

Effect of Renal Disease on Ambulatory Blood Pressure Monitoring

Efecto de la enfermedad renal sobre el monitoreo ambulatorio de la presión arterial

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ABSTRACT

Background: Chronic renal disease is a growing public health problem, not only for its progression to end-stage renal failure but for its close association with cardiovascular disease, especially hypertension. Currently, there is scarce information on ambulatory blood pressure monitoring (ABPM) in hypertensive patients with renal failure.

Objective: The aim of this study was to assess ABPM pulse pressure, circadian rhythm and blood pressure variability in a population of hypertensive patients with renal failure.

Methods: A cross-sectional study evaluated 123 consecutive ABPM performed in a Hypertension Service. The glomerular filtration rate was estimated using the abridged formula from the “Modification of diet in renal disease” (MDRD) study.

Results: A total of 123 hypertensive patients were evaluated (age 66 ± 7.5 years, 56% men), whose glomerular filtration rate was 64.5 ± 19.4 ml/min/1.73m². Thirty-seven percent of patients presented with renal failure with a glomerular filtration rate of 45 ± 12.5 ml/min/1.73m² vs. 76 ± 11.9 ml/min/1.73m² in patients without renal failure. Fifty-five hypertensive patients (44%) had elevated pulse pressure: 28 (60.9%) with renal failure vs. 27 (35%) without renal failure ($p < 0.005$). After adjusting for different variables, this difference remained significant. No differences were found in blood pressure variability or in the presence of non-dipper pattern.

Conclusions: The main ABPM characteristic in hypertensive patients with renal failure was a significant increase of pulse pressure. There was no greater prevalence of non-dipper pattern or increased blood pressure variability, as classically described for the general population of renal disease patients.

Key words: Ambulatory blood pressure monitoring – Renal failure – Pulse pressure

RESUMEN

Introducción: La enfermedad renal crónica es un problema creciente para la salud pública, no solo por su progresión a enfermedad renal terminal sino por su estrecha relación con la enfermedad cardiovascular, en particular con la hipertensión arterial. En la actualidad existen pocos datos acerca del monitoreo ambulatorio de la presión arterial (MAPA) en los pacientes hipertensos (PH) con insuficiencia renal (IR).

Objetivo: el objetivo del presente estudio fue evaluar la presión de pulso (PP), el ritmo circadiano y la variabilidad de la presión arterial en el MAPA en una población de PH con IR.

Materiales y métodos: Se realizó un estudio de corte trasversal donde se evaluaron 123 MAPAs consecutivos realizados en un servicio de Hipertensión Arterial y se estimó el filtrado glomerular (FG) a través de la fórmula abreviada proveniente del estudio “Modificación de la dieta en la enfermedad renal” (MDRDa).

Resultados: Se evaluaron 123 pacientes hipertensos (edad 66 ± 7.5 años, 56% sexo masculino). El FG de la población estudiada fue 64.5 ± 19.4 ml/min/1.73m². El 37% presentó IR con un FG de 45 ± 12.5 ml/min/1.73m² vs. 76 ± 11.9 ml/min/1.73m² en los pacientes sin IR. 55 PH (44%) presentaron PP elevada: 28 PH (60.9%) con IR vs. 27 PH (35%) sin IR, $p < 0.005$. Luego de ajustar por diferentes variables esta diferencia permaneció significativa. No hubo diferencias en la variabilidad de la presión arterial y en la presencia de patrón non dipper.

Conclusiones: En los pacientes hipertensos con IR observamos, como característica principal del MAPA, un aumento estadísticamente significativo de la presión de pulso. No se halló mayor prevalencia de patrón non dipper o aumento de la variabilidad de la presión arterial, lo que clásicamente está descripto para poblaciones de enfermos renales en general.

Palabras clave: Monitoreo ambulatorio de la presión arterial -Insuficiencia renal -Presión de pulso

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Abbreviations

PCr	Plasma creatinine	MDRD	Abridged formula from the "Modification of diet in renal disease" study
DM2	Type 2 diabetes mellitus	BP	Blood pressure
GFR	Glomerular filtration rate	MAP	Mean arterial pressure
HTN	Hypertension	SBP	Systolic blood pressure
BMI	Body mass index	HP	Hypertensive patient
RF	Renal failure	NDP	Non-dipper pattern
ABPM	Ambulatory blood pressure monitoring	PP	Pulse pressure

INTRODUCTION

Chronic renal failure (RF) has become a growing public health problem due to the progressive increase of its prevalence and the economic costs it entails, not only for the elevated number of dialysis or kidney transplant cases but also for its close association with cardiovascular disease. Effectively, patients with RF are more prone to present cardiovascular complications rather than progress to end-stage RF. At present, RF is considered a risk factor for the development of cardiovascular disease. (1)

More than 11% of the general adult population in the United States has impaired renal function and approximately 40% of these patients have a glomerular filtration rate (GFR) below 60 ml/min/1.73 m². (2) Australia, (3) Japan, (4) and Europe (5) show a prevalence of RF ranging between 6% and 11%. This is enhanced in higher risk individuals, as hypertensive patients (HP) and/or diabetic patients, in whom the incidence of RF reaches 50-60%. (6) In Latin America in general and particularly in our country there are no overall data on HF prevalence, although as the incidence of hypertension (HTN) and type-2 diabetes mellitus (DM2) -main contributors to the development of RF- is similar to that of the above-mentioned countries, it may be assumed that the prevalence of RF is similar to that in the rest of the world. A study performed in HP attending a Hypertension Service of the City of Buenos Aires (7) revealed the presence of RF in 19.6% of the population studied.

There is a strong relationship between HTN and RF. On one hand, HTN is very frequently found in RF patients, where 60% to 100% of patients present with HTN. (8) On the other hand, RF constitutes the most frequent cause of secondary HTN. (9) Moreover, HTN is the most clearly modifiable factor for the progression to chronic RF. (10) Thus, the correlation between HTN and RF is a truly deleterious circle both for the kidney as for the cardiovascular system.

There is ample evidence showing that blood pressure (BP) values obtained by 24-hour ambulatory blood pressure monitoring (ABPM) correlate better with target organ injury than BP obtained in the office, (11) making ABPM a better predictor of cardiovascular events. Recent studies have shown that the presence of a non-dipper pattern (NDP), increased pulse pressure (PP) in ABPM (12) and higher BP variability, (13) are variables associated with high cardiovascular risk.

According to the available information, most studies identifying ABPM characteristics in RF patients were performed in patients with end-stage renal disease, in dialysis/ transplant or with specific glomerular diseases. However, there are practically no studies showing ABPM characteristics in patients with RF secondary to DM2 and/or HTN.

The purpose of this study was to evaluate PP, BP circadian rhythm and variability in ABPM in a population of HP with renal injury attending a Hypertension Service.

METHODS

A cross-sectional study evaluating 123 consecutive ABPM was performed in a Hypertension Service during 3 months. All subjects aged over 50 years with BP \geq 140/90 mmHg, undergoing ABPM, were included in the study. Pregnant and type 1 diabetic patients were excluded from the analysis. The following data were obtained from the clinical records: sex, age, weight, height, waist circumference, family history of DM2, current smoking habit, average of three BP measurements in the office corresponding to the visit in which the ABPM device was withdrawn and antihypertensive medication. The following lab tests were done: lipid panel, blood glucose level, and the average of the last two plasma creatinine (PCr) measurements.

Methodology

Glomerular filtration rate was calculated using the abridged formula from the "Modification of diet in renal disease" (MDRD) study: (14)

$$186.3 \times (\text{PCr})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ in women}).$$

A GFR < 60 ml/min/1.73 m² was considered for RF, and the HP population was divided into two groups: HP with RF and HP without RF.

Plasma creatinine was assessed with the modified Jaffe method.

A validated automatic equipment (MEDITECH CARDIOTENS ABPM-04) was used to perform ABPM. (15). Ambulatory blood pressure monitoring with more than 80% effectiveness in BP measurements with respect to expected values, and at least one recorded measurement per hour was considered valid. The equipment was programmed to perform recordings every 15 minutes during the day (7:00 to 22:00 hours) and every 20 minutes during the night (22:00 to 7:00 hours). Then, for the analysis of BP circadian variability daytime and nighttime schedules were matched to those referred by the patient. A non-dipper pattern was defined as mean arterial pressure (MAP) reduction during nighttime below 10% of daytime value, (16) and elevated PP was considered for an average 24-hour PP greater than the

mean value of the study population. (10) Daytime systolic blood pressure (SBP) standard deviation was used as indicator of variability, and was considered elevated for values greater than 15 mmHg. (13, 17)

Statistical analysis

Statistical analysis was performed with Student's t test for continuous data with normal distribution, the chi-square test to compare nominal variables, and logistic regression analysis as appropriate, using Stata 9.0 statistical software package. A p value < 0.05 was considered as statistically significant.

Ethical considerations

The protocol was evaluated and approved by the Bioethics Institutional Board

RESULTS

A total of 123 HP with a mean age of 66 ± 7.5 years were evaluated. Among these patients, 69 (56%) were men, 46 (37.4%) had RF, 54 (44%) DM2, and 50 (41%) were obese [body mass index (BMI) ≥ 30 kg/m²]. Table 1 shows the general population characteristics.

The GFR of the study population was 64.5 ± 19.4 ml/min/1.73 m².

Forty six HP (37.4%) presented with RF, with a mean GFR of 45 ± 12.5 ml/min/1.73 m² vs. 76 ± 11.9 ml/min/1.73 m² in HP without RF (n=77, 62.6%). General characteristics showed that significant differences between both groups were only found for PCr and GFR, the latter variable being used to divide the groups. Table 2 shows ABPM and office BP measurements for the studied patients.

Fifty-five HP (44.7%) presented with elevated PP, 28 HP with RF (60.9%) vs. 27 HP without RF (35%), p<0.005. Hypertensive patients with RF had significantly higher 24-hour PP, (61 ± 11 vs. 56 ± 10 mmHg, p=0.007), as well as daytime (61 ± 11 vs. 56 ± 11 mmHg, p=0.009) and nighttime (61 ± 12 vs. 56 ± 11 mmHg, p=0.009) values. After adjusting for age, sex, presence of obesity, DM2, and 24-hour MAP, this difference continued to be significant (Table 3).

Higher SBP was observed during the nighttime period (131 ± 15 vs. 126 ± 14 mmHg, p=0.04).

Fifty-four HP (44%) presented with NDP, with no significant difference between patients with or without RF [25 HP with RF (54.3%) vs. 29 HP without RF (37.7%); p=ns].

Seventy-five HP (61%) had increased BP variability, without statistically significant difference between both groups [30 HP with RF (65.2%) vs. 45 without RF (58.4%); p=ns].

DISCUSSION

This study analyzed the main ABPM characteristics associated with HTN or DM2 in HP with RF that usually attend a Hypertension Service. Although several studies have tried to define the role of ABPM in the management of patients with RF, the difference is that most of these studies were performed in patients with end-stage RF, dialysis or transplant, (18-20) very different from the hypertensive patient who normally attends the consultation.

The ABPM analysis in our population showed that the HP group with RF presented with significantly higher 24-hour PP, both during daytime and nighttime periods, compared with the HP group without RF. No significant differences were found for NDP and BP variability.

Great arteries, in addition to their conduction function, transform pulsatile flow into continuous flow thanks to their viscoelastic properties. With the passage of time, arteries start losing their distensibility leading to increased SAP, reflex wave velocity and decreased diastolic BP, with the resulting selective increase of PP. The decreased elasticity of the great arteries has deleterious effects at the cardiovascular level. Therefore, increased PP is considered an independent risk predictor for cardiovascular disease (21), and its identification is essential for the evaluation of risk in the hypertensive patient.

In our study, HP with GFR < 60 ml/min/1.73 m² had significantly higher 24-hour PP, both during day-

Table 1. General characteristics of the study population

	Total (n=123; 100%)	With RF (n=46; 37.4%)	Without RF (n=77; 62.6%)	p
Age, years	66 ± 7.5	67 ± 8	65 ± 7	ns
Men, % (n)	56.1 (69)	50 (23)	59.7 (46)	ns
BMI, kg/m ²	28 ± 4	28 ± 4	29 ± 4	ns
Obesity, % (n)	40.7 (50)	41.3 (19)	40.3 (31)	ns
Waist circumference, cm	97 ± 13	99 ± 11	96 ± 15	ns
DM2, % (n)	43.9 (54)	47.8 (22)	41.6 (32)	ns
PCr, mg/dl	1.2 ± 0.51	1.6 ± 0.64	0.96 ± 0.15	< 0.001
GFR, ml/min/1.73 m ²	64.5 ± 19.4	44.9 ± 12.4	76.1 ± 11.9	<0.001

Continuous variables are expressed as mean ± standard deviation. Dichotomous variables are expressed as percentage (%) and number of patients (n). RF: Renal failure. BMI: Body mass index. DM2: Type 2 diabetes mellitus. PCr: Plasma creatinine. GFR: Glomerular filtration rate. ns: Not significant.

	Total (n=123; 100%)	With RF (n=46; 37.4%)	Without RF (n=77; 62.6%)	p
SBP	147 ± 15	148 ± 17	146 ± 14	ns
DBP	83 ± 11	81 ± 11	85 ± 11	0.046
24 hours				
Systolic	135 ± 12	137 ± 12	134 ± 12	ns
Diastolic	77 ± 9	76 ± 9	78 ± 9	ns
PP	58 ± 11	61 ± 11	56 ± 10	0.007
MAP	96 ± 9	96 ± 9	97 ± 8.5	ns
Daytime				
Systolic	138 ± 12	140 ± 12	138 ± 12	ns
Diastolic	80 ± 10	78 ± 10	82 ± 9	ns
PP	58 ± 11	61 ± 11	56 ± 10	0.009
MAP	100 ± 9	99 ± 9	100 ± 9	ns
Nighttime				
Systolic	128 ± 15	131 ± 15	126 ± 14	0.04
Diastolic	70 ± 10	70 ± 11	70 ± 10	ns
PP	58 ± 12	61 ± 12	56 ± 11	0.009
MAP	89 ± 10	91 ± 11	89 ± 10	ns
Elevated PP, % (n)	44.7 (55)	60.9 (28)	35 (27)	0.005
Non Dipper, % (n)	43.9 (54)	54.3 (25)	37.7 (29)	ns
Variability, % (n)	61 (75)	65.2 (30)	58.4 (45)	ns

Continuous variables are expressed as mean ± standard deviation (SD). Dichotomous variables are expressed as percentage (%) and number of patients (n). Blood pressure is expressed in mmHg. HP with RF: Hypertensive patients with renal failure. HP without RF: Hypertensive patients without renal failure. SBP: Office systolic blood pressure. DBP: Office diastolic blood pressure. PP: Pulse pressure. MAP: Mean arterial pressure. ns: Not significant.

	Odds ratio	95% CI	p
RF	2.58	1.12 to 5.95	0.03
Age	1.07	1.01 to 1.14	0.01
DM2	3.99	1.73 to 9.18	0.001
Obesity	0.66	0.29 to 1.51	ns
Sex	0.46	0.02 to 11.62	ns
24-hour MAP	1.03	0.98 to 1.08	ns

RF: Renal failure. DM2: Type 2 diabetes mellitus. 24-hour MAP: 24-hour mean arterial pressure assessed by ambulatory monitoring. CI: Confidence interval. ns: Not significant.

time and nighttime, independently of age and DM2, confounder factors on this variable, indicating that PP would be a distinctive characteristic in this type of patients. It has been shown that increased PP has a deleterious effect on renal function (22) behaving as an accelerator of renal aging. In a study by Fesler et al. (23) with follow-up of 129 HP during 6.5 years, the annual decrease of GFR was markedly and inversely correlated with PP, suggesting that stiffness developed in essential hypertension might accelerate the

fall of GFR with the passage of time. Therefore, PP evaluation by ABPM would be useful in HP with RF, facilitating risk estimation of RF progression.

In the general population, BP falls 10-20% during sleep. However, lack of nighttime BP fall (NDP) has been described in some healthy subjects and in certain diseases. This condition, associated with increased cardiovascular risk and greater injury in the target organ, is typically described in patients with RF. (24) However, again these descriptions are based on stud-

Table 2. Average systolic blood pressure and heart rate by day periods according to hypertension control defined by home-based blood pressure monitoring

Table 3. Relationship between elevated pulse pressure and renal disease. Multivariate analysis

ies performed in populations with high prevalence of patients with end-stage RF, dialysis or transplant. (19, 25) Although we found a high prevalence of NDP (44% of the study population), no significant differences were observed between HP with or without RF presenting this pattern (54.3% vs. 37.4%; $p=ns$). This is probably due to the population described, which is different from that in the literature, or else to the relatively low number of patients analyzed.

Twenty-four-hour BP variability is also related to cardiovascular disease, as there is evidence that BP variability closely correlates with target organ injury and that this effect is independent of mean BP values. (13) Blood pressure variability is greatly increased in patients on dialysis, in direct association to changes in intravascular volume in intra and interdialysis periods. (24) However, no studies were found evaluating the behavior of BP variability in hypertensive patients with different degrees of GFR. The study showed no significant differences in BP variability between both groups of patients. Therefore, although this study had a limited number of patients and the estimation of BP variability was controversial due to the scarce measurements obtained from ABPM, increased BP variability would not seem a distinctive element in HP with RF.

CONCLUSIONS

In the present study we evaluated PP, and BP circadian rhythm and variability from ABPM in a population of HP with RF attending a Hypertension Service. The results are interesting, as there are insufficient published data specifically assessing this type of patients.

The main characteristic observed in ABPM in HP with RF was a significant increase of PP, which could be used to evaluate the risk of progressive renal injury in these patients. However, we found no major prevalence of NDP or BP variability, as is classically described in populations of patients with RF.

These data should be corroborated with future studies with a higher number of patients, also analyzing the influence of PP in the progression of RF.

Conflicts of interest

None declared

(See author's conflicts of interest forms in the web / Supplementary Material)

REFERENCES

1. Wheeler D, Becker G. Summary of KDIGO guideline. What do we really know about management of blood pressure in patients with chronic kidney disease? *Kidney Int* 2013;83:377-83. <http://doi.org/x6s>
2. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 2003;41:1-12. <http://doi.org/bnrxr4>
3. Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, et al. Prevalence of kidney damage in Australian adults: the AusDiab Kidney Study. *J Am Soc Nephrol* 2003;14:S131-8.

<http://doi.org/dqq7dm>

4. Iseki K. The Okinawa Screening Program. *J Am Soc Nephrol* 2003;7 (Suppl 2): S127-30. <http://doi.org/b2xmbj>
5. Hillege HL, Janssen WM, Bak AA, Diercks GF, Grobbee DE, Crijs HJ, et al. Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *J Intern Med* 2001;249:519-26. <http://doi.org/chjbhr>
6. Brown WW, Peters RM, Ohmit SE, Keane WF, Collins A, Chen SC, et al. Early detection of kidney disease in community settings: the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis* 2003;42:22-35. <http://doi.org/ft6r5f>
7. Sarcona E, Díaz M. Evaluación de la función renal en pacientes hipertensos: subdiagnóstico de la enfermedad renal. *Rev Argent Cardiol* 2005;73:330-5.
8. Mailloux LU, Levey AS. Hypertension in patients with chronic renal disease. *Am J Kidney Dis* 1998;32(Suppl 3):S120-41. <http://doi.org/fhvzzk>
9. Campese VM, Mitra N, Sandee D. Hypertension in renal parenchymal disease: Why is it so resistant to treatment? *Kidney Int* 2006;69:967-73. <http://doi.org/fpg98h>
10. Meguid El Nahas A, Bello AK. Chronic kidney disease: the global challenge. *Lancet* 2005;365:331-40. <http://doi.org/bcgqjn>
11. Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. *Hypertension* 2000;36:394-9. <http://doi.org/x6t>
12. Verdecchia P, Angeli F, Gattobigio R. Clinical usefulness of ambulatory blood pressure monitoring. *J Am Soc Nephrol* 2004;15:S30-3. <http://doi.org/bp4br2>
13. Parati G. Blood pressure variability: its measurement and significance in hypertension. *J Hypertens* 2005;23 (Suppl):S19-25.
14. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;130:461-70. <http://doi.org/x6v>
15. Barna I, Kezei A, Dunai A. Evaluation of Meditech ABPM-04 ambulatory blood pressure measuring device according to the British Hypertension Society protocol. *Blood Press Monit* 1998;3:363-8.
16. Ohkubo T, Imai Y, Nagai K, Watanabe N, Minami N, Kato J, et al. Relation between nocturnal decline in blood pressure and mortality. The Ohasama Study. *Am J Hypertens* 1997;10:1201-7.
17. Sander D, Kukla C, Klingelhöfer J, Winbeck K, Conrad B. Relationship between circadian blood pressure patterns and progression of early carotid atherosclerosis. A 3-year follow-up study. *Circulation* 2000;102:1536-41. <http://doi.org/x6w>
18. Rahman M, Griffin V, Heyka R, Hoit B. Diurnal variation of blood pressure; reproducibility and association with left ventricular hypertrophy in hemodialysis patients. *Blood Press Monit* 2005;10:25-32. <http://doi.org/fsqczj>
19. Liu M, Takahashi H, Maruyama S, Mizuno M, Yuzawa Y, et al. Non-dipping is a potent predictor of cardiovascular mortality and is associated with autonomic dysfunction in haemodialysis patients. *Nephrol Dial Transplant* 2003;18:563-9. <http://doi.org/dpzkyk>
20. Prakash S, Chibber SK, Pande DP, Joshi S, Gupta KK, et al. Assessment of hypertension control in chronic kidney disease patients by ambulatory blood pressure monitoring. *J Assoc Physicians India* 2005;53:769-74.
21. Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. *Circulation* 1999;100:354-60. <http://doi.org/x6x>
22. Mimran A. Consequences of elevated pulse pressure on renal function. *J Hypertens* 2006;24(Suppl 3):S3-S7. <http://doi.org/dd8rp5>
23. Fesler P, Verhave JC, Ribstein J, du Cailar G, Mimran A. Pulse pressure is an independent determinant of renal function decline during treatment in essential hypertension [Abstract]. *J Am Soc Nephrol* 2005;16:60A.
24. Pickering TG, Thompson AM. The role of ambulatory blood pressure monitoring in chronic and end-stage renal disease. *Kidney Int* 2006;70:1000-7. <http://doi.org/cfck69>
25. Pickering TG. White-coat hypertension. *Curr Opin Nephrol Hypertens* 1996;5:192-8. <http://doi.org/cm6q27>