RESEARCH ARTICLE

Microalbuminuria: A potential marker in the assessment of cardiovascular risk

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Background: Microalbuminuria is an early marker of renal and cardiovascular damage, but it is underutilized in the management of hypertension.

Objective: To investigate the association between microalbuminuria, hypertension severity, left ventricular mass, and ischemic cardiopathy.

Methods: A retrospective study was conducted over six months in the cardiology department of the Cluj Heart Institute, including 54 patients: 34 with essential hypertension and 20 normotensive controls. Microalbuminuria, left ventricular mass, and the presence of ischemic cardiopathy were analyzed in relation to hypertension grade.

Results: Microalbuminuria was present in 20.93% of hypertensive patients, with prevalence increasing to 50% in grade III hypertension. Mean urinary albumin excretion was significantly higher in grade III hypertension compared with controls (57.31 ± 20.27 vs. 5.46 ± 1.33 µg/min, p = 0.0022). Left ventricular mass rose with hypertension severity, being significantly greater in grade II (p = 0.00685) and grade III (p = 0.00086) compared with grade I. No linear correlation was found between microalbuminuria and left ventricular mass. Ischemic cardiopathy was diagnosed in 32.36% of hypertensive patients, but microalbuminuria levels were not significantly different between those with and without ischemic cardiopathy.

Conclusions: Microalbuminuria correlates with hypertension severity and may represent a useful marker for early detection of cardiovascular risk. Routine measurement could support risk stratification and therapeutic decisions in hypertensive patients. Larger studies are warranted to confirm these findings.

Keywords: microalbuminuria, cardiovascular, marker, hypertension

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Introduction

Microalbuminuria, defined by the presence of small amounts of albumin in the urine, has maintained its definition since 1982, when the Viberty group presented values between 20-200 µg/min, as values above the upper limits of normal but below clinical proteinuria or an albumin-creatinine ratio between 30-300 mg/g [1,2].

As we well know, values >200 µg/min define clinical proteinuria, associated with cardiovascular diseases, hypertension, advanced renal damage, diabetes mellitus or obesity-related renal pathologies [3]. Microalbuminuria measurement is a useful tool in the management of these conditions, especially to prevent progression, but also an early predictor in determining these pathologies [1].

Physiologically, the glomerular capillary membrane acts as a filter with 5.5 nm pores and a negative electrical charge. The passage of albumin depends on size, shape, charge and transglomerular pressure. Albumin, a macromolecule with a weight of 69,000 da and a radius of 3.6 nm, has very low clearance (~0.1%), being the main protein in the body and being synthesized by hepatocytes, with a half-life of approximately 19 days. Albumine has multiple functions in the body, such as: maintaining colloid pressure, role in the transport of exogenous and endogenous substances, but also antioxidant action [4-7]. Under normal conditions, almost all filtered albumin is reabsorbed. An increase in the filtered level indicates functional alterations and determines increased secretion.

The secretion rate varies with position, physical exertion, blood pressure and diet, with daily fluctuations of 20-60% in both healthy individuals and diabetics or hypertensives, being lower at night compared to the day. The urinary excretion rate can be increased in all forms of hypertension (grade I, II or III), the severity of microalbuminuria being correlated with the severity of HTN and with the damage to target organs, for example left ventricular mass [8-10].

Hypertension has been increasing significantly in recent years in low- and very low-income areas, where studies estimate that approximately 1.04 billion people, or 31.5% of the population in these areas, currently suffer from hypertension [10,11]. It is the leading cause of cardiovascular disease and premature death in adults [12-14]. Studies suggest that the development of hypertension in adulthood is based on pathophysiological mechanisms that begin early in life, during childhood [12,15].

According to studies, albumin is investigated in an extremely small percentage of patients with hypertension (4%), despite the fact that the European Society of Cardiology recognizes albumin as one of the 5 pillars in the prevention of cardiovascular pathologies [4,16].

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The purpose of this paper is to present the link between albumin and hypertension, and thus to raise an alarm on the prevention of cardiovascular pathologies using albumin as a risk marker but also as a marker in the therapeutic management of hypertension.

Materials and methods

We conducted a retrospective study, over a period of 6 months, within the cardiology department of the Cluj Heart Institute, on a number of 54 patients, of whom 34 represented the study group (with hypertension) and 20 patients the control group.

Inclusion criteria for the study group: patients admitted to the cardiology department with essential hypertension (HTN).

Exclusion criteria for the study group: secondary hypertension or pathologies that may be associated with increased blood pressure, even if the patients currently had normal blood pressure values.

The inclusion criteria in the control group were patients without hypertension or pathologies associated with increased blood pressure values.

We aimed to determine the incidence and values of microalbuminuria in both groups, to see if microalbuminuria values increase in parallel with blood pressure values, to compare left ventricular mass values according to the severity of hypertension, to determine the incidence of ischemic cardiopathy in relation to the severity of hypertension, to compare microalbuminuria values in patients with hypertension and ischemic cardiopathy compared to those without ischemic cardiopathy, and to highlight a possible linear correlation between microalbuminuria and left ventricular mass.

Inclusion criteria: patients admitted to the cardiology department with essential hypertension.

Exclusion criteria: secondary hypertension or pathologies that may be associated with increased blood pressure, even if the patients currently had normal blood pressure values.

Results

The analysis of the two groups shows that the average age of the patients in the study group was 59.8 years, and in the control group it was 47.78 years. The female gender was significantly more representative (71%) compared to the male gender (29%) in the study group. The ratio regarding the environment of origin is approximately equal, between rural and urban. Most patients in the study group had grade III hypertension.

As for the severity of hypertension, 10 patients (29%) from the study group presented with hypertension grade I, 6 patients (18%) grade II and 18 patients (53%) grade III and 20.93% of the patients in the study presented with microalbuminuria. The microalbuminuria ratio varied depending on the degree of hypertension from 10% for stages I and II to 50% for those with grade III hypertension (Table 1).

Left ventricular mass was significantly higher in patients with grade II hypertension (p=0.00685) and in patients with grade III hypertension (p=0.00086) compared to patients with grade I hypertension. The mean values of LVH are presented in Table 2. No significant differences were found between LVH of patients with grade II hypertension and patients with grade III hypertension (Figure 1 and 2).

As we well know, HTN is associated with significant cardiovascular changes, and ischemic cardiomyopathy is an important complication that increases the morbidity and mortality rate in these patients. In our study group, 32.36% of patients had associated ischemic cardiopathy, with an incidence that was not associated with the severity of HTN, thus in patients with HTN grade I in the study, the incidence of ischemic cardiopathy was 30%, for those with HTN grade II, the incidence reached 50% and for patients with HTN grade III, the presence of IC was documented in 21.43% of patients

The average values of microalbuminuria were within the normal range in patients with grade I and grade II hypertension. Patients with grade III hypertension had microalbuminuria above the normal range. The difference between microalbuminuria found in the control group and that determined in patients with grade I hypertension was not statistically significant. A statistically significant difference was found between microalbuminuria determined in the control group and that of patients with grade III hypertension (p=0.0022). There was no statistically significant difference between microalbuminuria determined in patients with grade II hypertension and the control group (p=0.0394), as well as between microalbuminuria in patients with grade III hypertension and that of patients with grade II hypertension compared to patients with grade I hypertension. Patients with grade III hypertension had a significantly higher urinary albumin excretion compared to patients with grade I (p=0.03) and grade II (p=0.04) hypertension(Figure 3).

Although the microalbuminuria values determined in patients with HTN and IC are higher than in patients without IC (39.845+/-16.32 vs 19.68+/-6.64), this difference is not statistically significant (p- NS)(Figure 4).

The linear correlation index between the value of microalbuminuria and left ventricular mass was calculated.

Table 1. Average microalbuminuria values in patients with grade I, II and III and in the control group

Batch	Microalbuminuria (µg/min) Average +/- standard error
Control	5.46 +/- 1.33
HTN grade I	9.86 +/- 3.10
HTN grade II	13.12 +/- 5.40
HTN grade III	57.31 +/- 20.27

Table 2. Left ventricular mass in patients with HTN

HTN Severity	Left ventricular mass Average +/- standard error
Grade I	246.51 +/- 19.69
Grade II	343.65 +/- 26.96
Grade III	344.00 +/- 18.28

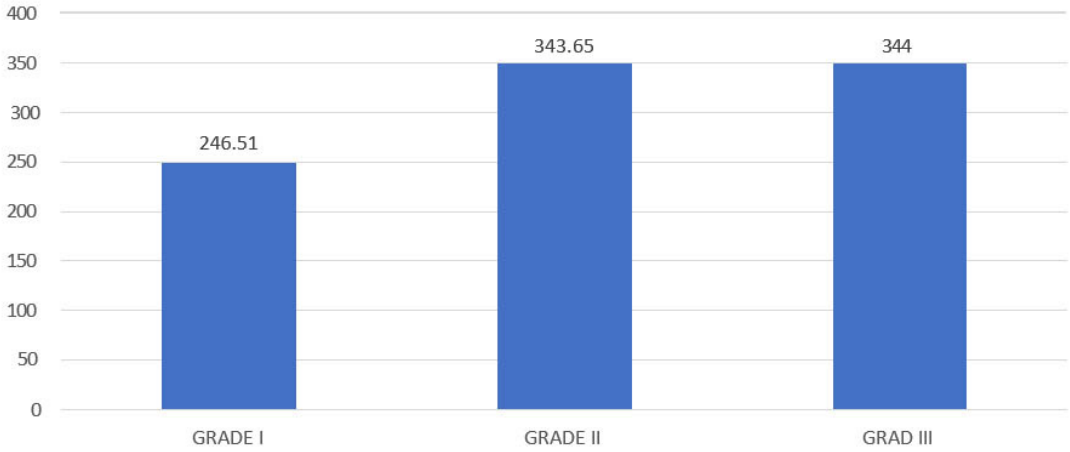

Fig. 1. Left Ventricular Mass acording to the HTN severity

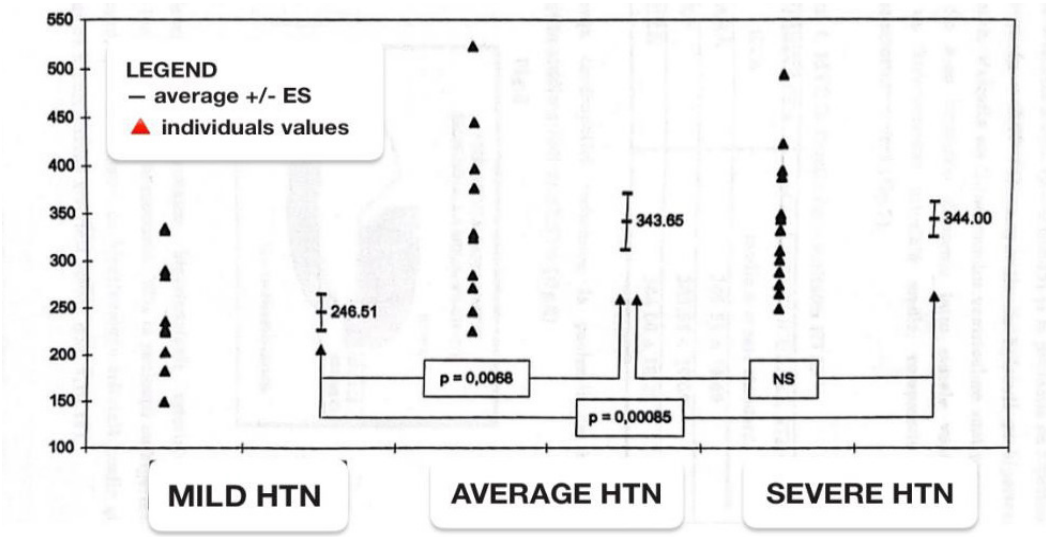

Fig. 2. Left Ventricular Mass acording to the HTN severity

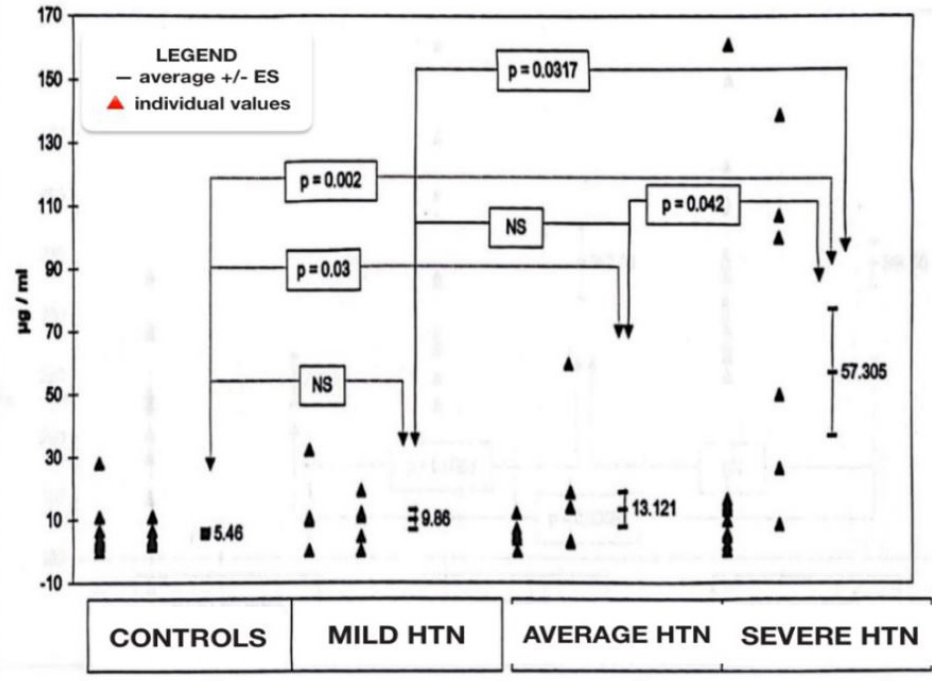

Fig.3. The relationship between hypertension and microalbuminuria

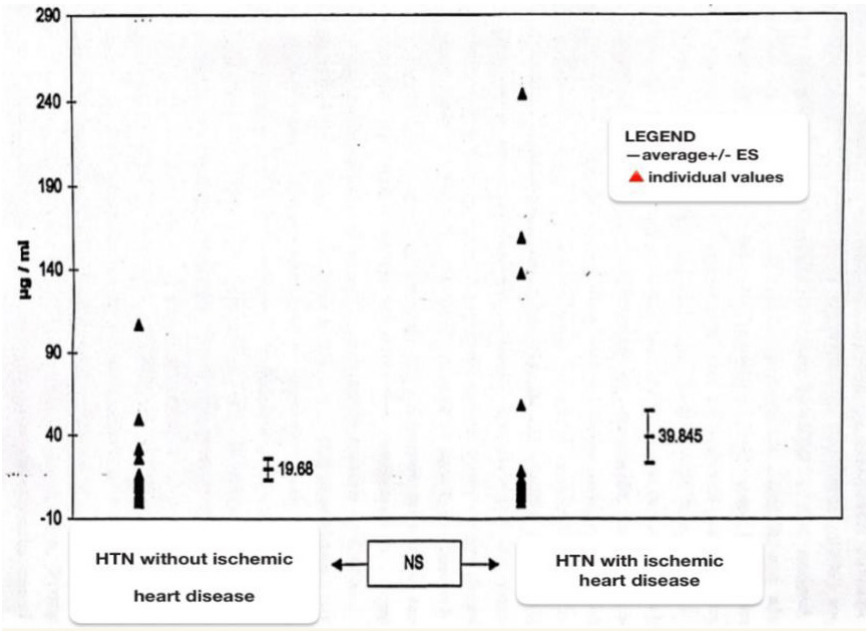

Fig. 4. The values of microalbuminuria in patients with hypertension and heart failure versus those without heart failure

No linear correlation was found between the increase in microalbuminuria and the increase in left ventricular mass (Figure 5).

Discussions

Hypertension is a real global health problem, with negative multisystemic repercussions, being an important factor in increasing morbidity and mortality [17,18]. Obesity, the definition of the unbalanced lifestyle of modern man, is an important cause for the occurrence of essential hypertension but also for the installation of chronic non-communicable diseases that associate hypertension and shorten life expectancy [19-21].

According to studies, the prevalence of microalbuminuria in patients with HTN varies between 8 and 40%. The incidence of microalbuminuria in the group of hypertensive patients studied was 20.39%, with a higher incidence in patients with HTN grade III-50% versus HTN grade I and II, but this difference did not reach the limit of statistical significance (p=0.07-NS). Thus, our study is in line with other specialized studies, which support the increase in the prevalence of microalbumin in parallel with the increase in blood pressure values [12,22].

The relationship between hypertension and microalbuminuria has also been studied in pediatric patients, due to the alarming increase in the prevalence of HTN in this age group. Thus, the analysis of a group of 306 children aged between 6 and 9 years, without cardiovascular or renal pathologies, shows a prevalence of 42.8% of prehypertension or hypertension, with a prevalence of microalbuminuria of 10.1% [12]. Numerous studies on this age group also suggest an association between blood pressure levels and microalbuminuria values, and The European Society of Hypertension recommends its routine measurement in the management of hypertension in the pediatric population [1,23].

The average EUA was within the normal range in patients with grade I hypertension (9.86+/-3.1 µg/min) and

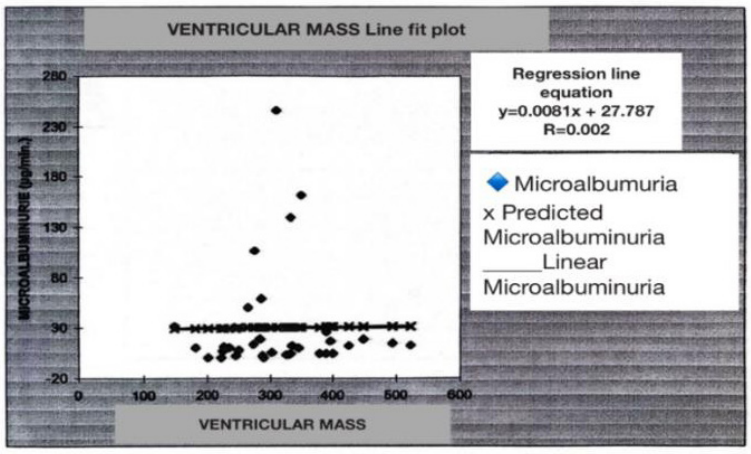

Fig. 5. The linear correlation index between the value of microalbuminuria and left ventricular mass

in those with grade II hypertension (13.12+/- 5.4 μg/min), but for grade III hypertension microalbuminuria was 57.31+/-20.27 μg/min, a significantly higher value compared to the control group (p=0.0022). Thus, we align ourselves with other studies that support that the severity of microalbuminuria correlates with the severity of hypertension and the degree of target organ damage.

Left ventricular mass, determined by echocardiography, is a common method for assessing the degree of left ventricular hypertrophy, especially in patients with hypertension [24,25]. It is proportional to the severity of hypertension and correlates with the severity of microalbuminuria.

The Framingham study confirms the association between left ventricular mass and cardiovascular morbidity or mortality, concluding that left ventricular hypertrophy is the most important risk factor for sudden death, congestive heart failure, acute myocardial infarction, and stroke [26,27]. Therefore, left ventricular hypertrophy is a risk factor for mortality and morbidity in patients with hypertension [28].

Left ventricular mass was significantly higher in patients with grade III hypertension (344.00+/-18.28g vs 246+/- 19.69g-p=0.00086) and grade II hypertension (343+/- 29.61g vs 246+/-19.69g-p-0.00685). In our study, the degree of left ventricular hypertrophy, expressed as left ventricular mass, was proportional to the severity of hypertension. The degree of left ventricular hypertrophy can also be influenced by the duration of hypertension or the degree of control, pharmacological or non- pharmacological, of blood pressure values [25,29].

It is known that left ventricular hypertrophy regresses under treatment with ACE inhibitors, beta- blockers and calcium channel blockers. In most studies in which a reduction in left ventricular hypertrophy was found, ACE inhibitors were used, representing the medication of choice [30]. The association between left ventricular hypertrophy and microalbuminuria represents an accumulation of two independent risk factors, correlated with increased cardiovascular morbidity and mortality, which may act through different mechanisms. Patients with HTN who present concomitant left ventricular hypertrophy and microalbuminuria should be treated and monitored carefully due to the accumulation of the aforementioned risk factors. We can state that microalbuminuria would represent a marker of the severity of vascular-endothelial damage in patients with essential HTN [12,31].

Microalbuminuria was also higher in patients with hypertension and ischemic heart disease compared to patients without ischemic heart disease (39.845 +/- 16.32 vs 19.68 +/- 6.64). This difference was not statistically significant (p-NS).

Boorsma and colab. present higher values of microalbuminuria and macroalbuminuria in patients diagnosed with heart failure [32].

The average EUA in hypertensive patients with ischemic heart disease did not exceed the value considered as the threshold for microalbuminuria (20 μg/ml). The finding that patients with HTN and ischemic heart disease presented microalbuminuria, and in those with ischemic heart disease the average EUA did not exceed the microalbuminuria threshold, confirms once again the role of microalbuminuria as a marker of the severity of vascular damage and thereby of the predisposition to atherosclerosis. A study of 45,006 patients from Korea with a history of coronary artery calcification demonstrated the association between coronary artery calcifications identified by imaging studies and the presence of albuminuria [33].

Mortality from acute coronary syndromes was associated with albuminuria in the TRACER study [34].

Increased microalbuminuria was significantly associated with the occurrence of carotid plaques (p- 0.035, OR-1.035, IC95%- 1.002-107) and in a study from Slovakia, we can thus state that microalbuminuria is a possible marker for assessing cardiovascular risk in both asymptomatic and symptomatic patients. [31]

Conclusions

Hypertension is a real health problem worldwide, being a leading cause of morbidity and mortality. It is part of the clinical picture of many chronic non-communicable diseases, either asymptomatic or symptomatic. The gray area, if we may say so, of hypertension is represented by asymptomatic patients, who benefit little or no from investigations, thus allowing elevated blood pressure values to persist without medical intervention for a long period of time, with negative effects on health.

Microalbuminuria could represent a rapid and early assessment marker both during hospitalization and during outpatient examinations or medical offices, correlated with the severity of arterial hypertension, but also a marker for personalized assessment of cardiovascular risk. Our study was consistent with other specialized studies, showing a statistically significant association between the degree of hypertension and cardiovascular damage with microalbuminuria values. The limitations of the study are represented by the small number of patients included in the study.

We consider more specialized studies, on larger samples, necessary so that the use of microalbuminuria as a marker for the severity of HTN becomes a common reality.

Authors' contributions

HA (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Writing – original draft; Writing – review & editing)

HM (Conceptualization; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing)

HD (Corresponding author) – (Conceptualization; Formal analysis; Investigation; Writing – review & editing)

Conflict of interest

None to declare.

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