ALBUMINURIA IS ASSOCIATED WITH LESS EFFORT TOLERANCE IN HYPERTENSION AND DIABETES

Juliana Maria Rodrigues Daniel[1]

Tani Roberto Neres Meira[2]

Marcia de Fatima Meira[3]

Silméia Garcia Zanati Bazan[4]

Roberto Jorge da Silva Franco[5]

Pasqual Barretti[6]

Luis Cuadrado Martin[7]

Abstract: Introduction: The presence of albuminuria is an adverse marker of renal dysfunction progression. Hypertension and diabetes mellitus predispose to albuminuria. However, not all hypertensive and diabetic patients have albuminuria, so it is relevant to identify risk factors associated to this abnormality. The acute effect of intense physical activity may lead to transient albuminuria. On the other hand, physical inactivity is associated with risk factors for albuminuria Objective: To analyze the association between activity levels or physical performance and albuminuria in hypertensive and/

---

1 Master by the Pathophysiology program in Internal Medicine, Faculty of Medicine of Botucatu and occupational physiotherapist;

2 Master by the Pathophysiology program in Internal Medicine, Faculty of Medicine of Botucatu, physiotherapist of the Municipality of Itaí and physiotherapist of the Municipality of Taguaí;

3 Nurse, specialist in urgent and emergency care and Public Health Management;

4 Cardiologist, professor of the Pathophysiology program in Internal Medicine at the Faculty of Medicine of Botucatu;

5 Nephrologist, professor of the Pathophysiology program in Internal Medicine at the Faculty of Medicine of Botucatu;

6 Nephrologist, professor of the Pathophysiology program in Internal Medicine at the Faculty of Medicine of Botucatu;

7 Nephrologist, professor of the Pathophysiology program in Internal Medicine at the Faculty of Medicine of Botucatu;

HEALTH & SOCIETY

or diabetic patients treated at basic health services. Methodology: A prospective cross-sectional study with hypertensives and/or diabetics subjects. The patients were evaluated in regard of albuminuria, clinical, laboratory and physical test performance variables. Results: There was no association between the degree of albuminuria and demographic, anthropometric, laboratory variables, functional capacity and level of physical activity. The degree of albuminuria was associated with systolic blood pressure, as well as the perception of effort, obtained by Borg Scale during the test in univariate analysis (odds ratio 4.11 with 95% confidence interval from 1.18 to 14.37, $p = 0.027$) and adjusted for systolic blood pressure and diabetes (odds ratio 3.02 with 95% confidence interval from 1.35 to 6.75; $p = 0.007$). Conclusion: there was association between albuminuria and perceived effort, as well with systolic blood pressure. There was not with association physical performance or level of activity. Further studies are needed to elucidate the association of albuminuria with Borg Scale.

Keywords: albuminuria, hypertension, diabetes, Borg scale.

INTRODUCTION

Moderately elevated albuminuria is defined as elimination of albumin above 30 mg within 24 hours urine and is an adverse marker of renal function evolution as well as cardiovascular outcomes (COSTA e RAMÔA, 2018; STEVENS e LEVIN, 2013). The development of albuminuria is due to abnormalities of glomerular capillaries and is associated with systemic endothelial dysfunction, which generally occurs due to the harmful effects of hypertension and diabetes mellitus (DM) (CRESTANI FILHO e RODRIGUES, 2013).

Other predisposing factors for albuminuria include African descent, male gender, smoking, obesity and aging (FELIX et al., 2016). However, not all hypertensive and diabetic patients have albuminuria, so it is relevant to identify other risk factors associated to this abnormality. The acute effect

of intense physical activity may lead to transient albuminuria. On the other hand, physical inactivity is associated with risk factors for albuminuria. However, we have not identified in the literature studies that have evaluated possible associations between activity levels or physical performance with albuminuria. Thus, the current study aims to analyze the association between activity levels or physical performance and albuminuria in hypertensive and / or diabetic patients treated at basic health units.

MATERIALS AND METHODS

A prospective cross-sectional study was conducted with a random sample of patients with hypertension and/or diabetes aged over 18 from a city of the state of São Paulo, Brazil, from June 2015 to February 2018. Patients under dialysis treatment, with cardiac arrhythmias, ischemic heart disease, musculoskeletal restrictions that precluded participation, presence of systemic diseases that could affect the kidneys were excluded, except for hypertension and DM. The study followed resolution 466/12 (compatible with Helsinki declaration) of the National Health Council and was approved by the local Research Ethics Committee, under the opinion CAAE: 42208815.3.0000.5411. All subjects signed the Informed Consent Form.

Initially, the subjects underwent clinical history, brachial blood pressure measurement and anthropometry. Albuminuria was measured within 24 hours, other laboratory tests performed were: serum creatinine and glycated hemoglobin. Glomerular filtration was estimated using the CKD epi equation (KIDNEY.ORG). Physical activity levels were measured by the International Physical Activity Questionnaire (IPAQ) in the abbreviated version (LEE et al., 2011). Functional capacity was assessed by the six-minute walk test (6MWT) (ATS, 2002). The modified Borg scale was used to analyze initial and final respiratory distress (BORG, 1982). Arterial stiffness properties were evaluated by pulse wave velocity (PWV) in the carotid-femoral segment (PWV-FC) and systolic and diastolic central arterial pressure (CAP) using Sphygmocor Medical®.

Patients were divided into two groups according to the presence or absence of moderately elevated albuminuria (> 30mg / 24h). These groups were compared by t-test, Mann-Withney or chi-square tests when appropriate. Variables that differed with p <0.05 were included in multiple logistic regression analysis, whose outcome variable was the presence of moderately elevated albuminuria. From the different modalities of blood pressure assessment, only one was chosen to compose the regression. The presence of DM and ethnicity were added to the model. Data were expressed as mean ± standard deviation, median (first quartile - third quartile) or frequency as appropriate, analyzed by the IBM SPSS 20 program and discussed at the significance level p <0.05.

RESULTS

There were invited 472 patients, of which 116 were eligible, 35 declined to participate and 81 completed the proposed evaluations. Table 1 shows the clinical, demographic and laboratory data. There was an association only between albuminuria and systolic blood pressure. Other variables did not present any association with albuminuria.

HEALTH & SOCIETY

Table 1. Clinical, demographic and laboratory data of hypertensive and / or diabetic patients in Basic Health Units according to the present or absence of significant albuminuria

	All	Normoalbuminurics	Albuminurics	p
	(n=81)	(n=63)	(n=18)	
Age (years)	62±11,5	62±11,0	62±13,4	0,971
Male (%)	33	32	39	0,571
Afro-Brazilians (%)	12	9	22	0,149
Diabetics (%)	46	44	50	0,676
Weight (kg)	73±14,2	72±12,6	77±18,7	0,189
Height (cm)	161±7,7	161±7,8	161±7,5	0,688
BMI (kg/m^2)	28,5±5,20	28,2±4,93	29,4±6,14	0,377
SBP (mm Hg)	137±22,3	133±17,9	151±30,1	0,002
DBP (mm Hg)	79±16,3	77±13,5	89±21,9	0,006
PWV-FC (m/s)	7,4±0,65	7,4±0,67	7,5±0,58	0,696
SCAP (mm Hg)	127±22,5	123±18,8	141±28,4	0,002
DCAP (mm Hg)	82±16,2	79±12,8	92±22,4	0,003
SpO$_2$ (%)	96±1,7	96±1,7	96±1,6	0,166
Glycated hemoglobin (%)	6,0±1,59	5,8±1,24	6,5±2,43	0,122
Creatinine (mg/dL)	1,1±0,31	1,1±0,31	1,2±0,32	0,228
Urea (mg/dL)	38±10,9	37±10,5	41±12,0	0,142
GFR (mL/min/1,73m^2)	65±21,9	66±21,7	64±23,2	0,716

BMI: body mass index, PWV-FC: femoral pulse wave velocity, SCAP: systolic central arterial pressure, DCAP: diastolic central arterial pressure, SpO2: blood oxygen saturation; GFR: glomerular filtration rate.

Table 2 shows the results of the 6MWT. There was an association between level of albuminuria and Borg scale at the end of 6MWT, as well as the diastolic and systolic blood pressures both before and at the end of the test.

Table 2. 6MWT results of hypertensive and diabetic patients in Basic Health Units according to the present or absence of significant albuminuria

	All	Normoalbuminurics	Albuminurics	p
	(n=81)	(n=63)	(n=18)	
Pre-6MWT				
SBP (mm hg)	136±18,5	133±13,10	149±27,7	0,001
DBP (mm hg)	80±14,9	77,9±11,52	89±21,6	0,005
BORG (median)	1(0-1)	1(0-1)	1(1-1)	0,814
Post-6MWT				
SBP (mm hg)	141±14,1	139±12,30	148±18,0	0,026
DBP (mm hg)	83±15,2	81,2±12,04	91±21,6	0,011
BORG (median)	3(2-3)	3(2-3)	4(3-4)	0,002
Travelled Distance (m)	324±29,0	324±29,4	325±28,5	0,872

Pre-6MWT: values obtained before the six-minute walk test; SBP: systolic blood pressure; DBP: diastolic blood pressure; End- 6MWT: values obtained at the end of the six-minute walk test; BORG: Borg dyspnea scale.

Logistic regression, with the outcome variable being the presence of moderately elevated albuminuria is shown in Table 3. It is observed that the association between Borg scale at the end of 6MWT and the presence of albuminuria remained even after adjusting for confusion variables. Figure 1 shows the frequencies of Borg scale according to albuminuria.

Table 3. Association between Borg scale and presence of albuminuria, adjusted for systolic blood pressure, diabetes and ethnicity

	RC	I.C.95% Lower	I.C.95% Upper	p
DM	1.30	0.40	4.23	0.661
Afro-Brazilians	2.57	0.50	13.27	0.258
Borg (points)	3.23	1.41	7.40	0.006
SBP (mmHg)	1.03	0.99	1.09	0.159

I.C: 95% confidence interval; RC: odds ratio; DM: presence of diabetes; Borg: Borg scale at the end of the six-minute walk test; SBP: systolic blood pressure after six-minute walk test.

HEALTH & SOCIETY

DISCUSSION

In the present study, albuminuria was associated with lower exercise tolerance in hypertensive and diabetic patients. This association remained even after adjusting for blood pressure levels. There was no association between different demographic, laboratory variables and albuminuria level.

Increased urine albumin excretion after intense physical activity is transient and has been demonstrated in a study published more than three decades ago (POORTMANS, 1984). Elevation of albuminuria up to 30 minutes after physical activity is considered normal, even in athletes, and may remain for up to 48 hours (SAEED et al., 2012). The current study found no association between the degree of albuminuria and the level of physical activity, assessed by IPAQ or functional capacity, analyzed by the 6MWT.

Albuminuria is associated with high blood pressure, diabetes mellitus and increased cardiovascular risk, as well as endothelial dysfunction (ZANELLA, 2006), which is implicated in the development of CKD (MORAES et al., 2009). This dysfunction could potentially elucidate the highest Borg scale indices found in albuminuric patients in this study (SALERMO, PARRAGA e MCLN-TYRE, 2017).

A study in hypertensive patients showed an association between albuminuria and age, obesity, dyslipidemia and diabetes. That study also pointed out that the presence of albuminuria may represent an important predictor of coronary artery disease (SILVA et al., 2008). It is of note that effort dyspnea is an early sign of coronary disease and mediated by transient diastolic dysfunction in ischemia (GIPSON et al., 2019), which could explain the finding of this study. On the other hand, diastolic dysfunction was associated with albuminuria in a large cross-sectional study (KATZ et al., 2014).

Some limitations of this study should be mentioned. Although we attribute the patients' albuminuria to hypertension and diabetes, they were not submitted to renal biopsy to confirm the diagnosis for ethical reasons, but they are unlikely to have primary glomerulopathies, since patients

with albuminuria above 2.0g/24h were excluded. It is also worth mentioning that associations in cross-sectional studies do not means a causal relationship. Interventional studies are necessary to establish cause and effect relationship. Finally, we did not perform evaluations that could elucidate possible mechanisms involved in this association that will be addressed in a future study.

In conclusion, the present study analyzed the predictors of albuminuria in the hypertensive and / or diabetic population. No associations were found with functional capacity, physical activity level, demographic and laboratory variables, except for the greater perception of effort by Borg scale in the walking test. Further work is needed to elucidate the possible pathophysiological mechanisms of the observed association.

ETHICAL CONSIDERATION

The study followed resolution 466/12 (compatible with Helsinki declaration) of the National Health Council and was approved by the local Research Ethics Committee, under the opinion CAAE: 42208815.3.0000.5411. All subjects signed the Informed Consent Form.

DISCLOSURE:

Conflict of interest: None of the authors has any conflict of interest for this publication. Registration trail: N/A.

Animal study: N/A.

Referências bibliográficas

Costa P, Ramôa A. Renal injury in patients with hypertension: study in primary health care in the Braga region. Rev Port Med General Fam. 2018; 34: 242-6.

Stevens PE, Levin A. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013; 158: 825-30.

Crestani Filho VJ, Rodrigues RAC. Progression of chronic kidney disease: outpatient experience in Santarém - Pará. J Bras Nefrol. 2013; 35: 99-106.

Felix KT., et al. Individual long-term albuminuria exposure during angiotensin receptor blocker therapy is the optimal predictor for renal outcome. Nephrol Dial Transplant. 2016; 31: 471–77.

Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. Int J Behav Nutr Phys Act. 2011; 8: 8-15.

Matsudo S, Araujo T, Matsudo V., et al. Questionario Internacional de Atividade Física (IPAQ): estudo de validade e reprodutibilidade no Brasil. Revista Brasileira de Atividade Física & Saúde. 2001; 5: 5-18.

ATS. Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002; 166: 111–17.

Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982; 14: 377-81.

Poortmans, JR. Exercise and renal function. Sports Med. 1984; 1:125-33.

Saeed F Pavan PN, Devaki K, Mahendrakar L, Holley JL. Exercise-induced proteinuria?
The of family practice. 2012; 61:23-6.

Zanella MT. Microalbuminuria: cardiovascular and renal risk factor underestimated in clinical practice. Arq Bras Endocrinol Metab. 2006; 50: 313-321.

Moraes CE, Cerolli CF, Silva, VS, Franco RJS, Habermann, F, Matsubara, BB, Martin, LC. Predictors of chronic renal failure in patients in a hypertension center. Rev Assoc Med Bras. 2009; 55: 257-62.

Salermo FR, Parraga G, Mclntyre CW. Why Is Your Patient Still Short of Breath? Understanding the Complex Pathophysiology of Dyspnea in Chronic Kidney Disease. Semin Dial. 2017; 30: 50-7.

Silva RP., et al. Microalbuminuria dosage in hypertensive patients and in patients with coronary disease. Arq. Bras. Cardiol. 2008; 90: 108-113.

Gipson GT, Carbone S, Wang J. Impaired delivery of cholesterol effluxed from macrophages to hepatocytes by serum from CKD patients may underlie increased CVD risk. Journal Pre-proof. 2019; 19: 1-36.

Katz DH, Selva VRAJ, Aguilar FG., et al. Association of low-grade albuminuria with adverse cardiac mechanics: findings from the hypertension genetic epidemiology network (HyperGEN) study. Circulation. 2014; 129: 42-50.