

Factors associated with the presence of resistant arterial hypertension in patients with stage 5 chronic kidney disease undergoing renal replacement therapy treated at a high-complexity health institution in the city of Pereira in the year 2022–2023

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Abstract

Introduction: Resistant arterial hypertension (RAH) is described as a significant risk factor for the development of chronic kidney disease (CKD). Currently, it is defined as blood pressure that remains at or above 140/90 mm Hg and is uncontrolled despite the use of three classes of antihypertensive drugs at their maximum tolerated doses.

Objective: To identify the risk factors associated with the presence of RAH in patients with stage 5 CKD undergoing replacement therapy, treated at a high-complexity healthcare institution in the city of Pereira during the period 2022–2023.

Methodology: A cross-sectional descriptive study with an analytical intent was conducted, including a total of 255 patients with stage 5 CKD receiving care at a renal unit and undergoing hemodialysis in the city of Pereira. Data were collected through medical records, identifying patients who met the inclusion criteria. Data analysis was performed using SPSS software, generating frequency distribution tables, variable cross-tabulations, chi-square tests, odds ratios (OR), and bivariate and multivariate logistic regression analysis.

Results: The prevalence of RAH was 44%. The most frequent etiology of CKD was arterial hypertension. Among sociodemographic variables, 61.7% of patients were male, 87.5% were from Pereira, and the average age was 61 years (range: 24–89 years). Additionally, 58.2% were single, 78.1% were enrolled in the subsidized healthcare system, and 80.1% had completed only primary education. Regarding clinical variables, 59.6% had diabetes,

44.1% presented with RAH, 82.7% were at high cardiovascular risk, 54.7% had cardiovascular disease, and 1.7% had cerebrovascular disease; 38.3% were overweight, and 73.0% were non-adherent to treatment. Statistically significant associations ($p \leq 0.005$) were found in variables such as age, use of two classes of antihypertensives, and use of three pharmacological groups. Relationships between variables were determined through bivariate analysis and risk estimation (OR). Multivariate analysis was used to describe the probability of associations between crossed variables.

Conclusions: In the studied population of stage 5 CKD patients undergoing hemodialysis during the 2022–2023 period, the prevalence of RAH was 44%. The use of two classes of antihypertensive drugs was considered a protective factor against this condition, whereas the use of three antihypertensive drugs was identified as a risk factor for the development of RAH.

Keywords: Resistant hypertension, CKD, risk factor, ABPM, ACE inhibitors, ARBs, CCBs.

Resumen

Introducción: la hipertensión arterial (HTA) resistente se describe como un factor de riesgo importante para el desarrollo de enfermedad renal crónica (ERC). Actualmente, se define como hipertensión arterial que persiste en rangos tensionales superiores o iguales a 140/90 mm Hg, no controlada a pesar del uso de tres grupos farmacológicos de antihipertensivos a dosis máxima.

Objetivo: determinar los factores de riesgo asociados a la presencia de HTA resistente en pacientes con ERC estadio 5 en terapia de reemplazo, atendidos en una institución de salud de alta complejidad de la ciudad de Pereira en el período 2022-2023.

Metodología: se realizó un estudio descriptivo transversal con intención analítica, considerando un total de 255 pacientes con ERC estadio 5 atendidos en una unidad renal y en terapia de hemodiálisis en la ciudad de Pereira. La recolección de datos se realizó a través de historias clínicas, identificando a los pacientes que cumplieran con los criterios de inclusión. Para el análisis de los datos se utilizó el programa SPSS, generando tablas de distribución de frecuencias, cruces de variables, pruebas de chi cuadrado, odds ratio (OR) y análisis bivariado y multivariado mediante regresión logística.

Resultados: la prevalencia de HTA resistente fue del 44%. La etiología más frecuente de ERC fue la hipertensión arterial. Entre las variables sociodemográficas, se encontró que el 61.7% de los pacientes eran hombres,

el 87.5% procedían de Pereira y la edad promedio fue de 61 años (rango: 24–89 años). Además, el 58.2% eran solteros, el 78.1% pertenecían al régimen subsidiado y el 80.1% tenían nivel educativo de primaria. En cuanto a las variables clínicas, el 59.6% tenían diabetes, el 44.1% presentaban HTA resistente, el 82.7% tenían alto riesgo cardiovascular, el 54.7% enfermedad cardiovascular y el 1.7% enfermedad cerebrovascular; el 38.3% tenían sobrepeso y el 73.0% no se adherían al tratamiento. Se encontró significancia estadística ($p \leq 0.005$) en variables como edad, uso de dos grupos de antihipertensivos y uso de tres grupos farmacológicos. La relación entre variables se determinó mediante análisis bivariado y el cálculo del riesgo (OR). En el análisis multivariado se describió la probabilidad de asociación entre las variables cruzadas.

Conclusiones: en la población estudiada de pacientes con ERC estadio 5 en hemodiálisis durante el período 2022–2023, la prevalencia de HTA resistente fue del 44%. El uso de dos grupos farmacológicos antihipertensivos se consideró un factor protector frente a esta condición, mientras que el uso de tres fármacos antihipertensivos se identificó como un factor de riesgo para el desarrollo de HTA resistente.

Palabras clave: HTA resistente, ERC, factor de riesgo, MAPA, IECAS, ARA II, BCC.

Introduction

Resistant arterial hypertension (RAH) is a non-communicable chronic disease that has a significant impact on the deterioration of patients' renal function. It is defined as a persistent elevation of systolic and diastolic blood pressure values equal to or greater than 140/90 mmHg, despite the use of three or more antihypertensive drugs from different pharmacological classes, such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), and calcium channel blockers (CCBs), in combination with diuretics—whether thiazide or potassium-sparing. Even when administered at the maximum tolerated dose and at the appropriate frequency, these medications fail to control elevated blood pressure levels, significantly increasing cardiovascular risk (1).

This study aims to provide detailed information on the prevalence of this condition in patients with end-stage chronic kidney disease undergoing hemodialysis as renal replacement therapy, taking into account sociodemographic and clinical variables associated with both resistant hypertension and chronic kidney disease (CKD) (2).

Methodology

A descriptive cross-sectional study with an analytical-relational approach was conducted to establish the association between demographic and clinical risk factors for resistant hypertension. The study analyzed the total population of patients with stage 5 chronic kidney disease (CKD) undergoing renal replacement therapy through hemodialysis. It was carried out at a tertiary-level healthcare institution, a referral center for renal replacement therapy in the city of Pereira, Colombia.

Data collection: Institutional permission was requested to access medical records. Data collection was conducted over a period of eight months, with a weekly dedication of two hours, retrieving retrospective data from the medical records of patients treated between 2022 and 2023. These records were stored in the unit's information system, and manual data extraction was performed by the study's author. Personal patient information, including sociodemographic and clinical variables, was included to build the database.

Data Tabulation and Statistical Analysis

An electronic database was created using Microsoft Excel 2021, version 16.55, and subsequently exported to SPSS software, version 26, licensed by the University of Caldas, for statistical analysis. A descriptive analysis of each variable was initially performed. Qualitative variables were expressed as absolute and relative frequencies, while quantitative variables were described using measures of central tendency and dispersion, such as mean, standard deviation, mode, median with confidence intervals, and minimum and maximum values for each distribution. The normality of distribution for quantitative variables was assessed using the Kolmogorov-Smirnov statistical test.

Subsequently, in order to identify factors associated with resistant arterial hypertension, the association between the dependent variable and the independent variables was evaluated using chi-square tests, considering statistical significance at a $p\text{-value} < 0.05$. Risk estimation was performed using the odds ratio (OR) or prevalence ratios, along with their 95% confidence intervals.

Finally, a multivariate analysis was conducted, including statistically significant variables, through a binary logistic regression model with backward stepwise selection. The objective was to confirm the association between the dependent variable (resistant hypertension) and the statistically signifi-

cant independent variables, while also controlling for confounding factors.

Sample: The study included the total number of patients with stage 5 chronic kidney disease who met the study's selection criteria.

Inclusion criteria: Patients diagnosed with stage 5 chronic kidney disease undergoing renal replacement therapy via hemodialysis. Patients of both sexes, aged 18 years and older, treated at a high-complexity healthcare institution in the city of Pereira during the 2022–2023 period. Patients diagnosed with both arterial hypertension and stage 5 chronic kidney disease, including those with additional underlying comorbidities.

Exclusion criteria: Patients with stage 5 chronic kidney disease undergoing peritoneal dialysis, due to the outpatient nature of follow-up in these cases. Patients under 18 years of age with a diagnosis of stage 5 chronic kidney disease.

Results

The prevalence of resistant arterial hypertension in the population with stage 5 chronic kidney disease undergoing hemodialysis therapy was 44.0%.

11. Etiology of CKD:

The most prevalent etiologies of stage 5 chronic kidney disease (CKD) were hypertension (HTN), accounting for 46.7% of cases, followed by diabetes, with 33.3%. The prevalence of resistant hypertension was 44%, with hypertension being the most frequent etiology of CKD at 46.7%.

Regarding sociodemographic variables, 61.7% of the patients were male, 87.5% were from Pereira, and the average age was 61 years, ranging from 24 to 89 years. In terms of marital status, 58.2% were single. Concerning the health insurance scheme, 78.1% were enrolled in the subsidized regime, and 80.1% had completed primary education as their highest level of schooling.

Among clinical variables, 59.6% of patients had diabetes, 44.1% presented with resistant hypertension, 82.7% had a high cardiovascular risk, 54.7% had cardiovascular disease, 1.7% had cerebrovascular disease, 38.3% were overweight, and 73.0% showed poor treatment adherence.

Statistical significance was determined using a p-value ≤ 0.005 for the variables age, use of two classes of antihypertensive drugs, and use of three pharmacological classes of antihypertensives. The relationship between variables was established through bivariate analysis, and risk was calculated using the odds ratio (OR). In the multivariate analysis, the probability of association found between variables was described.

For the binary logistic regression model, the backward stepwise method was used. In the multivariate analysis, it was demonstrated that the variables "use of one or two classes of antihypertensive drugs" and "use of three or more classes of antihypertensive drugs" were associated with resistant hypertension. In step 2 of the model, the variable "over 50 years of age" was removed, indicating that there was no association between this independent variable and the dependent variable (resistant hypertension) after adjusting for potential confounding factors. The following section presents the corresponding graphs and result tables:

Figure 1. Percentage distribution of the etiology among patients with stage 5 chronic kidney disease

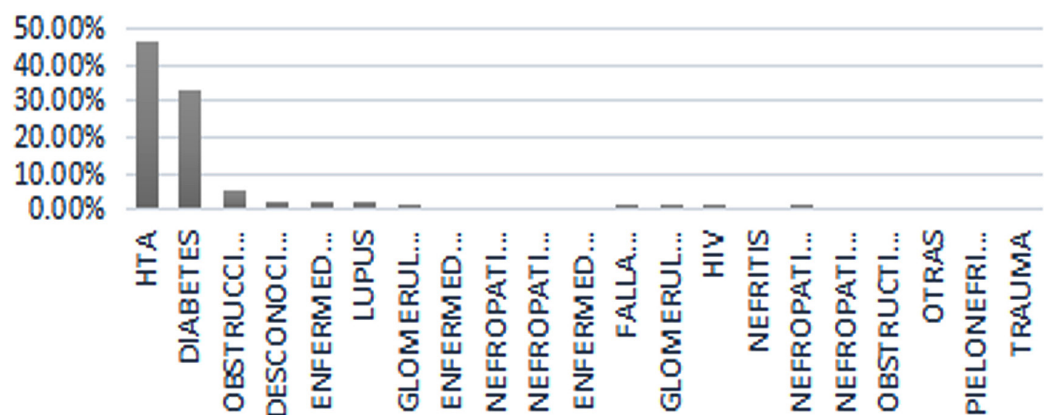


Table 1. Absolute and percentage distribution of sociodemographic variables in patients with stage 5 chronic kidney disease.

QUALITATIVE VARIABLES		NUMBER	PERCENTAGE
Demographic variables			
Gender	Male	158	61,7
	Female	97	37,9
Origin	Pereira	224	87,5
	Santa Rosa	6	2,3
	Belen de Umbría	3	1,2
	La Virginia	2	0,8
	Dosquebradas	1	0,4
	Apia	1	0,4
	Other departments	19	7,4
Age by age group	20 a 29 years	8	3,1
	30 a 39	19	7,4
	40 a 49	28	10,9
	50 a 59	46	18,0
	60 a 69	65	25,4
	70 a 79	70	27,3
	>80	18	7,0
Average 61			

SD 15.1 Median 63 Minimum V 24 Maximum V 89 Pba Kolmogorov 0.95 Normal distribution			
Marital status	Single	149	58,2
	Married	65	25,4
	Free union	21	8,2
	widower	13	5,1
	Divorced	8	3,1
Affiliation regime	Subsidized	200	78,1
	Contributory	46	18,0
	Exception	8	3,1
	Individual	1	0,4
Educational level	No studies	3	1,2
	Primary	205	80,1
	Secondary	42	16,4
	Technical	1	0,4
	Professional	4	1,6

*Own elaboration.

Table 2. Absolute and percentage distribution of clinical variable frequencies in patients with chronic kidney disease.

		FREQUENCY	PERCENTAGE
BMI (Body Mass Index) Average: 24.8 SD (Standard Deviation): 5.1 Median: 23.8 Min. value: 15.1 Max. value: 51	Normal weight - Underweight	157	61,3
	Obesity - Overweight	98	38,3
Diagnosis of HTN in years	0-9	145	56,6
	10-19	75	29,3
	20-29	25	9,8
	>30	11	4,3
Diabetes	Yes	103	59,6
	No	152	40,4
Smokes	Yes	30	11,7
	No	225	87,9
Hypertension	Yes	252	98,8
	No	3	1,2
Resistant hypertension (RH)	Yes	113	44,1
	No	142	55,5
Cardiovascular risk	Very high	5	2,0
	High	211	82,7
	Moderate	32	12,5
	Low	5	2,0
	No risk	2	0,8
Cardiovascular disease	Yes	140	54,7
	No	115	44,9
Cerebrovascular disease	Yes	4	1,6
	No	251	98,4
Treatment adherence	Yes	67	27,0
	No	188	73,0
Use of 1 or 2 groups of Antihypertensive	Yes	136	53,1
	No	119	46,5
Use of 3 or more Antihypertensive groups	Yes	111	43,0
	No	144	56,3

*Own elaboration.

Table 3. Sociodemographic risk variables associated with Resistant Hypertension in patients with stage 5 chronic kidney disease.

Demographic variables		YES (N° %)	NO N° %)	X2 p		OR (IC)
Gender	Male	73(46,2)	85(53,8)	0,59	0,43	1,22 (0,73-2,0)
	Female	40(41,2)	57(58,8)			
Age Older than 50	YES	80 (40,0)	118 (60,0)	6,0	0,013	0,47(0,25-0,86)
	NO	33 (60,0)	22 (40,0)			
Education level	Primary	87(41,8)	121 (58,2%)	2,8	0,09	0,58 (0,3-1,1)
	Secondary-Professionall	26(55,3)	21(44,7)			
High BMI	YES	50 (47,2)	56 (52,8)	3,3	0,68	1,6 (0,9-2,7)
	NO	48 (35,6)	87(64,4)			
Marital status	With couple	37(32,74)	49 (57,0)	0,08	0,7	0,9(0,5-1,5)
	Without couple	76(67,3)	93 (65,5)			
Smoke	YES	15 (50,0)	15 (50,0)	0,44	0,5	1,3(0,6-2,8)
	No	98 (43,6)	127 (56,4)			
Health affiliation regime	Subsidized	84 (42,0)	116 (58)	2,01	0,156	1,54 (0,84-2,8)
	Contributory	29 (56,7)	26 (47,3)			

*Own elaboration.

Table 4. Clinical risk variables associated with Resistant Hypertension in patients with stage 5 chronic kidney disease.

Risk Factors	RESISTANT HYPERTENSION					
		YES (N° %)	NO (N° %)	X2	p	OR (Odds Ratio / Prevalence Ratio)
Diabetes	YES	45 (43,7)	58 (56,3)	0,027	0,86	1,0 (0,63-1,7)
	NO	68 (44,7)	84 (52,6)			
Use of Antihypertensive	YES	109 (44,5)	136 (55,5)	0,078	0,77	1,2 (0,33-4,3)
	NO	4 (40,0%)	6 (60,0)			
	YES	6 (4,4)	130 (95,6)	188	0,00	

Risk Factors	RESISTANT HYPERTENSION					
Use of 1 or 2 Antihypertensive groups	NO	107 (89,9)	12 (10,1)			0,0055 (0,018 - 0,014)
Use of 3 or more Antihypertensive groups	YES	103 (92,8)	8 (7,21)	187	0,000	172,5 (65,7 - 452,6)
	NO	10 (6,9)	134 (93,1)			
Cardiovascular risk	YES	63(55,7)	77(54,2)	0,019	0,8	0,43 (0,21-0,88)
	NO	50(44,2)	65(45,8)			
Cardiovascular disease	YES	63 (45,0)	77 (55,0)	0,05	0,8	1,06 (0,64-1,7)
	NO	5,0 (43,5)	65 (56,5)			
Cerebrovascular disease	YES	1 (25,0)	3 (75,0)	0,6	0,43	0,41 (0,04-4,03)
	NO	112 (44,6)	139 (55,4)			
Treatment adherence	YES	29 (42)	40 (58)	0,200	0,65	1,1 (0,6-1,9)
		84 (45,2)	102 (54,8)			

*Own elaboration

Table 5. Binary Logistic Regression

Variables en la ecuación

		B	Error estándar	Wald	gl	Sig.	Exp(B)
Paso 1 ^a	>50	,391	,634	,380	1	,537	1,478
	USODE30MASGRUPOS DEANTIHIPERTENSIVOS	2,867	,688	17,361	1	,000	17,588
	USODE10DOSGRUPOS ANTIHIPERTENSIVOS	-3,132	,691	20,523	1	,000	,044
	Constante	,154	2,170	,005	1	,943	1,167
Paso 2 ^a	USODE30MASGRUPOS DEANTIHIPERTENSIVOS	2,791	,669	17,383	1	,000	16,302
	USODE10DOSGRUPOS ANTIHIPERTENSIVOS	-3,120	,688	20,552	1	,000	,044
	Constante	,739	1,935	,146	1	,702	2,094

a. Variables especificadas en el paso 1: >50, USODE30MASGRUPOSDEANTIHIPERTENSIVOS, USODE10DOSGRUPOSANTIHIPERTENSIVOS.

Las variables no están en la ecuación

		Puntuación	gl	Sig.
Paso 2 ^a	Variables >50	,382	1	,537
	Estadísticos globales	,382	1	,537

a. Variables eliminadas en el paso 2: >50.

*Own elaboration

Discussion

The aim of this study was to determine the relationship between factors associated with resistant hypertension (RH) in patients with stage 5 chronic kidney disease (CKD) undergoing renal replacement therapy, treated at a high-complexity healthcare institution in Pereira, Colombia. The prevalence of resistant hypertension was found to be 44%, a percentage higher than that reported in specific studies such as the 2018 scientific statement from the American Heart Association (AHA), where prevalence ranged from 12% to 15% in patients with resistant hypertension (4).

The average age of the patients in this study was 61 years, with the highest proportion of cases occurring in individuals over 70. The Kolmogorov-Smirnov test showed that age did not follow a normal distribution. These results are comparable to those of a study conducted at a university hospital in Egypt, where a higher incidence of CKD was reported in elderly patients, with an average age of 62.1 years (24).

Regarding sociodemographic variables, 61.7% of the patients were male, most were from Pereira, and 58.2% were single. The predominant health insurance scheme was the subsidized regime (78.1%), and 80% of the patients had completed only primary education. These factors may influence disease understanding and adherence to antihypertensive treatment. Furthermore, the average body mass index (BMI) was 24.8, indicating overweight. This condition is documented as a factor associated with hypertension, as individuals with a BMI ≥ 30 kg/m² are twice as likely to develop resistant hypertension (25).

Regarding tobacco use, 89.7% of the patients were non-smokers. However, recent studies have indicated that nicotine use, even though vaping devices increases blood pressure levels. It is recommended that patients with resistant hypertension cease smoking to reduce associated cardiovascular events (25).

Hypertension was identified as the main cause of CKD, followed by diabetes mellitus. Globally, diabetes is the most common etiology of CKD; however, the results of this study highlight the significance of hypertension in the development of this condition. It is estimated that 65%–75% of obese patients develop hypertension, which is considered an important predictor of CKD and a risk factor for diabetes mellitus (26).

A total of 82.4% of patients with CKD presented a high cardiovascular risk. Elevated blood pressure is not only a risk factor but also a predictor of

cardiac, cerebral, and vascular complications such as coronary artery disease, heart failure, atrial fibrillation, and stroke. Additionally, lack of adherence to pharmacological treatment was identified as a significant risk factor. Adherence may be affected by economic barriers, complex medication regimens, and associated chronic conditions such as depression and cognitive dysfunction (25).

Despite the importance of adherence, it is currently difficult to assess in clinical practice due to challenges in follow-up, clarity of antihypertensive management protocols, and the lack of a standardized and clinically available method or test. Pill counting, the most commonly used method in clinical trials, is associated with an overestimation of adherence. Other methods include electronic monitoring and drug metabolite analysis, which are not widely available in the country.

Efforts to improve medication adherence are essential to reduce the risk of disease and its secondary complications. Therefore, patient education should also be promoted to enhance self-awareness of medical conditions and the need for appropriate care.

With regard to the strict monitoring and control of antihypertensive medication intake, therapeutic efforts by physicians to reduce pill burden are also important, as studies have shown a significant inverse relationship between the number of antihypertensive pills and medication adherence. In this regard, a study involving patients with poorly controlled hypertension who were provided with tools such as standard care and even a smartphone app that offered reminder alerts, compliance reports, and optional peer support, found that patients receiving the intervention showed improved self-reported adherence; however, the intervention did not affect blood pressure control (25).

Similarly, the use of fixed-dose combinations or extended-release formulations has been reported as effective in improving adherence. Therefore, adjusting prescriptions to once-daily regimens using fixed-dose combinations to reduce the total pill count may help improve medication adherence in patients with hypertensive disease (25).

In the present study, resistant hypertension, as the dependent variable, showed a statistically significant association. The use of one or two antihypertensive drugs was identified as a protective factor against resistant hypertension, in contrast to the clinical variable “use of three pharmacological groups of antihypertensives,” which behaved as a risk factor for resistant

hypertension. This was confirmed through binary logistic regression, which showed that patients on a pharmacological regimen involving three classes of antihypertensive drugs had a 17.5 times greater risk of developing resistant hypertension, likely related to poor adherence to antihypertensive treatment regimens.

Lack of adherence to antihypertensive medication is one of the main contributing factors to uncontrolled blood pressure. Studies have indicated that more than 30% of adults taking antihypertensive drugs exhibit low adherence within the first year of treatment. A meta-analysis on the prevalence of nonadherence among adults with resistant hypertension, which included 42 studies with a total of 71,353 participants, showed a mean prevalence of 37%, with wide variation across studies ranging from 3% to 86%. Various factors were evaluated, including socioeconomic status, demographics, and environmental conditions, all of which were found to be associated with nonadherence to pharmacological treatment (25).

Hypertension is considered an important cardiovascular risk factor in the general population, but even more so in patients with chronic kidney disease (CKD). Furthermore, the absence of cardiovascular risk factors is considered a protective factor in the CKD population. In this regard, it is recommended that the pharmacological treatment of resistant hypertension be individualized, with the prescription of an optimal or maximally tolerated combination of long-acting renin-angiotensin system inhibitors, calcium antagonists, and thiazides or similar drugs (25).

The treatment of resistant hypertension requires optimization of medication regimens through dose adjustments, the addition of drugs from different classes, or the use of fixed-dose combinations. Lifestyle modifications, such as weight loss, regular exercise, and a low-sodium diet, are also important for elderly patients. This research highlighted the need and importance of establishing protocols that include identification, risk factors, diagnosis, pharmacological treatment, and lifestyle modifications focused on individualized management of patients with resistant hypertension. Furthermore, it is essential to carry out proper follow-up through outpatient blood pressure monitoring in order to obtain objective results (25).

Finally, although in this study the variable "nonadherence to pharmacological treatment" was not considered statistically significant, the proportion of nonadherent patients was higher than that of adherent patients, with 73% being nonadherent. This is relevant as it acts as an important risk factor

identified in the study of the population. Therefore, it is suggested that non-adherence should be measured and controlled in future protocols developed for patients with CKD and associated hypertension, in order to verify the treatment regimen, the number of combined antihypertensive drugs for each specific case, appropriate formulation, daily schedule, and adjustments and follow-up conducted by the treating specialist (25).

The treatment of resistant hypertension should include optimization of pharmacological regimens and lifestyle modifications, such as weight loss, regular exercise, and a low-sodium diet. It is crucial to establish protocols that include the identification of risk factors, diagnosis, personalized treatment, and rigorous follow-up, utilizing methods such as outpatient blood pressure monitoring to obtain more objective results (25).

Regarding the statistical analysis, the use of one or two groups of antihypertensive drugs was identified as a protective factor against resistant hypertension, while the use of three or more drug classes was associated with a significant increase in risk (OR=17.5). This may be related to poor adherence to complex antihypertensive treatment regimens (26).

Finally, although the variable "nonadherence to pharmacological treatment" was not statistically significant, the 73% of nonadherent patients represents a relevant percentage. This finding suggests the need to assess adherence as part of future protocols for patients with CKD and hypertension. Implementing strategies such as patient education, simplifying regimens, and using fixed-dose combinations may improve adherence and reduce the risk of associated complications (26).

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Conflicts of Interest: None.

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