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Nighttime blood pressure dipper pattern is more frequent in type 2 diabetes with normal renal function compared to chronic kidney disease

Dana Mihaela Ciobanu [1], Cornelia Bala [1,2]*, Alice Sfâra [2], Ştefan Cristescu [2], Ioan Andrei Vereşiu [1,2], Gabriela Roman [1,2]

[1] Iuliu Hatieganu University of Medicine and Pharmacy, Faculty of Medicine, Department of Diabetes and Nutrition, Cluj-Napoca, Romania
[2] Emergency Clinical County Hospital Cluj, Romania

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Abstract

It has been reported that patients with non-dipper blood pressure pattern have worse kidney function compared to patients with normal dipper pattern. In our observational study, we aimed to investigate the prevalence of dipping pattern of nocturnal systolic blood pressure and 24-hour blood pressure control in patients with type 2 diabetes and normal renal function CKD(-) (n=90) compared to their peers with diabetic chronic kidney disease CKD(+) (n=90). All patients underwent 24-hour ambulatory blood pressure monitoring (ABPM). We found that nighttime blood pressure dipper pattern was significantly more frequent in patients with type 2 diabetes and normal renal function compared to their peers with diabetic chronic kidney disease (27.7% vs. 13.3%; p=0.016). Mean systolic blood pressure during daytime, nighttime and 24-hour periods were significantly higher in the CKD(+) group, although the percentage of patients achieving 24-hour blood pressure control was not statistically different in two study groups. Our study could have clinical implications regarding recommendations for ABPM and the choice of drug regimens in hypertensive patients with diabetes and CKD.

Keywords: type 2 diabetes; chronic kidney disease; ambulatory blood pressure monitoring

Introduction

Chronic kidney disease (CKD) affects one out of three patients with diabetes. Increased blood pressure (BP) is a common find in type 2 diabetes and worsens CKD progression [1]. 24-hour ambulatory BP monitoring, the gold standard for BP assessment [2], has been established to have prognostic importance, with a particular interest in nighttime systolic BP and BP control [3,4]. The non-dipper nocturnal BP pattern was related with renal damage in patients with CKD, suggesting that special attention should be given to these patients [5,6]. In the Hygia Project, a cross-sectional study which

* Correspondence to: Cornelia BALA,
Address: 2 Clinicilor Street, 400006, Cluj-Napoca, Romania.
Tel.: +4 072 260 5501; Fax: +4 026 459 4455
e-mail: cbala@umfcluj.ro

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included 10271 hypertensive patients irrespective of their diabetes study, it has been reported that the prevalence of non-dipper status was inversely related to kidney function; moreover, significant increase in the proportion with non-dipper status was reported with each increasing stage of worsening CKD [7]. Whether this findings apply to patients with type 2 diabetes remains to be further clarified. We aimed to investigate the prevalence of dipping pattern of nocturnal systolic blood pressure and 24-hour blood pressure control in patients with type 2 diabetes and normal renal function compared to their peers with diabetic chronic kidney disease.

Patients and methods

Study Design and Patients

This was a cross-sectional study performed in the Department of Diabetes and Nutrition, Emergency Clinical County Hospital, Cluj-Napoca, Romania. 180 consecutive adult patients previously diagnosed with type 2 diabetes according to the American Diabetes Association criteria [8] were enrolled between July 2013 and February 2014. For the purpose of this analysis, the patients were divided into two groups according to the presence of diabetic chronic kidney disease according to KDIGO guidelines: normal renal function group CKD(-) (n=90) and diabetic chronic kidney disease group CKD(+) (n=90) [1]. Patients were not included if they had: unstable cardiovascular conditions, secondary hypertension, renal failure, malignancies or were pregnant.

The study was conducted in accordance with International Conference on Harmonization Good Clinical Practice guidelines and Declaration of Helsinki. The study protocol was approved by the local Ethics Committee of the Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania. All patients provided written informed consent before any study procedure.

Study Protocol

Data on age, sex, duration of diabetes and hypertension was collected during patients' interviews and from patients' medical files. Hypertension was diagnosed in the presence of office BP of ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic or the use of antihypertensive drugs [2]. Weight, height and abdominal circumference were measured in fasting state, light dress and with no shoes, and body mass index was calculated. Fasting serum creatinine was collected and assessed in all patients using a commercially available method (Hitachi, Roche Diagnostics). Glomerular filtration rate was estimated (eGFR) using MDRD formula by accessing www.mdrd.com. One morning urine sample was collected in each patient for detecting qualitative urinary albumin.

24-Hour Ambulatory Blood Pressure Monitoring

After blood samples collection, all study participants underwent 24-hour ambulatory BP monitoring using a validated and calibrated automatic device (Hol-CARD CR-07; Aspel, Poland). The protocol of 24-hour ambulatory BP monitoring was described in a study we previously published [9]. The BP control and systolic BP dipper pattern were evaluated during 24-hour ambulatory BP monitoring according to 2018 ESH/ESC guidelines for the management of arterial hypertension guideline recommendations. Dipper pattern was considered present when mean nighttime systolic BP decreased by >10% of the mean daytime systolic BP value [2].

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation or number and percentages after assessing the distribution using Kolmogorov-Smirnov test. Group comparisons of all variables were performed using ANOVA, chi-square test and Kruskall-Wallis tests. Correlations were performed using Pearson coefficient. Statistical analyses were performed using R 2.15.1 program. Statistical significance threshold was considered $p<0.05$.

Results

Characteristics of the study participants

The characteristics of the study groups are presented in Table 1. The groups, CKD(-) and CKD(+), had comparable age, male percentage, body mass index and abdominal circumference. Diabetes and hypertension durations were significantly higher in the CKD(+) group. Estimated GFR was significantly higher in the

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Table 1. The characteristics of the study groups.

Variables	CKD(-) group (n=90)	CKD(+) group (n=90)	p-value
Age (years)	59.4±6.7	61.1±8.1	0.06
Male n, (%)	40 (44.4)	36 (40.0)	0.55
Diabetes duration (years)	8.8±8.1	11.7±8.3	0.019
Hypertension duration (years)	7.5±6.0	10.4±6.7	0.003
Body mass index (kg/m^2)	31.6±4.8	31.7±5.2	0.41
Abdominal circumference (cm)	108.5±11.4	107.9±12.4	0.06
eGFR MDRD (ml/min/1.73m^2)	78.2±12.7	62.9±21.8	0.001
Albuminuria n, (%)	0.0 (0.0)	64 (71.1)	<0.001

CKD, chronic kidney disease; eGFR MDRD, estimated glomerular filtration rate using MDRD formula. Values are means ± standard deviation or number and percentages.

CKD(-) group, while albuminuria was present only in the CKD(+) group.

24-Hour Ambulatory Blood Pressure Monitoring

The 24-hour ambulatory systolic and diastolic BP in the two study groups are presented in Figure 1 and Figure 2. Mean systolic and diastolic BP during daytime, nighttime and 24-hour periods were higher in the CKD(+) group, but the statistical significance was reached only for systolic BP.

We found that nighttime BP dipper pattern was significantly more frequent in the CKD(-) group compared to CKD(+) group (Figure 3).

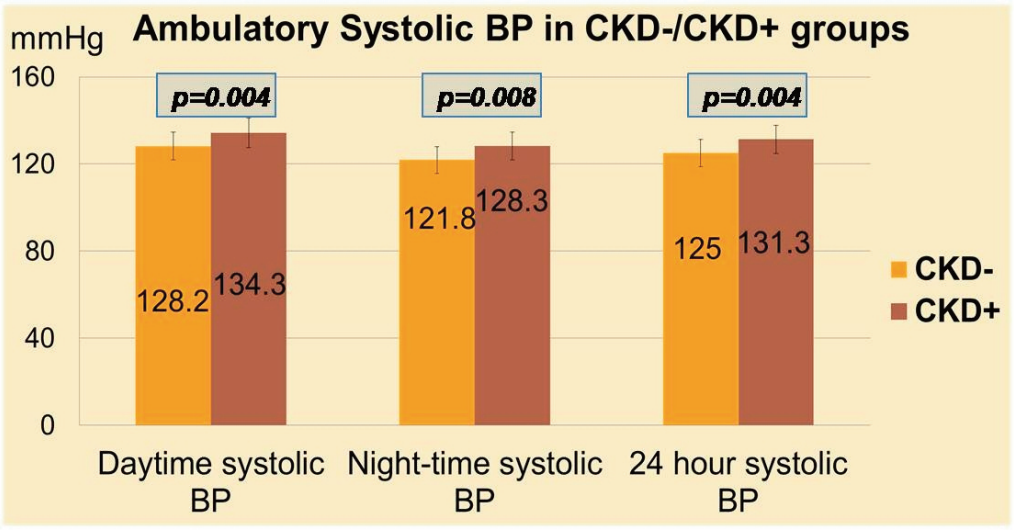

Figure 1. The 24-hour ambulatory systolic blood pressure in the study groups.

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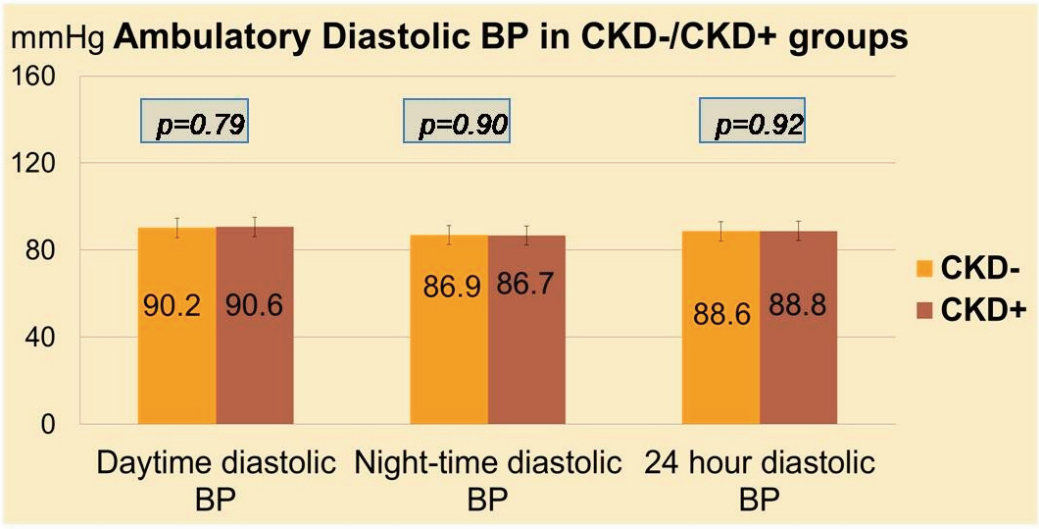

Figure 2. The 24-hour ambulatory diastolic blood pressure in the study groups.

When assessing BP control during 24-hour ambulatory BP monitoring according to the 2018 ESH/ESC guidelines for the management of arterial hypertension, we observed there were no differences în the percentages of patients achieving daytime, nighttime and 24-hour BP control between the study groups (Table 2).

In the study population, the dipper pattern was inversely associated with type 2 diabetes and hypertension durations, the presence of albuminuria, but not with estimated glomerular filtration rate or age (Table 3).

Discussions

We hypothesized that patients with type 2 diabetes and CKD might have a higher prevalence of non-dipper nighttime BP pattern compared to patients with type 2 diabetes and normal renal function. Our results suggest that increased nighttime systolic BP might play pathogenic role in renal function worsening in patients with type 2 diabetes, independently of 24-hour ambulatory BP control. However, due to the cross-sectional design of the study, we cannot rule out that the pres-

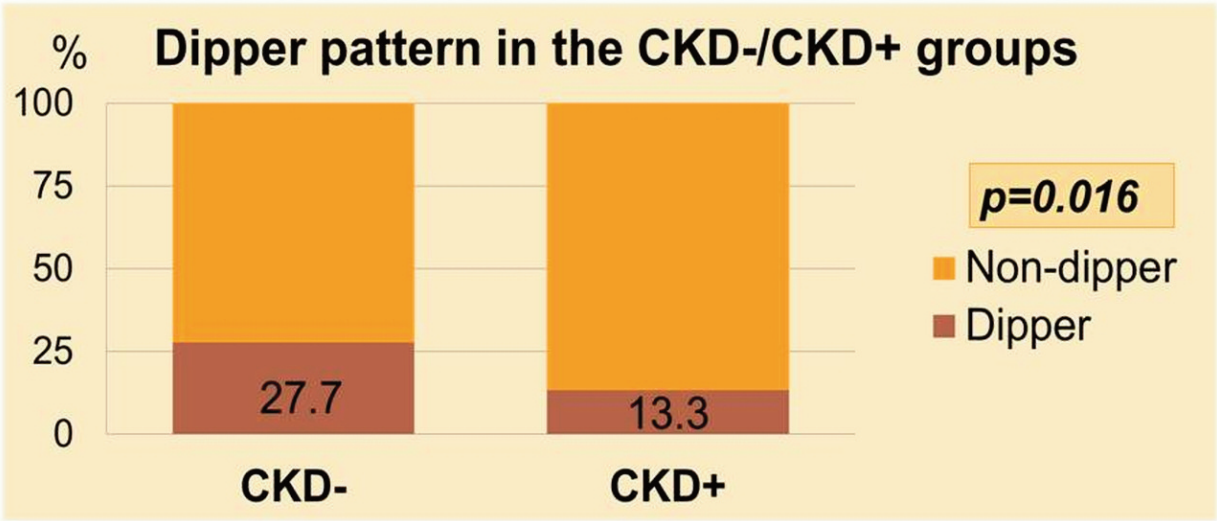

Figure 3. The prevalence of nighttime blood pressure dipper pattern in the study groups.

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Table 2. The 24-hour blood pressure control in the study groups.

Blood pressure control	CKD(-) group (n=90)	CKD(+) group (n=90)	p-value
Daytime BP control (<135/85mmHg)*	23 (25.6%)	27 (30.0%)	0.51
Nighttime BP control (<120/70mmHg)*	2 (2.2%)	2 (2.2%)	1.0
24-hour BP control (<130/80mmHg)*	17 (18.9%)	20 (22.2%)	0.58

BP, blood pressure. Values are number and percentages. * According to 2018 ESH/ESC guidelines for the management of arterial hypertension.

ence of CKD associated to diabetes and hypertension might have also worsened nighttime BP control. Previous studies reported that prevalence of non-dipper status was inversely related to kidney function in the general population, but no data were specifically reported for patients with diabetes [6,7]. Our observation confirms similar results in patients with type 2 diabetes.

Elevated nighttime BP was associated with increased risk of developing hypertension target organ damage, adverse cardiovascular and renal outcomes in patients with normal kidney function [3]. In patients with CKD, non-dipper BP pattern was related to severe renal damage and cardiovascular injuries [5]. When analysing the prevalence of dipper pattern in our study population, we found lower prevalence in patients with normal renal function and even lower prevalence in patients with CKD compared to the prevalence reported in previously mentioned studies (37.1% and 36.1 %, respectively) [3,5]. Our results indicating elevated nighttime systolic BP in patients with CKD and type 2 diabetes might suggest that our population might be at even higher risk of developing the renal and cardiovascular complications. Thus, our observation emphasis the need of ambulatory BP monitoring in type 2 diabetes patients in order to detect and further address for treatment management the patients with increased nighttime systolic BP. Patients concomitantly having CKD may be seen as a higher risk group and be prioritized for ambulatory BP monitoring in low resources settings.

Table 3. The correlations of the dipper pattern in the study population.

	Dipper pattern	
	r coefficient (Pearson)	p-value
Diabetes duration	- 0.22	0.003
Hypertension duration	- 0.16	0.03
Albuminuria	- 0.15	0.048
Age	0.11	0.17
eGFR	0.09	0.26

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

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In the our type 2 diabetes study population, we also report a lower percentage of patients with controlled 24-hour BP compared to the percentage of patients with controlled BP reported in a representative sample of Romanian adults enrolled in SEPHAR II study (25.0 %) [10], and an even lower percentage compared to the percentage recently reported in SEPHAR III study (30.8 %). Moreover, it is estimated that BP control will further increase up to 36.6% in the year 2020 in the Romanian population [11]. A possible explanation of the difference between our results and the results of SEPHAR studies might be related to the method used to assess BP control: we used 24-hour ambulatory BP monitoring, while office BP monitoring was used in the published SEPHAR studies that assessed the percentages of hypertensive patients achieving BP control. Also, the our sample population consisted of type 2 diabetes patients, while the SEPHAR studies enrolled persons from the general population having only 12.2% prevalence of diabetes in the overall study group and 17.5% in the hypertensive group.

Nocturnal variations of BP were closely related to the presence of type 2 diabetes and hypertension [12,3]. We observed that the dipper pattern was inversely correlated with type 2 diabetes and hypertension duration, suggesting that increased nocturnal systolic BP is more likely to be found in patients with longer duration of these diseases.

The dipper pattern of nighttime BP inversely correlated with presence of albuminuria in our study including patients with type 2 diabetes with normal renal function and chronic kidney disease, respectively. Significant interaction between albuminuria and the presence of kidney dysfunction on the changes of 24-hour BP were observed. Albuminuria was reported to be an independent predictor of 24-hour BP changes in persons with renal dysfunction, but not in those with normal renal function. Also, albuminuria was associated with the non-dipper pattern progression, after exclusion of non-dippers at baseline [13]. Albuminuria was reported to be accompanied by striking higher nighttime systolic BP, particularly in patients with hypertension and diabetes with very high albuminuria and low eGFR [14]. Although we performed an observational study, our results confirm the findings of these recent prospective studies investigating the relation between albuminuria and nighttime BP; however, we did not find a significant relation between dipper pattern of nighttime BP and renal function evaluated using eGFR as a continuous variable.

Our study has several implications for the management of our hypertensive patients with type 2 diabetes. First, it draws the attention to the need of ambulatory BP monitoring in this category of patients in order to detect dipper and non-dipper systolic BP pattern with confirmed implication on their further renal and cardiovascular risk. Second, it identifies patients with concomitant CKD as a subgroup at higher-risk for non-dipper pattern that should represent a priority for the access to ambulatory BP monitoring and further adjustment of antihypertensive regimens. The overall BP control in hypertensive patients with type 2 diabetes is still sub-optimal and efforts should be made to improve the quality of care in this category of patients.

Conclusions

We found that nighttime systolic blood pressure dipper pattern was significantly more frequent in patients with type 2 diabetes and normal renal function compared to their peers with diabetic chronic kidney disease. Mean systolic blood pressure during daytime, nighttime and 24-hour periods were significantly higher in the CKD(+) group, although the percentage of patients achieving 24-hour blood pressure control was not significantly different in the two study groups.

Declarations of interest

The authors declare that they have no conflict of interest.

List of abbreviations

ABPM, ambulatory blood pressure control

BP, blood pressure

CKD, chronic kidney disease

eGFR MDRD, estimated glomerular filtration rate using MDRD formula

ESH/ESC, European Society of Hypertension/ European Society of Cardiology

KDIGO, Kidney Disease: Improving Global Outcomes

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