

## MICROALBUMINURIA AS A SPECIAL PROGNOSTIC MARKER FOR HEART FAILURE

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✓ **Resume,**

*Numerous works in recent decades have been devoted to the study of the clinical, including prognostic, importance of microalbuminuria (MAU), methods for its detection and quantification, as well as therapeutic measures aimed at combating this pathological condition.*

**Keywords:** microalbuminuria, prognostic marker, heart failure, pathological condition.

## ЮРАК ЕТИШМОВЧИЛИГИДА МИКРОАЛЬБУМИНУРИЯ ПРОГНОСТИК МАРКЕР СИФАТИДА

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✓ **Резюме,**

*Охириги йилликда олиб борилган кўп сонли клиник - прогностик текширишлар натижаларига кўра, микроальбуминурия юрак етишмовчилигини даволаш мақсадида, патологик жараёнга қарши курашишда прогностик маркер сифатида қабул қилинди.*

**Калит сўзлар:** микроальбуминурия, прогностик маркер, юрак етишмовчилиги, патологик ҳолатлар.

## МИКРОАЛЬБУМИНУРИЯ КАК СПЕЦИФИЧЕСКИЙ ПРОГНОСТИЧЕСКИЙ МАРКЕР ПРИ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

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✓ **Резюме,**

*Многочисленные работы в последние десятилетия посвящены исследованию клинической, в том числе прогностической, значимости микроальбуминурии (МАУ), методов ее выявления и количественного определения, а также лечебных мер, направленных на борьбу с данным патологическим состоянием.*

**Ключевые слова:** микроальбуминурия, прогностический маркер, сердечной недостаточности, патологический состояния.

### Introduction

Numerous works in recent decades are devoted to the study of the clinical, including prognostic, importance of microalbuminuria (MAU), methods for its detection and quantification, as well as therapeutic measures aimed at combating this pathological condition. The interest in the problem is explained by the fact that UIA is regarded as one of the earliest unfavorable prognostic signs and risk factors for the development of target organ damage in such widespread diseases as arterial hypertension (AH) and diabetes mellitus (DM). At the same time, according to the Copenhagen City Heart Study-3 [7,8], and a lower excretion of albumin in the urine may also indicate an increased risk of cardiovascular disease (CVD) and cardiovascular death.

UIA is the most important early sign of kidney damage, reflecting the initial stages of vascular pathology (endothelial dysfunction, atherosclerosis), and invariably correlates with an increase in the incidence of CVS and mortality. According to clinical studies, even a slight increase in the excretion of albumin in the urine is associated with a significant increase in the risk of cardiovascular events, including fatal ones. Progressive increase in the level of UIA unambiguously indicates a worsening of the vascular condition and, accordingly, causes an additional risk increase [6,9]. In connection with this, UIA is recognized as an independent factor of

cardiovascular risk and the earliest (preclinical) sign of the defeat of such vulnerable target organs as the kidneys.

MAU is a consequence of the increased loss of albumin from the blood plasma through the endothelium and is therefore defined as a marker of the development of systemic endothelial dysfunction. And endothelial dysfunction is characteristic for early stages of atherosclerosis and is directly related to increased cardiovascular risk [5,6,9,15]. Recently, a relationship of microalbuminuria with pronounced coronary atherosclerosis has been established according to angiography [10]. In one of the LIFE (Losartan Intervention for Endpoint reduction in hypertension) [15], it was found that increased urinary protein excretion is clearly associated with left ventricular hypertrophy, regardless of age, sex, race, blood pressure (BP), the presence of diabetes, smoking, the level of creatinine in the blood. Especially often, UIA is detected with diabetes and hypertension. According to various data, UIA is found in 10-40% of patients with type 1 diabetes and in 15-40% of patients with type 2 diabetes [6,9,14].

For example, in the EUCLID (EURODIAB controlled trial of lisinopril in insulin dependent diabetes), MAU was determined in approximately 15% of 530 patients with type 1 diabetes [11]. The frequency of detection of UAS increases with the duration of the disease with diabetes of both types. In a major UK study UKPDS (United Kingdom Prospective Diabetes Study),

UIA was detected in 12% of patients with newly diagnosed type 2 diabetes and in almost 30% of patients with a disease duration of more than 12 years [12]. Detection of new cases of UIA in patients with diabetes may range from 1 to 3% per year. Under the supervision of most studies, among untreated patients with mild and moderate hypertension, the prevalence of MAU varies from 15 to 40%, averaging about 25%. The frequency of detection of UAS is higher in patients with newly diagnosed AH and with inadequate antihypertensive therapy. In a large-scale i-SEARCH study (2007) involving about 22,000 patients from 1750 centers, UIA was found in the majority of patients with AH: in 53-71% of cases, with the highest urinary protein excretion rates recorded with uncontrolled AH [2]. In the DIABHYCAR study (2003), it was reliably demonstrated that the detection of UIA is associated with a high risk of developing heart failure [13]. In the MICROHOPE study (Microalbuminuria, Cardiovascular and Renal Outcomes Heart Outcomes Prevention Evaluation), patients with baseline microalbuminuria had a significantly higher risk of major cardiovascular manifestations, total mortality and hospitalizations associated with heart failure compared with patients who did not initially have an MAU, regardless of the presence of diabetes mellitus [4].

According to a study by Johan Arnlov et al. (2005), microalbuminuria increases the risk of cardiovascular disease and cardiovascular mortality by more than 3 times [1]. The results of the PREVEND (Prevention of Renal and Vascular Endstage Disease) study provided conclusive evidence that UIA is a potent predictor of cardiovascular mortality in the population, regardless of other risk factors [3].

It is curious that the relationship between microalbuminuria and cardiovascular morbidity was detectable even at very low urinary protein excretion rates. So, in

the study Copenhagen City Heart-3, the risk of coronary heart disease and cardiovascular death increased (regardless of the presence of arterial hypertension, diabetes and renal pathology) already at a albuminuria level  $> 4.8 \mu\text{g}/\text{min}$ , which is significantly lower than the generally accepted lower threshold for the diagnosis of microalbuminuria ( $20 \mu\text{g}/\text{min}$ ) [7]. Numerous experimental, clinical and epidemiological studies indicate that microalbuminuria is one of the most important independent risk factors for cardiovascular and cerebrovascular events, as well as death from them.

## Materials and methods

UIA is understood as the level of excretion of albumin in urine from 30 to 300 mg/day (or from 20 to 200  $\mu\text{g}/\text{min}$ ). In European countries, the ratio of albumin to creatinine in urine is often used to determine protein loss in urine-microalbuminuria is often indicated by the numbers 2.5-30 mg / mmol in men and 3.5-30 mg / mmol in women [6]. The determination of albumin excretion in the urine is carried out in the morning or daily portions of urine. The level of albuminuria has a high variability - up to 30%, which is affected by: physical activity, fever, as well as concomitant pathology: uncontrolled hypertension and hyperglycemia, heart failure. Levels of albuminuria, regarded as microalbuminuria, are used to diagnose the condition of all categories of patients and healthy individuals.

The study involved 30 patients (22 men and 8 women) undergoing heart failure in cardiology for heart failure (III-IV class in the New York Heart Association (NYHA)) (Table 1). The average age of the patients was 66.5 years. Diabetes mellitus was noted in 14 patients (46.7%), arterial hypertension in 23 patients (76.7%). 5 patients (16.7%) had nodiabetes mellitus, no arterial hypertension.

Table 1.

**Distribution of patients by sex, age and concomitant pathologies.**

№	Quantity	Average age	Diabetes	Hypertension	Absence of concomitant pathology
Man	22(73%)	63,23	10	15	5
Female	8 (27%)	68,25	4	8	-

The examination included electrocardiography (ECG), echocardiography (EchoCG), a biochemical blood test, and microalbuminuria in morning urine (in  $\mu\text{g}/\text{min}$ ). The albuminuria level was determined by turbidimetric method using a biochemical analyzer "HITACI cobac c 311" (Roche) using Tina-Qant diagnostic kits.

## Results of the research

The number of patients with microalbuminuria was 17 (57%). In 9 patients, the albumin level in urine did not exceed  $20 \mu\text{g} / \text{min}$  - the norm (30%). Four patients had macroalbuminuria, a level above  $200 \mu\text{g} / \text{min}$  (13%) (Figure 1-2). Repeated hospitalization was observed in 8 patients with microalbuminuria and in 1 patient with macroalbuminuria. Lethal outcome was recorded in 1 patient with microalbuminuria and in 2 patients with macroalbuminuria.

## Conclusion

Thus, the conducted studies once again confirmed that patients with initial UIA had a higher risk of total mortality, repeated hospitalizations associated with heart failure than patients without UIA. Based on these data, it can be concluded that UIA is an early preclinical sign of endothelial vascular dysfunction and a reliable marker of high cardiovascular risk.

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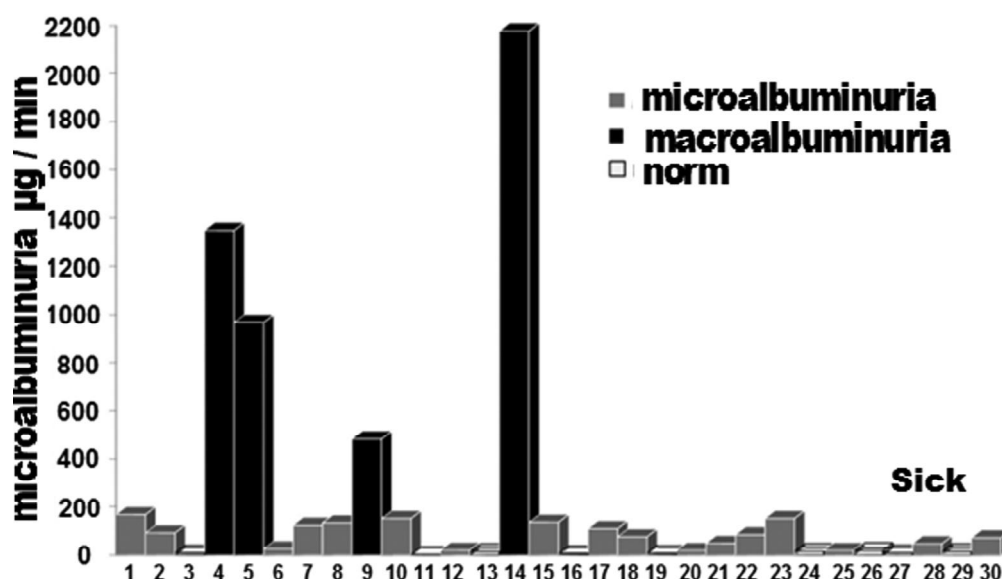


Figure 1. The level of albumin in the urine of patients

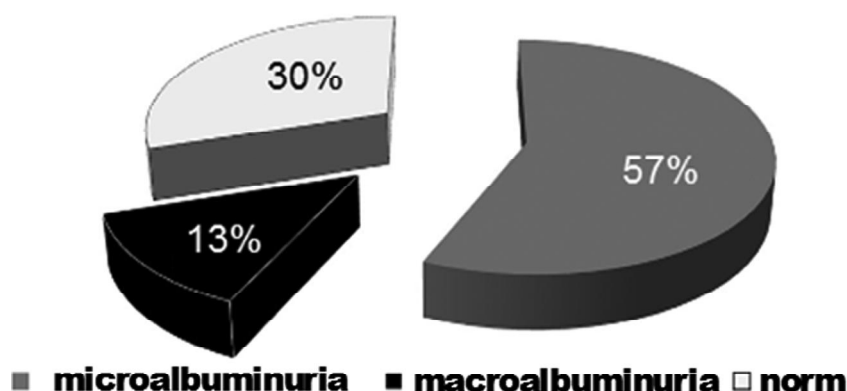


Fig. 2. Percentage ratio of patients with different levels of albumin in the urine

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