed for each patient. Before ABPM, patients were educated about the details of Holter use, including the device itself, maintaining their prescribed dose and type of anti-hypertensive medication(s), and continuing their daily activities. The ABPM period was 24 hours, and during this time BP was measured every 30 minutes while awake and once per hour at night during sleep. Each patient was asked about what time they normally wake in the morning and go to sleep at night, and the ABPM device was adjusted accordingly.

Ethical considerations

The study protocol was approved by the Research Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1394.s85). The design and objectives of the study were explained to all participants and written informed consent was obtained. Clarification was provided to all participants that they were free to leave the study whenever they wished. Assurance was provided to all participants that their information would be kept confidential and analyzed anonymously.

Statistical analysis

Results of quantitative variables were presented as mean ± standard deviation and categorical variables were summarized as frequencies and percentages. Comparisons between the variable means were by paired *t* test. *P* values of 0.05 or less were considered statistically significant.

Bland–Altman graphs were used to evaluate the agreement between measured parameters, compare two clinical measurements with specified errors, and compare measurement method to the reference method, especially when the methods contained some inherent degree of error. Bland–Altman graphs are thus useful for evaluating differences between measurements obtained by two methods versus the means of the measurements. In this method of analysis, smaller differences between methods result in obtained points on the graph (or mean differ-

ences) being closer to the x axis zero. When calculating the Bland–Altman limits of agreement, we considered all observations that fell outside the accepted range to represent disagreement between the two methods. Data analysis was performed with PASW Statistics version 18.0 for Windows (IBM Corp., Armonk, USA).

Results

A total of 70 patients with CKD stage 3 or 4 were initially enrolled in our study. The demographic characteristics, results of laboratory examinations, and medical and drug history of patients are shown in Table 1. Six patients refused to undergo 24-hour ABPM. Among the remaining 64 patients, 39 (60.9%) were men and 25 (39.1%) were

Table 1. Baseline characteristics and results of laboratory examinations of study participants

Variable	Data (n = 64)
Age (yr)	59.3 ± 13.6
Sex, male	39 (60.9)
Weight (kg)	76.2 ± 13.8
Body mass index (kg/m ²)	28.1 ± 4.2
Smoking	4 (6.2)
eGFR (mL/min/1.73 m ²)	33.7 ± 11.0
Underlying renal disease	
Diabetes mellitus	27 (42.2)
Hypertension	25 (39.1)
Renal stone	10 (15.6)
Glomerulonephritis	2 (3.1)
Laboratory examinations	
Blood urea nitrogen (mg/dL)	30.2 ± 10.2
Creatinine (mg/dL)	2.1 ± 0.6
Potassium (mg/dL)	4.6 ± 0.5
Calcium (mg/dL)	9.2 ± 0.7
Uric acid (mg/dL)	6.7 ± 1.5
Hemoglobin (g/dL)	12.8 ± 1.8
Anti-hypertensive drugs	
ACEI	7 (10.9)
ARB	46 (71.9)
Alpha blocker	2 (3.1)
Beta blocker	17 (26.6)
Calcium channel blocker	37 (57.8)
Diuretic	6 (9.4)

Data are presented as mean ± standard deviation or number (%). ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate.

women, with a mean age of 59.3 (standard deviation [SD], ± 13.6) years and mean BMI of 28.1 (± 4.2) kg/m². The final study cohort included 27 (42.2%) patients with diabetes mellitus, 25 (39.1%) with HTN, 10 (15.6%) with

a history of nephrolithiasis, and two (3.1%) with a history of glomerulonephritis. With respect to anti-hypertensive medications, 37 patients (57.8%) were being treated with a calcium channel blocker, seven (10.9%) with an angiotensin converting enzyme inhibitor, 17 (26.6%) with a beta-blocker, two (3.1%) with an alpha-blocker, 46 (71.9%) with an angiotensin receptor blocker, and six (9.4%) with a diuretic. No patients in our study were being treated with an erythropoietin-stimulating agent. Four (6.3%) patients were current smokers. The mean \pm SD estimated GFR of the patients enrolled in our study was 33.7 \pm 11.0 mL/min/1.73 m² (range, 15.5–55.3 mL/min/1.73 m²).

Table 2. Blood pressures measured by three different methods in patients with chronic kidney disease

Blood pressure	Method		
	Manual office	Automated office	Awake ambulatory
Systolic blood pressure (mmHg)	156.6 \pm 17.8*	148.8 \pm 18.6*	140.2 \pm 19.0
Diastolic blood pressure (mmHg)	88.9 \pm 13.2*	84.1 \pm 14.0*	78.6 \pm 13.2

Data are presented as mean \pm standard deviation.

*P value < 0.001 compared with awake ambulatory measurements.

Table 2 shows the results of the BP measurements obtained during the study. The mean systolic BP was 156.6 \pm 17.8 mmHg by MOB measurement, 148.8 \pm 18.6 mmHg by AOBP measurement, and 140.2 \pm 19.0 mmHg by awake

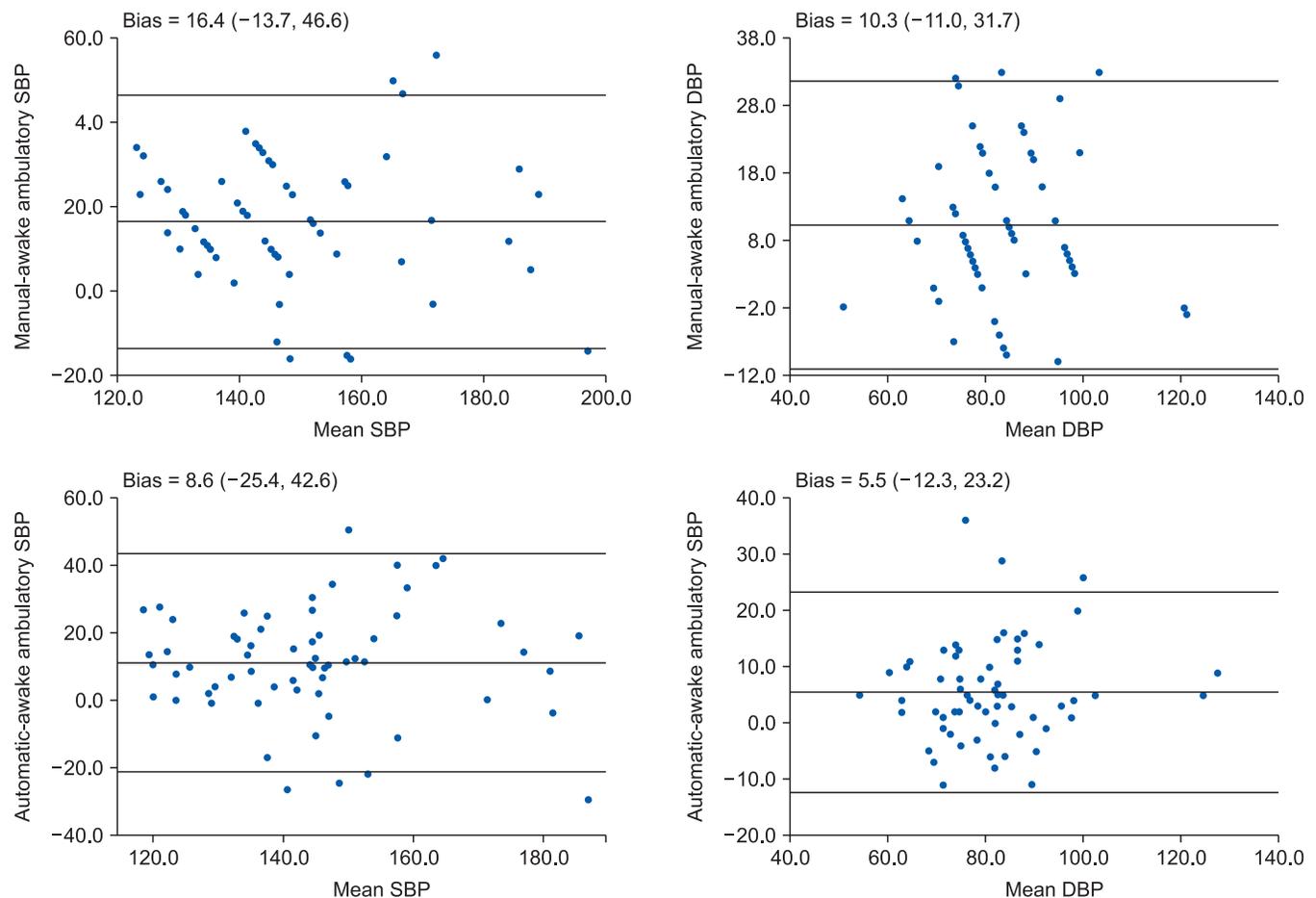


Figure 1. Bland–Altman plots, demonstrating the difference between ambulatory blood pressure measurements and the manual office blood pressure or automated office blood pressure (AOBP) methods vs. mean values. The upper panels display the manual vs. ambulatory systolic and diastolic blood pressure (SBP and DBP) and the lower panels present AOBP vs. ambulatory SBP and DBP measurements.

ABPM. The mean diastolic BP was 88.9 ± 13.2 mmHg by MOBP measurement, 84.1 ± 14.0 mmHg by AOBP measurement, and 78.6 ± 13.2 mmHg by awake ABPM. Pairwise comparison of mean values demonstrated a significant difference between both the MOBP and AOBP methods with awake ABPM ($P < 0.001$ for both, Table 2). The mean 24-hour ABPM systolic and diastolic BPs were 140.0 ± 19.4 and 78.4 ± 13.2 mmHg, respectively.

The mean difference between MOBP measurements and awake ABPM was 16.4 mmHg (95% confidence interval [CI], 12.6–20.1) for systolic BP and 10.3 mmHg (95% CI, 7.6–13.0) for diastolic BP (both $P < 0.001$). The mean difference between AOBP measurements and mean awake ABPM for systolic BP was 8.6 mmHg (95% CI, 4.3–12.8) and 5.5 mmHg for diastolic BP (95% CI, 3.3–7.7) ($P < 0.001$ for both).

The mean difference between systolic MOBP and systolic ABPM measurements was significantly greater than the mean difference between systolic AOBP and systolic awake ABPM measurements (16.4 vs. 8.6 mmHg, $P < 0.001$). The difference for diastolic BP for MOBP was greater than for AOBP (10.3 vs. 5.5 mmHg, $P < 0.001$).

Bland–Altman graphs were used to compare mean awake ambulatory systolic BP measurements with both MOBP and AOBP measurements relative to the mean differences between these readings and ABPM recordings (Fig. 1). The bias of systolic MOBP readings was 16.4 mmHg (2SD –13.7, 46.6), while the bias of AOBP measurements was 8.6 mmHg (2SD –25.4, 42.6).

Discussion

Blood pressure plays a significant role in the pathogenesis of CKD [4]. The hazard ratio of CKD increases with higher HTN stage [6], as does the increased risk of resistant HTN in patients with CKD [8]. Thus, accurate assessment of BP is of great importance for diagnosing HTN. BPs can be measured by various methods, including MOBP monitoring, AOBP monitoring, and ABPM [17,22–24]. Among these options, ABPM is considered the best method for determining BP in patients with CKD. Gorostidi et al [17] showed that office BP control leads to misclassification of BP in one out of three hypertensive patients with CKD, whereas ABPM control rates were much better than office-based rates. However, the use of ABPM for monitoring HTN treatment is impractical in

the long-term. AOBP measurements are more strongly associated with ABPM measurements than conventional MOBP measurements in hypertensive patients without CKD. However, the role of the AOBP technique has not been satisfactorily studied in patients with CKD. Thus, in the present study, we aimed to evaluate the accuracy of AOBP in patients with CKD.

To the best of our knowledge, only one study to date has simultaneously compared ABPM, MOBP, and AOBP [27], although various studies have compared MOBP/AOBP methods with ABPM in patients without CKD [23–25]. In our study, we observed lower systolic and diastolic BP recordings with ABPM compared to MOBP and AOBP, with significant differences noted between both the MOBP and AOBP methods and that of the ABPM method. Consistent with these results, previous studies comparing AOBP and MOBP measurements reported higher mean BPs recorded by MOBP methods [24,25]. Nevertheless, researchers have determined that AOBP recordings correlate with awake ABPM more than MOBP measurements, and have therefore suggested using AOBP measurements in the primary care setting [22–25].

We observed a significant difference between mean BPs measured by the AOBP method and mean awake ABPM in the present study; however, the bias was less than that of MOBP measurements (8.6 vs. 16.4). Agarwal [27] studied the relationship between BP according to method of measurement in the SPRINT trial and routine BP measurements in patients with CKD. In the SPRINT trial, five minutes of seated rest in a quiet room was followed by three oscillometric measurements without an observer in the room [28]. Agarwal [27] concluded that the specified SPRINT trial method resulted in substantially lower BPs than routinely measured single recordings in the clinic. Interestingly, this result is different from not only our study, but from previous studies on AOBPs as well. However, there are some important differences between our study and the study by Agarwal [27]. First, they included CKD patients with BPs less than 140/90 mmHg. Second, routine BP was measured in the supine position by a validated device on the same day after an automated BP was obtained. In our study, we enrolled CKD patients with an office BP greater than 130/90 mmHg. In addition, MOBP measurements were performed prior to AOBP measurements using a sphygmomanometer with the patient in a seated position, consistent with common practice in the

office.

The accuracy of BP measurements by automated devices is influenced by several factors, including the device itself and the patients' condition [24]. The device used in the study by Agarwal [27] was the Omron HEM 907 oscillometric monitor (Omron Healthcare, Kyoto, Japan). Conversely, we utilized a Microlife automated blood pressure monitor. Other automated devices including the PharmaSmart PS-2000 (PlasmaSmart, New York, USA) have been studied, and they do not record BPs that are significantly different from those of awake ambulatory BPs [29]. Although this observation is not consistent with the results of our study, we hypothesized that the Microlife blood pressure monitor may reduce patient stress and decrease the incidence of WCHT owing to the fact that it measures BP several times during a short period and reports a mean of those measurements.

Many of the studies discussed above recruited their study subjects from primary care patients. However, if those same studies had included patients with documented CKD as was done in our study, different BP results might have been obtained. In addition, talking while measuring BP, recording only a single BP, rapid cuff deflation, and digit preference all negatively influence the accuracy of MOBP measurement in daily practice. On the other hand, automated devices record multiple BP readings without the need for a physician or nurse to be physically present, which may decrease the probability of WCHT [22]. Consistent with the results of our study, a comparison of MOBP with AOBP methods using a Dinamap 8100 machine (Critikon, Tampa, USA) showed good agreement, with significantly lower mean BP levels recorded by the AOBP method [30].

Correctly diagnosing HTN is essential, especially in patients with CKD, as these patients have increased risk of HTN and its associated complications, in addition to greater abnormalities during ABPM [6,16]. Although ABPM is the gold standard for BP monitoring, it is only suggested for primary diagnosis and drug adjustment use, because it is difficult to perform routinely [20]. Thus, many studies focusing on HTN in patients with CKD have suggested that patient education and home BP monitoring may be superior to BP monitoring [18]. Although we observed significant fluctuations in ABPM measurements, we also found that the MOBP and AOBP techniques were not as accurate as ABPM. Thus, our results

suggest that further interventions including both patient education and continuous BP monitoring are useful for patients with CKD.

Successive evaluation of BP in the same patients by three measurements was a significant strength of the study, as it allowed us to minimize interpersonal differences as a confounding factor. In addition, all MOBP measurements were performed by a single observer, which limited inter-observer bias. There were some limitations to our study as well, including non-randomization of patients, small sample size, and the cross-sectional nature of the study. Thus, future randomized crossover trials are needed to better evaluate the accuracy of MOBP/AOBP measurements in patients with CKD.

In conclusion, the significantly higher mean BPs recorded by the MOBP and AOBP methods compared to ABPM for patients with CKD in our study support the use of ABPM, at least for primary diagnosis of HTN and monitoring anti-hypertensive therapy. However, because ABPM is not practical for routine use, BPs obtained by automated methods appear to be more accurate than those obtained manually.

Conflicts of interest

All authors have no conflicts of interest to declare.

Acknowledgments

The present article was extracted from the thesis written by Ghasem Haghghi, submitted for a subspecialty in internal medicine. The study was financially supported by Shiraz University of Medical Sciences (Grant No.93-01-01-7562). The authors appreciate the collaboration of Dr. Saeedeh Pourahmad, a biostatistician who supervised the statistical analysis.

Authors' contributions

Shahrokh Ezzatzadegan Jahromi designed the study, performed the literature search, and prepared the manuscript. Shahrokh Ezzatzadegan Jahromi and Ghasem Haghghi had full access to all of the study data and are responsible for the integrity of the data. Shahrokh Ezzatzadegan Jahromi and Vahid Ebrahimi participated in the preparation of the manuscript, statistical analysis,

and data interpretation. Jamshid Roozbeh supervised the study design and data interpretation. All authors have read and confirmed the final version of the manuscript.

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