

## Research Article

# Comparison of Daily Home Blood Pressure Variability in Type 2 Diabetes Mellitus Patients With and Without Diabetic Nephropathy

 Onur Tunca,<sup>1</sup>  Elif Dizen Kazan,<sup>2</sup>  Sinan Kazan<sup>1</sup>

<sup>1</sup>Department of Nephrology, Afyonkarahisar Health Sciences University Faculty of Medicine, Afyonkarahisar, Türkiye

<sup>2</sup>Department of Internal Medicine, Afyonkarahisar Health Sciences University Faculty of Medicine, Afyonkarahisar, Türkiye

### Abstract

**Objectives:** In this study, we aimed to compare daily home blood pressure (BP) variability in Type 2 diabetes mellitus patients with and without diabetic kidney disease (DKD).

**Methods:** We reviewed all Type 2 diabetic patients' files admitted to the nephrology outpatient clinic between January 2021 and January 2022. Patients who applied to our outpatient clinic with 10-day BP measurements at home were included in the study. Patients with  $\geq 30$  mg/g albumin excretion were defined as patients with DKD. Patients with albumin excretion  $< 30$  mg/g were defined as patients without DKD. Systolic and diastolic BP variability was evaluated with the average real variability (ARV).

**Results:** The study was conducted with a total of 243 Type 2 diabetes mellitus patients. The mean age of the patients was  $55.4 \pm 14.9$  years. Systolic ARV (SysARV) was found statistically significantly higher in patients with DKD ( $p=0.009$ ). SysARV was also found to be statistically significantly higher in patients with severe albuminuria than in patients with moderate albuminuria ( $p<0.001$ ). Diastolic ARVs was found to be similar between patients with and without DKD and in albuminuria groups in patients with DKD ( $p=0.289$  and  $p=0.171$ , respectively).

**Conclusion:** The present study shows that systolic BP variability is higher in patients with DKD. Type 2 diabetic patients with higher SysARV can be followed more closely in terms of DKD.

**Keywords:** Albuminuria, blood pressure, diabetes mellitus, diabetic nephropathy

**Cite This Article:** Tunca O, Dizen Kazan E, Kazan S. Comparison of Daily Home Blood Pressure Variability in Type 2 Diabetes Mellitus Patients With and Without Diabetic Nephropathy. EJMI 2023;7(3):215–218.

Diabetic kidney disease (DKD) is the major cause of end-stage renal disease worldwide. It is mostly diagnosed with the presence of albuminuria in clinical practice and may be accompanied by a decline in the estimated glomerular filtration rate (eGFR).<sup>[1]</sup> The presence of albuminuria is considered evidence of increased glomerular permeability to macromolecules.<sup>[2]</sup> Albuminuria excretion values between 30 and 300 mg/g are defined as moderately increased al-

buminuria, and patients with this amount of albuminuria have an increased risk of mortality, cardiovascular mortality, acute kidney injury, chronic kidney disease progression, and end-stage renal disease, even if the eGFR is normal.<sup>[3–6]</sup>

Blood pressure (BP) control has an important place in preventing the progression of DKD. There is a close relationship between BP and poor kidney outcomes in Type 1 and Type 2 diabetic patients.<sup>[7, 8]</sup> While the BP target is  $< 130-80$

**Address for correspondence:** Onur Tunca, MD. Afyonkarahisar Saglik Bilimleri Universitesi Tip Fakultesi, Nefroloji Anabilim Dalı, Afyonkarahisar, Türkiye

**Phone:** +90 532 391 12 31 **E-mail:** dronurtunca@hotmail.com

**Submitted Date:** November 17, 2022 **Revision Date:** January 20, 2023 **Accepted Date:** January 25, 2023 **Available Online Date:** March 21, 2023

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mmHg in patients with DKD, this target is <140–90 mmHg in patients without DKD.<sup>[9]</sup> Although BP targets are clear to prevent DKD progression, BP is dynamic data, and changes are detected between BPs measured at different times in the same patient. BP variability is a current issue and has proven to be a risk factor for morbidity and mortality.<sup>[10, 11]</sup> We could not find any study comparing BP variability in Type 2 diabetic patients with and without DKD.

In this study, we aimed to compare daily home BP variability in Type 2 diabetic patients with and without DKD.

## Methods

### Patients

The electronic files of all Type 2 diabetic patients admitted to the nephrology outpatient clinic between January 2021 and January 2022 were reviewed retrospectively. Patients who applied to our outpatient clinic with 10-day BP measurements at home were included in the study. Those who already have DKD, have Type 1 diabetes mellitus, are younger than 18 years old, are over 80 years old, are pregnant, use any antihypertensive drug, including inhibitors of the renin-angiotensin-aldosterone system, have clinical findings suggestive of non-diabetic glomerular disease, patients with a history of febrile illness within a week and heart failure were not included in the study. A total of 243 patients who met the criteria were evaluated. According to the albumin excretion in the spot urine, the patients were grouped into those with DKD and those without DKD. All complete blood counts of patients were analyzed with an automatic analyzer (Cobas 6000, Roche Diagnostics International AG, Rotkreuz, Switzerland).

### Definition of DKD and Calculation of Variability

Patients with  $\geq 30$  mg/g albumin excretion were defined as patients with DKD. Patients with albumin excretion <30 mg/g were defined as patients without DKD. DKD patients were then grouped into those with moderately increased albuminuria (albuminuria between 30 and 300 mg/g) and those with severely increased albuminuria (albuminuria  $\geq 300$  mg/g).

Average real variability (ARV) was used for variability evaluation. While calculating ARV, nine  $\Delta$ ARV values were obtained from house measurements for 10 consecutive days. The ARV value was calculated by taking the arithmetic average of these nine  $\Delta$ ARV values. ARV formula=

$$ARV = \frac{1}{\sum_{k=2}^n w_k} \sum_{k=2}^n w_k \times |BP_k - BP_{k-1}|$$

n= the number of BP measurements and  $w_k$  is the time interval between  $BP_k$  and  $BP_{k-1}$ .

## Statistical Analyses

Categorical variables were presented as percentage and frequency. The Shapiro–Wilk test was used to check the normal distribution in continuous variables. Mean and standard deviations were used to present continuous variables with normal distribution, and continuous variables without normal distribution were presented as median and interquartile range. Mann–Whitney U test was used in comparisons between the two groups if there was no normal distribution, and the independent sample t-test was used if there was a normal distribution. All the p-values presented were bidirectional and the values with  $p < 0.05$  were expressed as statistically significant. Statistical analyzes were performed with SPSS 26.0 (IBM Corp. 2019 IBM SPSS Statistics for Windows, version 26.0. Armonk, NY: IBM Corp.) package program.

## Results

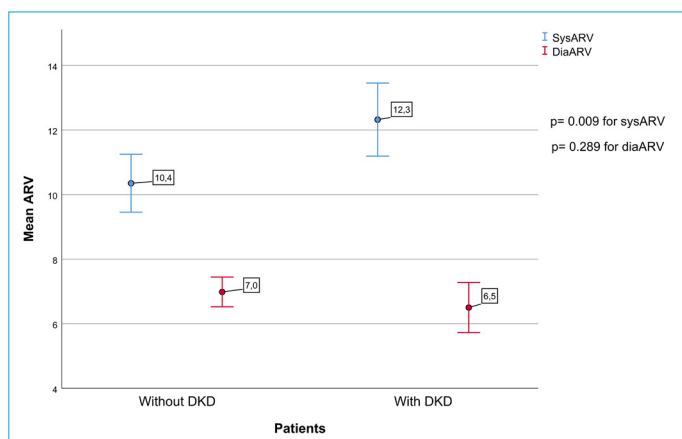
The study was conducted with 243 Type 2 diabetic patients. The mean age of the patients was  $55.4 \pm 14.9$  years. Of the patients, 153 were men (63%). DKD was found in 84 (34.6%) of the patients. While 64 (76.2%) of 84 patients with DKD had moderate albuminuria (30–300 mg/g), 20 (23.8%) had severe albuminuria ( $\geq 300$  mg/g). Patients with DKD had a higher rate of smoking than patients without DKD. Table 1 shows the comparison of the general characteristics of the groups.

While diastolic ARVs (DiaARV) were similar in patients with or without DKD, systolic ARV (SysARV) was found statistically significantly higher in patients with DKD ( $p = 0.289$ , and  $p = 0.009$ , respectively). Fig. 1 shows the comparison of DiaARV and SysARV among patients with or without DKD.

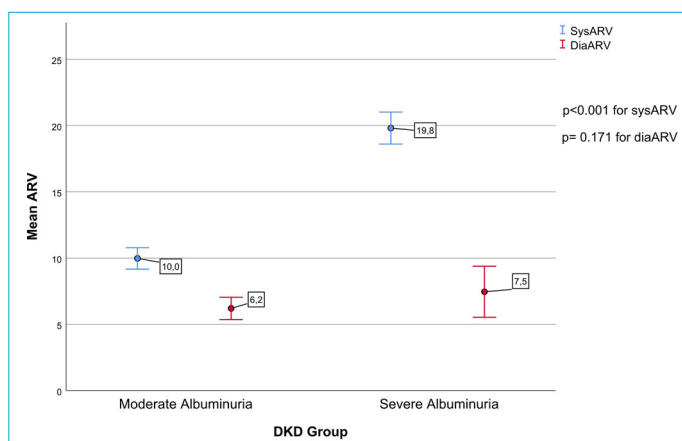
**Table 1.** The comparison of general characteristics between groups

Characteristics	With DKD n= 84	Without DKD n=159	p
Age (years)	56.35±14.8	54.9±14.9	0.458
Male gender (%-n)	58.3-49	65.4-104	0.328
Smoking (% , n)	28.6-24	15.1-24	0.097
BMI (kg/m2)	26.1±2.9	25.7±2.6	0.298
Hemoglobin (g/dL)	12.02±2.6	12.7±2.3	0.053
Creatinin (mg/dL)	0.84±0.2	0.86±0.2	0.548
HbA1c (%)	7.47±0.6	7.21±0.7	0.003
Albuminuria (mg/g)	187.8±90.5	17.54±4.8	<0.001
Office sysBP (mmHg)	125.9±13.1	124.1±13.2	0.294
Office diaBP (mmHg)	84.7±6.3	84.2±5.9	0.568

DKD: Diabetic kidney disease; BMI: Body mass index; HbA1c: Glycated hemoglobin A1c; SysBP: Systolic blood pressure; DiaBP: Diastolic blood pressure.



**Figure 1.** The comparison of ARVs between patients with or without DKD.



**Figure 2.** The comparison of ARVs between DKD groups.

When patients with DKD were compared among themselves, SysARV was found to be statistically significantly higher in patients with severe albuminuria than in patients with moderate albuminuria ( $p < 0.001$ ). DiaARV was similar between albuminuria groups ( $p = 0.171$ ). Fig. 2 shows the comparison of ARVs among patients with DKD.

## Discussion

Systolic and diastolic BPs are both risk factors for DKD, they are also risk factors for the progression of DKD if they cannot be controlled. The ideal BP targets in diabetic patients still vary between guidelines.<sup>[9, 12, 13]</sup> In recent years, in addition to BP measurements, some parameters such as BP variability are thought to be important for target organ damages.<sup>[14, 15]</sup> Diastolic and SysARV values were found higher in hypertensive patients with microalbuminuria than in hypertensive patients without microalbuminuria in Mulè et al.'s study.<sup>[16]</sup> However, in their study, diabetes was more common in the group with microalbuminuria.

In our study, all patients were diabetic, and we found that

the only difference between our patients with and without DKD was SysARV. Another difference between our study from Mulè et al.'s study is that ARV was calculated with 24-h ambulatory BP measurements (ABPM) in their study, whereas ARV was calculated with 10-day home BP measurements in our study. ABPM reflects short-term BP variability and is more demanding than home BP measurement for both patients and health-care professionals.

BP variability can be calculated in many different ways, such as the difference between the minimum and maximum values, coefficient variation, standard deviation, and ARV.<sup>[17, 18]</sup> In a review of 19 studies in which the relationship of ARV with organ damage was summarized, it was emphasized that high ARV values were associated with cardiovascular events and clinical or subclinical organ damage in 17 studies.<sup>[19]</sup> Our findings are also similar to these studies in the literature.

In our study, daily home BP variability in Type 2 diabetic patients with DKD was found to be higher in systolic measurements than in Type 2 diabetes patients without DKD, while daily BP variability in diastolic measurements was found to be similar. In this respect, our findings are similar to the Angiotensin II Antagonist Losartan (RENAAL) study and the Reduction of Endpoints in non-insulin-dependent diabetes mellitus. One arm of the RENAAL study investigating the effects of BP levels on DKD found that high systolic BP was associated with renal outcomes, but not diastolic BP.<sup>[20]</sup>

It was shown years ago by Weir et al.<sup>[21]</sup> that salt-induced systolic BP increases could lead to proteinuria by affecting renal hemodynamics. Our study also shows that SysARV values are higher in patients with DKD than in patients without DKD, and also it is higher in patients with severe albuminuria when compared to patients with moderate albuminuria. In addition; Kitagawa et al.<sup>[22]</sup> showed that isolated systolic hypertension leads to a 2.4-fold increase in risk for the development of DKD. We think that the high SysARV values in patients with DKD in our study may also be due to isolated systolic hypertension in this patient group.

The biggest limitations of our study are its retrospective design and the small number of patients. Moreover, a cause-effect relationship cannot be established according to our findings due to retrospective design. Larger prospective studies may reveal the relationship between ARV and DKD more clearly.

## Conclusion

We found that SysARV was higher in patients with DKD. It was observed that SysARV increased as the severity of DKD increased. Type 2 diabetic patients with higher SysARV can be followed more closely in terms of DKD. In addition, we have shown that daily home BP measurements can be used

in BP variability and still have an important place in treatment planning.

### Disclosures

**Ethics Committee Approval:** The study was approved by Afyonkarahisar Health Sciences University Clinical Research Ethics Committee (Meeting date: November 04 2022, Meeting number: 2022/14, Decision number: 521). Since the study was retrospective, there was no patient consent and the study was conducted in accordance with the Declaration of Helsinki.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – O.T., E.D.K., S.K.; Design – O.T., E.D.K., S.K.; Supervision – O.T., S.K.; Materials – O.T., E.D.K.; Data Collection – O.T., S.K.; Analysis and/or Interpretation – O.T., E.D.K.; Literature Search – O.T., S.K.; Writing – O.T., E.D.K., S.K.; and Critical Review – O.T., S.K.

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