

The Effect of Visit-to-Visit Blood Pressure Variability on Renal Function in Geriatric Chronic Kidney Disease

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Objective: The visit-to-visit variability (VTV) of blood pressure (BP) has been recognized as a risk factor for cardiovascular events and chronic kidney disease (CKD). The objective of this study is to evaluate the association between the VTV of BP and changes in estimated glomerular filtration rate (eGFR) in elderly CKD patients at different stages of renal function.

Materials and Methods: For 60 months, we analyzed the medical records of 105 patients with and without diabetes and hypertension. Systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP) were examined. A multivariable linear regression model was used to analyze the correlation between eGFR and the VTV of BP.

Results: No differences were demonstrated between the groups in the clinical characteristics. Mean SBP and DBP were not significant between the groups, and we observed no decrease in renal function. A significant negative correlation between PP and eGFR was observed in the total CKD population with a P of .010 (95% CI: -0.20, -0.03) and a correlation coefficient of -0.11.

Conclusion: Our study shows no statistical significances in terms of the VTVs of BP in any of the geriatric groups, with no significant decreases in renal function. However, we observed a significant negative correlation between PP and eGFR. We demonstrated that if a VTV of BP does not occur, there is no decrease in eGFR. [*P R Health Sci J* 2023;42(2):127-131]

Key words: Blood pressure, Chronic disease, Glomerular filtration rate, Geriatrics

Hypertension is one of the greatest health concerns worldwide. It is a major contributor to the development of coronary artery disease, heart failure, cerebrovascular accidents, chronic kidney disease (CKD), and death (1,2). Of interest, in the elderly population, blood pressure (BP) variability constitutes a major risk for the development of cardiovascular disease and disability. In recent years, BP variability over several clinical visits has acquired a prognostic value and is recurrent instead of being a random phenomenon. It is being used as a prognostic indicator of cardiovascular and renal disease (3,4).

Independent of mean BP and dietary and medication adherence, visit-to-visit variability (VTV) of BP has emerged as an important risk factor for cardiovascular events and death (5,6). Using ambulatory BP measurements over a 24-hour period, a study revealed an increased risk of left ventricular hypertrophy over a 7-year follow-up, with increased diurnal BP variability (7). Several other studies have confirmed that the VTV of BP confers a high risk for myocardial infarction and death (8–12). In this regard, the National Health and Nutrition Examination Survey study reported an increase in all-cause

mortality associated with the VTV of BP (13). Other reports have shown a decline in cognitive function and increased risk for dementia in individuals over 65 years of age with an increased VTV of BP (14,15). More recently, studies confirmed (in a large group of patients) that the VTV of BP is a prognostic risk factor for cardiovascular events (16,17).

Further studies have also examined the relationship between the VTV of BP and renal outcomes, both in patients with and those without pre-existing CKD. Some investigators showed that higher BP variability was associated with new-onset CKD in patients with and in those without diabetes mellitus

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(DM) (18,19). Other investigators have reported that high BP variability is a novel risk factor for the development and progression of diabetic nephropathy in diabetic patients without CKD (20,21). Indeed, diabetic patients have shown an association of such variability with more clinically impactful renal outcomes, such as the development of end-stage renal disease (ESRD) (22,23). Nonetheless, this association has, essentially, been limited to diabetic individuals with CKD.

In a previous experience, we explored the VVV of BP in diabetic and non-diabetic CKD patients at 3 specific CKD stages, namely, CKD 3A, CKD 3B, and CKD 4 (24). We observed no statistically significant decline in renal function in any of the CKD groups as VVV of BP was not identified. However, it is unclear whether such a relationship would be found elderly patients. Thus, we proceeded to evaluate the above-described association in our geriatric population of CKD patients.

Materials and Methods

A cross-sectional retrospective analysis was done of the medical records of 105 patients aged 60 to 80 years receiving treatment at the Chronic Kidney Disease Clinic of the University District Hospital in San Juan. The patients were divided into 3 groups according to their renal function; eGFR was determined by the 4-variable Modification of Diet in Renal Disease formula, and the changes in eGFR were analyzed during the study period of 60 months. Group I included patients with CKD stage 3A, which latter is defined as having an eGFR from 45 to 59 mL/min/1.73M2. Group II comprised those with CKD stage 3B (eGFR from 30 to 44), and group III was composed of patients with CKD stage 4 (eGFR from 15 to 29). All patients with history of CKD stage 1, CKD stage 2, CKD stage 5, ESRD, as well as those younger than 60 years of age, those older than 80 years of age, and those with a history of malignancy were excluded. Each group consisted of 35 patients, for a total of 105 patients.

To increase the precision of the VVV of BP estimates, data collection was restricted to patients with no fewer than 5 visits from January 2010 through December 2015. Blood pressure and eGFR were collected at each visit, and pulse pressure (PP) was calculated (in mmHg, individually) from each of the 5 BP measurements. The demographic and clinical information included age, gender, height, weight, body mass index (BMI), history of hypertension, baseline BP, history of DM, and baseline serum creatinine level. At the beginning of the study, baseline BP and serum creatinine values were determined and were then compared to other measures taken during the study. Our study was approved by the Institutional Review Board (A8660216) of the University of Puerto Rico Medical Sciences Campus.

Blood pressure and heart rate were measured and recorded simultaneously by trained nursing staff at the CKD clinic for a period of 60 months (January 2010 through December 2015), following the acceptable standards of clinical nephrology care.

The mean office BP and the VVV of BP, expressed as intra-individual standard deviation (SD) and coefficient of variation (CV) ($CV = SD/\text{mean office BP over 5 visits} \times 100 [\%]$), were measured over the 60 months of observation (which included no fewer than 5 visits). Ideal BP parameters were utilized following the guidelines of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, the American Heart Association, and the Kidney Disease Outcomes Quality Initiative (25–27). Dietary counseling on sodium restriction was offered as part of the usual clinical care, and antihypertensive medications were given as required. The primary outcome was the rate of decline in renal function, estimated by fitting a regression line through the eGFR measurements at the beginning and at the end of the observation period. A decrease of more than 30% in eGFR was categorized as significant.

The analyses were performed using the program Stata 14.0. Clinical characteristics were compared using chi-square (for categorical variables); ANOVA and Bonferoni tests were used for continuous variables. Linear regression analyses of the slope of the eGFR were performed. Spearman and Pearson correlation tests were also done.

Results

No differences were observed in the 3 groups studied in terms of the demographic characteristics, including the age, sex, and BMI of the study participants by CKD stage (Table 1). As can be seen in Table 2, the mean SBP, DBP, and PP were not significant. The mean SBP in patients with CKD 3A was 139.2; in those with CKD 3B, it was 139.9 and was 143.2 in those with CKD 4. The P value was not significant. The mean DBP was 77.9 in patients with CKD 3A, 77.0 in those with CKD 3B, and 75.5 in those with CKD 4; the P value was not significant. The mean PP

Table 1. Demographic characteristics of study participants by CKD stage (n = 105)

Characteristic	CKD Stage			P value
	CKD 3A (n = 35)	CKD 3B (n = 35)	CKD 4 (n = 35)	
Age (mean) n (95% CI)	68 (66–70)	69 (67–71)	69 (67–71)	.6461 ^A
Sex				
Male n (%)	20 (57)	19 (54)	23 (66)	
Female n (%)	15 (43)	16 (46)	12 (34)	.5990 ^X
BMI, kg/m ² n (95% CI)	30 (28–32)	29 (27–30)	28 (26–30)	.4490 ^A
History of DM				
Yes n (%)	16 (46)	16 (46)	17 (49)	.8500 ^X
History of Hypertension				
Yes n (%)	27 (77)	28 (80)	26 (74)	.9620 ^X

CKD: chronic kidney disease; BMI: basal metabolic index [kg/M²]; DM: diabetes mellitus; ^Xchi-squared test; ^A1-way ANOVA. Data are reported as mean with a confidence interval of 95%.

Table 2. Clinical measures of study participants by CKD stage (n = 105)

Measure	CKD Stage			P value
	CKD 3A (n = 35)	CKD 3B (n = 35)	CKD 4 (n = 35)	
Creatinine	1.4 (1.3–1.5)	1.7 (1.6–1.8)	2.6 (2.3–2.8)	<.001 ^A
SBP ¹	140 (133–148)	142 (135–148)	149 (141–157)	.2423 ^A
DBP ²	79 (75–83)	75 (71–79)	78 (74–82)	.2671 ^A
eGFR ³	51 (50–53)	39 (37–41)	24 (23–25)	<.001
PP ⁴	64 (58–69)	67 (60–73)	70 (64–77)	.3199 ^A
SBP ¹	137 (129–145)	139 (132–146)	145 (135–154)	.4050 ^A
DBP ²	76 (72–81)	78 (74–81)	76 (72–81)	.8643 ^A
eGFR ³	51 (48–54)	37 (35–39)	24 (23–26)	<.001 ^A
PP ⁴	61 (54–67)	62 (56–67)	68 (60–77)	.2348 ^A
SBP ¹	138 (131–145)	140 (134–147)	142 (135–149)	.7408 ^A
DBP ²	77 (73–81)	74 (71–78)	76 (72–80)	.6557 ^A
eGFR ³	48 (45–50)	39 (37–41)	25 (24–27)	<.001 ^A
PP ⁴	61 (54–68)	66 (60–72)	66 (60–72)	.4921 ^A
SBP ¹	138 (132–144)	138 (129–146)	141 (132–149)	.8583 ^A
DBP ²	77 (74–81)	78 (74–83)	75 (71–78)	.4060 ^A
eGFR ³	47 (45–50)	38 (36–41)	25 (24–27)	<.001 ^A
PP ⁴	61 (55–66)	60 (53–66)	66 (58–74)	.3907 ^A
SBP ¹	144 (137–150)	140 (134–146)	139 (132–147)	.6403 ^A
DBP ²	79 (75–83)	80 (76–83)	72 (68–77)	.0170 ^A
eGFR ³	49 (47–52)	38 (36–41)	24 (22–25)	<.001 ^A
PP ⁴	64 (59–70)	61 (56–65)	67 (60–74)	.2876 ^A

CKD: chronic kidney disease; ¹SBP: systolic blood pressure (mmHg); ²DBP: diastolic blood pressure (mmHg); ³eGFR: estimated glomerular filtration rate (mL/min/1.73m²); ⁴PP: pulse pressure (mmHg). ^A1-way ANOVA. Data are reported as mean with a confidence interval of 95%.

was 62.1 in patients with CKD 3A, 63.0 in those with CKD 3B, and 67.6 in those with CKD 4; the P value was not significant.

The result of the correlations was examined using the Spearman test with Holm corrections to adjust for multiple comparisons based on an alpha value of 0.05. Table 3 presents the correlations of clinical characteristics with eGFR by CKD stage. When we analyzed the eGFR of each of the groups (CKD 3A, 3B, and 4) with the different pressure variables (SBP, DBP, and PP) of each one, no statistical relationship was found between them. However, when we analyzed the total population of patients older than 65 years with CKD, we observed a significant negative correlation between eGFR and PP ($r_s = -.11$; $P = .010$; 95% CI [-0.20, -0.03]). The correlation coefficient between eGFR and PP was -.11, indicating a weak effect. This correlation indicates that as PP increases, eGFR tends to decrease significantly. These observations are illustrated in Figure 1.

Table 3. Correlations between eGFR and Systolic blood pressure, Diastolic blood pressure, and Pulse pressure by CKD stage

Variable	CKD stage 3A rho	P value	CKD stage 3B rho	P value	CKD stage 4 rho	P value	CKD Total rho	P value
SBP	-0.04	.629	-0.06	.418	0.05	.516	-0.07	.0928
DBP	0.03	.687	-0.04	.579	0.09	.228	0.07	.0600
PP	-0.05	.518	-0.09	.248	0.03	.743	-0.11	.010

CKD: chronic kidney disease; SBP: systolic blood pressure (mmHg); DBP: diastolic blood pressure (mmHg); PP: pulse pressure (mmHg)

Discussion

Our study showed no statistically significant VVV of BP in any of the geriatric CKD patients. The VVV of SBP was not linked to a decrease in renal function in CKD 4 patients, while in CKD 3A and CKD 3B patients, it was associated with a non-statistically significant decline in renal function. The VVV of PP exhibited a similar pattern. Our results demonstrated that in the absence of VVV of BP, the eGFR would not be expected to decrease. These observations are in accordance with those of the study of Yokota et al; this team studied 69 diabetic CKD patients, though without analyzing them by CKD stage, which individuals demonstrated no decline in renal function in the presence of VVV of BP (20). In contrast to the findings of this study, our results, which explored 105 patients, were observed in both diabetic and non-diabetic CKD patients at 3 specific CKD stages. In addition, as shown in Table 1, age and BMI did not vary between the studied groups. In addition, Lasserson et al, in a 5-year retrospective cohort study of a spectrum of CKD patients, showed that the worsening of renal function was associated with small increases in the VVV of BP (28).

Upon our analysis of the total population of patients older than 65 years with CKD, we observed a significant negative correlation between eGFR and PP. In our previous study on CKD patients, the VVV of PP exhibited a weak correlation observed in all the stages of CKD, but with a tendency for significance (24). Comparing both studies, we found that this significantly negative correlation was observed because there was a larger sample studied in this elderly population. This correlation may be associated with increased vascular calcification, such as is reported in elderly patients, as well as in advanced CKD stages (29,30).

Other studies have looked into renal variables. One such was a retrospective cohort study of 354 participants with diabetes that demonstrated that the coefficient of variation of SBP positively correlated with age, duration of diabetes, and changes in urinary albumin excretion (31). A post hoc analysis from the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan study and the Irbesartan Diabetic Nephropathy Trial by McMullan et al demonstrated significant increased risk at renal end points with an SBP

greater than 140 mmHg and a PP greater than 70 mmHg. The adjusted risk for ESRD or death increased with a hazard ratio of 1.96 (95% CI: 1.40–2.74) (32). Furthermore, the TRial Of Preventing Hypertension emphasized that the number and timing of visits and the device used to measure BP influence VVV and need to be considered when researchers are designing, interpreting, and comparing studies (33).

A recent study by Wang et al in 207 hospitalized male elderly and 277

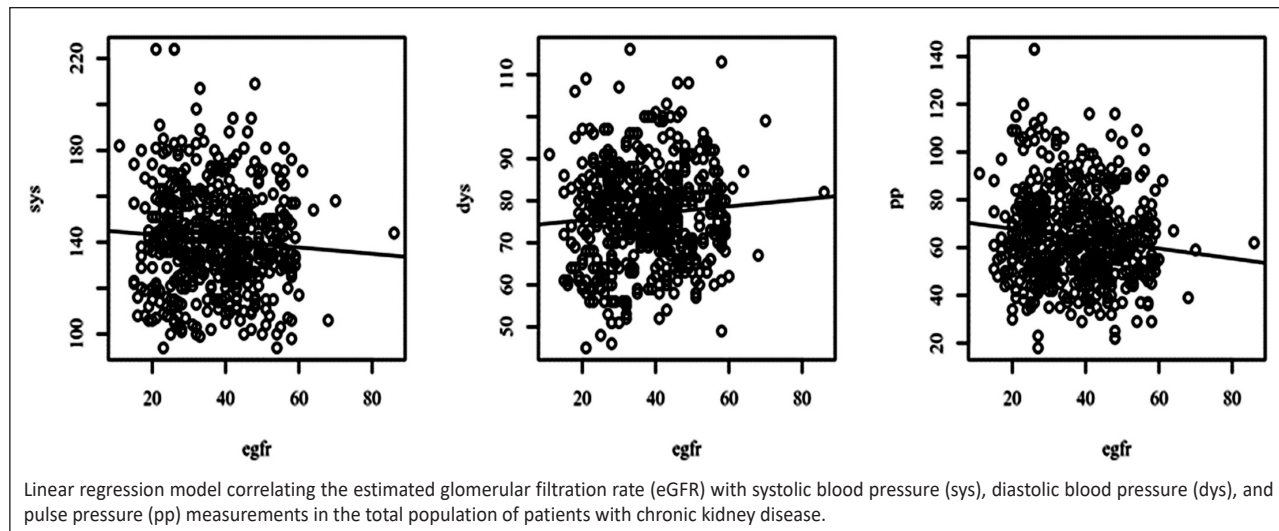


Figure 1. Scatterplots between each variable, with the regression line added

hospitalized male very elderly patients, all with a controlled BP and all using ambulatory BP monitoring, disclosed that the only independent variable associated with a decline in renal function was the 24-hour SBP variability (34). Although we know very little of the mechanism involved in the VVV of BP, there are 2 distinct factors which may explain them in the elderly patient: namely, autonomic dysfunction and arterial stiffness. These abnormalities are more prevalent in the elderly than in younger populations.

In addition to these reported findings, further analyses divided the elderly patients into 3 groups based on eGFR (eGFR > 90, eGFR < 90 to \geq 60, eGFR < 60). In these 3 groups, they observed no differences when associating renal function with the VVV of BP. This finding supports the observations of our study regarding the different stages of CKD in the elderly population.

However, several limitations were reported in the Wang study; for example, it was a cross-sectional observational study with a small sample size, and only male subjects were included (all of whom were hospitalized and restricted from undertaking any kind of physical activity). In contrast, our study had specific limitations. It also had a small sample size but it had a retrospective observation period. In addition, in terms of our own study, the number and timing of the patient visits may be another limiting factor to consider.

Conclusion

Our present study demonstrates that the VVV of BP was not correlated with a decline of renal function in a 60-month period in elderly CKD patients at 3 different stages of renal dysfunction. We believe that these patients' good control of their BP during the period of observation contributed to preserving their renal function. These findings may serve as a stimulus to investigate VVV in a large population of elderly CKD patients to associate the progression and severity of CKD.

Resumen

La variabilidad entre visita a visita en la presión arterial (PA) ha sido reconocida como un factor de riesgo para los eventos cardiovasculares y la enfermedad renal crónica (ERC). Objetivo: Evaluar la relación entre la VVV en PA con cambios en la tasa de filtración glomerular estimada (TFGe) en envejecientes con diferentes estadios de ERC. Metodología: Analizamos los expedientes de 105 pacientes por espacio de 60 meses. Presión arterial sistólica (PAs), diastólica (PAd) y de pulso (PP) fueron examinadas. Modelos de regresión lineal se utilizaron para correlacionar la TFGe y VVV en PA. Resultados: Las características demográficas no revelaron diferencias entre los tres grupos de ERC. La media de la PAs y PAd no fueron significativas entre los grupos y no se observó un deterioro en la función renal. Se observó una correlación negativa significativa en la PP y la TFGe en la población total de ERC ($p = 0.010$, IC 95% [-0.20, -0.031] y -0.11 coeficiente de correlación). Conclusión: Nuestro estudio no demostró significancias estadísticas en la VVV de PA en los tres grupos y no se observó un deterioro significativo en la función renal. Podemos esperar que la TFGe no disminuya si no se observa VVV en la PA.

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