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Uric acid as a link between renal dysfunction and both pro-inflammatory and prothrombotic state in patients with metabolic syndrome and coronary artery disease

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Abstract

Background: Hyperuricaemia has long been known to be associated with cardiovascular disease, and it is particularly common in patients with kidney disease, metabolic syndrome and diabetes mellitus. Metabolic syndrome is associated with pro-inflammatory and prothrombotic state.

Aim: To examine the association between renal function, serum uric acid and markers of both pro-inflammatory and prothrombotic state in patients with diabetes mellitus (DM), metabolic syndrome and coronary artery disease.

Methods: The study population consisted of 91 patients (58 men, 33 women) aged 57.6 ± 10.3 years with metabolic syndrome and type 2 DM. Patients were selected from a large group of patients scheduled for routine coronary angiography between 2006 and 2009. The patients were evaluated for the common risk factors for atherosclerosis: smoking, hypertension, DM, family history and hyperlipidaemia. Laboratory tests included complete blood counts, serum urea and creatinine, aminotransferases, C-reactive protein (CRP), fibrinogen, uric acid, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting glucose, glycated haemoglobin (HbA1c), glomerular filtration rate (GFR) and urinary protein. We also measured body mass, height, waist circumference, hip circumference and calculated body mass index (BMI) and waist-to-hip ratio (WHR).

Results: The following significant correlations were observed: body mass *vs* serum creatinine ($r = 0.291$; $p = 0.009$), WHR *vs* serum creatinine ($r = 0.672$; $p < 0.001$), WHR *vs* GFR ($r = –0.706$; $p < 0.001$), WHR *vs* uric acid ($r = –0.341$; $p = 0.001$), WHR *vs* uric acid ($r = 0.295$; $p = 0.05$), BMI *vs* CRP ($r = 0.231$; $p = 0.031$), WHR *vs* CRP ($r = 0.236$; $p = 0.024$), serum creatinine *vs* uric acid ($r = 0.362$; $p < 0.001$), GFR *vs* uric acid ($r = –0.341$; $p = 0.001$), uric acid *vs* CRP ($r = 0.251$; $p = 0.016$), CRP *vs* fibrinogen ($r = 0.470$; $p < 0.001$), CRP *vs* platelet count ($r = 0.282$; $p = 0.04$) and HbA1c *vs* platelet count ($r = 0.263$; $p = 0.0112$). Multiple stepwise regression analysis showed that uric acid level was independently associated with WHR, GFR and CRP.

Conclusions: In patients with ischaemic heart disease, DM and metabolic syndrome, obesity, particularly visceral obesity, is associated with renal dysfunction and elevated markers of pro-inflammatory state. Renal dysfunction co-exists with elevated serum uric acid. Elevated serum uric acid is associated with markers of pro-inflammatory state. Markers of pro-inflammatory state correlate with prothrombotic markers such as serum fibrinogen and platelet count. Uric acid should be taken into consideration as a link between renal dysfunction and both pro-inflammatory and prothrombotic state in patients with metabolic syndrome and coronary artery disease.

Key words: metabolic syndrome, diabetes mellitus, uric acid, inflammation, prothrombotic state

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INTRODUCTION

Obesity and obesity-related metabolic syndrome are associated with the development of end-stage renal disease. Body mass index (BMI) values exceeding 25 kg/m^2 have been associated with the risk of end-stage renal disease even when adjusted for the presence of diabetes mellitus (DM) and hypertension [1]. Renal dysfunction is one of the strongest predictors of cardiovascular (CV) events and CV risk. Large studies investigating nearly a million subjects have shown an independent and discrete association between various degrees of renal dysfunction and the risk of CV events [2].

The traditional CV risk factors are not always suitable for the assessment of patients with metabolic syndrome. This also applies to some of the recently studied risk factors associated with the pathogenesis of atherosclerosis [3]. It is therefore justified to look for novel factors that would predict CV risk before the development of overt renal dysfunction on the one hand and adverse CV events on the other.

Clinical and epidemiological studies have unequivocally confirmed the association between high levels of uric acid and the severity of coronary artery atherosclerosis [4]. There is also a strong association between serum uric acid and waist-to-hip ratio (WHR), a manifestation of visceral obesity which is a component of metabolic syndrome [5]. On the other hand, uric acid is a novel and independent predisposing factor of renal dysfunction in the general population [6].

Inflammation is characterised by elevated levels of acute phase proteins, such as fibrinogen and C-reactive protein (CRP), and elevated levels of such cytokines as IL-6 and TNF-α. All these biomarkers, which are CV risk factors at the same time, are markedly elevated in patients with metabolic syndrome and DM [7]. Elevated fibrinogen, in addition to the other coagulation factors, reflects the increased prothrombotic tendency so typical of visceral obesity [8].

The aim of our study was to evaluate the association between renal function, serum uric acid and markers of pro-inflammatory and prothrombotic state in patients with DM and metabolic syndrome.

METHODS

Study population

A total of 91 patients (58 men and 33 women) aged 57.6 ± ± 10.3 years with DM and metabolic syndrome were included in the study. The diagnosis of metabolic syndrome was based on the NCEP ATP III criteria [2], which include the following abnormalities: (1) visceral obesity, defined as waist circumference ≥ 102 cm in men and ≥ 88 cm in women; (2) fasting glucose ≥ 100 mg/dL or hypoglycaemic treatment; (3) systolic blood pressure (SBP) ≥ 130 mm Hg or diastolic blood pressure (DBP) ≥ 85 mg, or antihypertensive treatment in hypertensive patients; (4) triglycerides ≥ 150 mg/dL or lipid-lowering treatment; and (5) HDL-cholesterol < 40 mg/dL in men and < 50 mg/dL in women, or cholesterol-lowering treatment.

The study population was selected from patients admitted for elective coronary arteriography or coronary angioplasty. Patients who, in addition to DM, met at least two of the above diagnostic criteria for metabolic syndrome were eligible.

Study assessments

A detailed history was taken from all the patients, including the risk factors for atherosclerosis, such as hypertension, lipid abnormalities, DM, smoking, a family history of CV disease, and signs of atherosclerosis in various locations. The patients also underwent a physical examination including the measurement of SBP and DBP using the Korotkoff method.

Body mass, height, waist circumference and hip circumference were measured and the values of BMI were calculated from the following formula: BMI [kg/m^2] body mass [kg]/body surface area (BSA) [m^2], where BSA was calculated from the Gehan and George formula as follows: BSA [m^2] = 0.0235 × × (body mass [kg])$^{0.51456}$ × height [cm]$^{0.42246}$. The WHR was calculated form the following formula: WHR = waist circumference [cm]/hip circumference [cm].

In addition, all the patients underwent fasting blood sampling prior to coronary arteriography. Complete blood cell counts and serum levels of standard parameters were measured. The HbA1c concentration was measured in whole blood by turbidimetry method (Roche). Glomerular filtration rate (GFR) was calculated from the modification of diet in renal disease (MDRD) formula [9]: GFR [mL/min/1.73 m^2] = 186 × × serum creatinine$^{-1.154}$ × age$^{-0.203}$ × F, where F = 1 in men and F = 0.742 in women. The 24-hour proteinuria levels were measured from the following formula: protein (mg/dL × × 24-hour urine collection)/100, where protein was determined by turbidimetry.

Statistical analysis

The results were analysed with the use of Statistica 6.0 PL. The values are presented as means ± SD or as absolute and relative frequencies. We performed analysis of correlation calculating the coefficients of correlation. We also performed multivariate regression analysis in order to establish the association between uric acid levels and other variables. The following independent variables were included in the regression model: BMI, WHR, platelet count, serum urea, serum creatinine, CRP, fibrinogen, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting glucose, HbA1c, GFR. A p value < 0.05 was considered significant.

RESULTS

Table 1 summarises the principal clinical characteristics of the study population. The BMI and WHR values show that obesity in the study population was of visceral nature. It is

Table 1. Clinical and angiographic characteristics of the study population

Age [years]	57.6 ± 10.3
Males	58 (63.7%)
Duration of diabetes mellitus [years]	11.35 ± 10.51
Body mass [kg]	84.9 ± 14.8
Height [cm]	168.1 ± 7.8
Body mass index [kg/m^2]	30.2 ± 6.0
Waist-to-hip ratio	0.97 ± 0.11
Hypertension	87 (95.6%)
Coronary artery disease	72 (79.1%)
Heart failure	34 (37.2%)
Atrial fibrillation	23 (25.3%)
History of myocardial infarction	42 (46.2%)
Haemorrhagic stroke	2 (2.2%)
Ischaemic stroke	7 (7.7%)
Family history of cardiovascular disease	29 (31.7%)
Smoking	26 (28.6%)
No changes in the coronary arteries	19 (20.9%)
One-vessel disease	17 (18.7%)
Two-vessel disease	30 (33.0%)
Three-vessel disease or left main stem disease	25 (27.5%)

also important that the most common clinical abnormalities in the study population were angiographically confirmed coronary artery disease (79.1%) and hypertension (95.6%).

Laboratory results in the study population are summarised in Table 2. The mean serum creatinine and mean serum urea values were normal in the presence of reduced GFR. Mean serum CRP and mean serum uric acid were both markedly elevated. Lipid profiles were characterised by elevated triglycerides and markedly reduced HDL-cholesterol accompanied by normal values total cholesterol and LDL-cholesterol. The remaining biochemistry parameters were within normal ranges.

There was a significant correlation between body mass and serum creatinine (Fig. 1). A significant correlation was also demonstrated between WHR and renal function parameters, namely serum creatinine and GFR (Figs. 2, 3). Both obesity-related parameters, BMI and WHR, significantly correlated with serum CRP (Table 3). The WHR was significantly associated with uric acid (Fig. 1).

A close association between uric acid and renal function represented by serum creatinine (Table 3) and GFR (Fig. 2) was documented. Uric acid was also closely associated with CRP (Fig. 3). Prothrombotic markers, namely serum fibrinogen and platelet count, were associated with serum CRP

Table 2. Laboratory results in the study population

Parameter	Mean	Minimum	Maximum	SD
RBC [million/μL]	4.47	3.0	5.89	0.57
WBC [thousand/μL]	7.6	2.1	15.1	2.34
HGB [g/dL]	13.3	9.6	17.0	1.59
HCT [%]	38.96	28.80	49.0	4.44
PLT [thousand/μL]	273.76	146.0	717.0	88.84
Serum urea [mg/dL]	49.05	17.1	226.8	28.19
Serum creatinine [mg/dL]	1.06	0.40	2.6	0.42
eGFR [mL/min/1.73 m^2]	73.69	28.3	139.6	24.46
24-hour urinary protein [g/24 h]	1.12	0	3.47	0.53
AST [U/L]	26.01	11.0	106.0	12.24
ALT [U/L]	26.39	10.0	99.0	14.82
Total cholesterol [mg/dL]	169.49	64.0	330.0	48.35
HDL-cholesterol [mg/dL]	43.98	4.0	103.0	14.13
LDL-cholesterol [mg/dL]	95.47	121.0	249.0	43.97
Triglycerides [mg/dL]	150.11	49.0	596.0	81.15
Glucose [mg/dL]	144.87	57.0	345.0	55.41
HbA1c [%]	7.58	4.27	15.49	1.63
CRP [mg/L]	6.94	0.5	33.7	7.58
Fibrinogen [g/L]	4.7	2.58	8.87	1.24
Uric acid [mg/dL]	6.68	2.9	12.1	1.81

RBC — red blood count; WBC — white blood count; HGB — haemoglobin; HCT — haematocrite; PLT — platelets; GFR — glomerular filtration rate; AST — aspartate transferase; ALT — alamine transferase; HDL — high density protein; LDL — low density protein; HbA1c — glycated haemoglobin; CRP — C-reactive protein

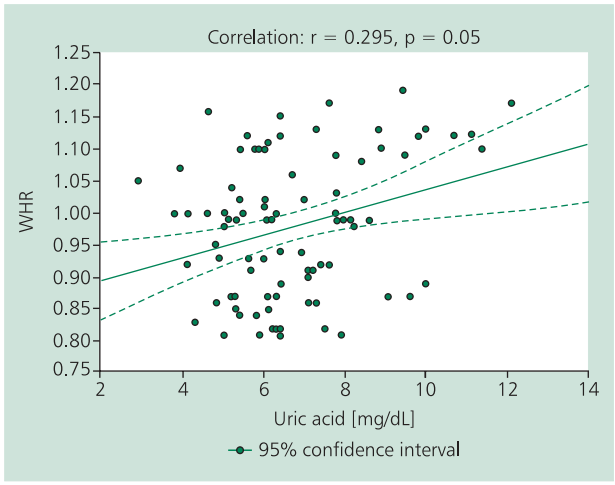

Figure 1. The association between uric acid and waist-to-hip ratio (WHR)

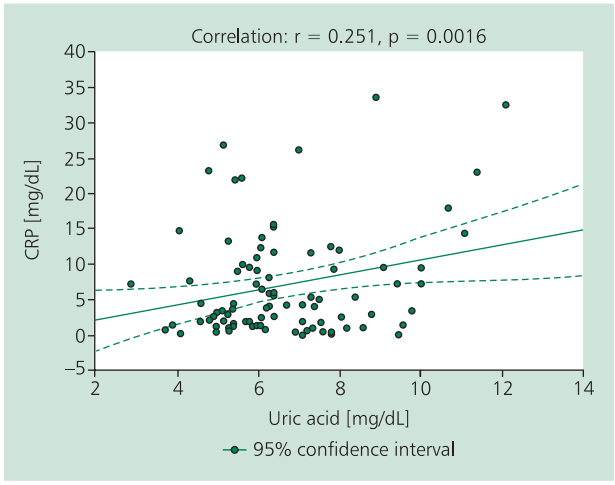

Figure 3. The association between uric acid and C-reactive protein (CRP)

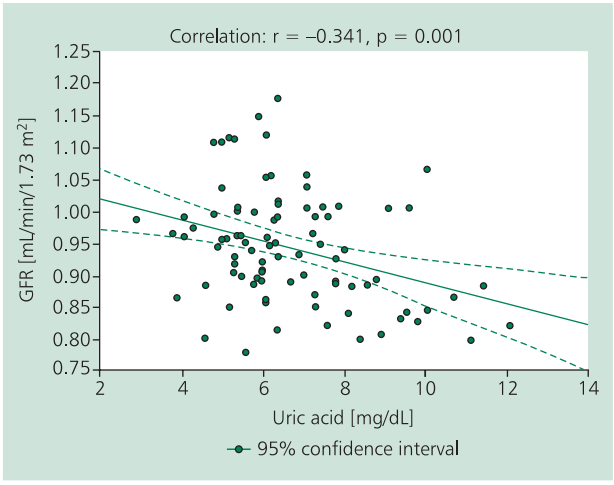

Figure 2. The association between glomerular filtration rate (GFR) and uric acid

Table 3. Significant correlations between the assessed parameters

Compared parameters	r	P
Body mass *vs* serum creatinine	0.291	0.009
WHR *vs* serum creatinine	0.672	< 0.001
WHR *vs* serum urea	0.500	< 0.001
WHR *vs* GFR	–0.706	< 0.001
BMI *vs* CRP	0.231	0.031
WHR *vs* CRP	0.236	0.024
WHR *vs* fibrinogen	0.237	0.024
Serum creatinine vs uric acid	0.362	< 0.001
CRP *vs* fibrinogen	0.470	< 0.001
CRP *vs* platelet count	0.282	0.04
HbA1c *vs* platelet count	0.263	0.012

WHR — waist-to-hip ratio; BMI — body mass index; rest abbreviations as in Table 2

(Table 3). Platelet count was associated with glycaemic control defined by HbA1c (Table 3).

The independent factors affecting uric acid levels in multivariate regression analysis were WHR, GFR and CRP (Table 4).

DISCUSSION

We showed that serum creatinine negatively correlated with body mass. When we corrected body mass for BSA this correlation disappeared, as BMI did not correlate with GFR, serum creatinine or serum urea. This is in contrast to data from literature. The Framingham study showed that BMI was one of the risk factors of chronic renal failure [10]. Furthermore, a Swedish study showed an association between BMI, especially at a young age, and elevated serum creatinine [11]. The untoward effects of obesity on the risk of renal failure are maintained even after such unquestionable risk factors for renal dysfunction as hypertension and DM have been excluded [12].

The study population was characterised by mild renal dysfunction (mean GFR was reduced, while serum creatinine and urea were both normal). These are far more sensitive parameters than BMI in predicting renal dysfunction in this patient group, as confirmed by the study by Pinto-Sietsma et al. [13], who demonstrated that even non-obese patients are at risk of reduced glomerular filtration and microalbuminuria, if they are constitutively characterised by visceral obesity. Me-

Table 4. Multivariate regression analysis

Dependent variable	Independent variables	B	Standard error	β	P
Uric acid	WHR	0.42	0.26	0.28	0.039
	GFR	–2.97	0.55	0.52	0.001
	CRP	1.19	0.28	0.27	0.009

Abbreviations as in Table 2

tabolic syndrome is associated with a high risk of renal dysfunction even in the absence of abnormal glucose metabolism. A prospective nine-year observation of 2110 patients with metabolic syndrome selected from a group of more than 15,000 patients enrolled in the Atherosclerotic Risk in Communities (ARIC) study showed a significantly higher incidence of renal failure in this patient group even in the absence of type 2 DM [1].

The pathogenetic causes of renal failure in the course of metabolic syndrome are unclear. Hyperfiltration and proteinuria observed in the initial stage of metabolic syndrome and associated with obesity are two examples of these factors. Hyperfiltration is one of the early effects of metabolic syndrome, most likely resulting from the increased production of insulin and IGF-1 [14]. The significance of proteinuria was emphasised by the studies by Morales et al. [15], which showed that following unilateral kidney resection proteinuria seldom developed in patients with BMI exceeding 25 kg/m^2. Weight reduction, on the other hand, reduces proteinuria. Observational data also demonstrate the significance of elevated triglycerides accompanied by reduced HDL-cholesterol [16]. It turns out that this pattern, typical of metabolic syndrome, is not only associated with atherogenic effects. Mesangial cells of the renal glomerulus are structurally and functionally similar to vascular smooth muscle cells and respond similarly to lipid abnormalities, except in the case of mesangial cells this results in glomerulosclerosis rather than atherosclerosis.

Our study showed an association between obesity and inflammation. The CRP significantly correlated not only with BMI, but — more importantly — with WHR, which defines visceral obesity, so typical of metabolic syndrome. Adipose tissue has been shown to exhibit high endocrine activity. Fat cells produce and release over 50 active substances into the circulation. They are involved in the regulation of energy balance, lipid metabolism, insulin sensitivity, immune response, angiogenesis, vascular function, arterial blood pressure, coagulation and acute inflammation [8]. There is an extensive body of evidence to support the usefulness of CRP in the assessment of CV risk in various stages of both metabolic syndrome and type 2 DM. The significance of obesity in triggering the pro-inflammatory state is also emphasised by prospective studies. They have demonstrated that reducing body mass decreases other markers of inflammation and corrects insulin resistance, which is one of the principal metabolic manifestations of metabolic syndrome [17, 18]. It may therefore be assumed that it is the inflammation that links obesity, especially visceral obesity typical of metabolic syndrome, with the development of atherosclerosis [19].

Studies conducted in the past several years provided new evidence to support the observation that elevated uric acid is a novel yet well-established CV risk factor and a risk factor for renal dysfunction [20]. Elevated uric acid is a constant abnormality found in patients with metabolic syndrome [21]. The widespread character of hyperuricaemia has prompted certain investigators to suggest that overproduction or insufficiently rapid elimination of uric acid might be the underlying cause of metabolic syndrome [22], as studies have shown that uric acid levels and reduced uric acid clearance in hypertension are proportional to the severity of insulin resistance, which is the key manifestation of metabolic syndrome [23]. Insulin resistance results in excess circulating insulin, which most likely stimulates uric acid transporter and increases sodium reabsorption, which is associated with increased uric acid reabsorption. Furthermore, hyperinsulinaemia increases intracellular pH, drives the sodium-hydrogen ion exchanger, resulting in stimulation of anion and urate reabsorption. Hence, in metabolic syndrome, elevated uric acid may be observed before overt DM develops.

Our study showed that even relatively mild renal dysfunction promotes increased serum concentration of uric acid. Multivariate regression analysis showed a significant and independent association between uric acid and WHR or GFR. The relationship between renal function and uric acid has been known for a long time. It is, in fact, an interrelation, as excess uric acid impairs renal function and insufficient kidneys filter uric acid out of the circulation to a lower degree. Numerous studies demonstrated that elevated uric acid is an independent risk factor for renal failure in the general population [24]. The significance of uric acid is further emphasised by studies showing that reducing its concentration with allopurinol results in a slower development of renal failure and in a parallel reduction of CV risk [25]. This is most likely associated with the decreasing CRP as a result of uric acid-lowering treatment.

Our study showed that in patients with metabolic syndrome there is an association between uric acid and renal

function on the one hand, and inflammation on the other. Inflammation is an important risk factor for CV mortality and CRP is one of the most sensitive markers of CV events, even more sensitive than the classic LDL-cholesterol [26]. Not so long ago the liver was considered to be the main source of CRP. However, recent studies have revealed another, potentially very abundant source of CRP, namely human vascular cells stimulated by inflammatory cytokines [27].

Uric acid has long been known to be a CV risk factor. Recently, a close association between elevated uric acid and numerous markers of inflammation has been noticed, such as white blood cells, including neutrophils, interleukins, TNF-α or CRP [28]. What is more, uric acid has also been shown to directly stimulate the production of inflammatory mediators, such as CRP, in vascular cells [29]. These findings suggest that uric acid is an actual endothelium-injuring factor. It is therefore justified to consider uric acid an important risk factor for hypertension and vascular disease. It is particularly important in cases where excess uric acid is found in the setting of pro-oxidative atherogenic environment, as is the case with metabolic syndrome, type 2 DM or CV disease. There, uric acid, which in chemical terms is an antioxidant, paradoxically begins to act as a pro-oxidant, which results in lipoprotein oxidation in the atheromatous plaque promoting its growth and destabilisation [30].

It is beyond doubt that metabolic syndrome and type 2 DM both contribute to hypercoagulability. It is associated with the increased number of platelets and their overactivity, increased PAI-1 (resulting in impaired intrinsic fibrinolysis) and elevated fibrinogen. Evidence of the direct prothrombotic properties of uric acid have been sparse so far. A study by Kanellis et al. [31] showed that uric acid can increase cyclooxygenase-2-dependent formation of thromboxane. The direct toxic effect of uric acid on vascular endothelium also plays a role, which may result in a potent prothrombotic activity.

Given the association between uric acid and the formation of CRP presented above one cannot ignore its significance as a potential prothrombotic factor. Although we did not demonstrate any direct association between uric acid and the markers of prothrombotic state, the very association between uric acid and CRP and between CRP and fibrinogen level and platelet count suggests the possibility of a pathogenetic continuity that positions uric acid as the initial cause of these essential associations. The CRP and therefore inflammation have been proved to be potential mediators of prothrombotic factor activation in patients with metabolic syndrome. In obesity, the biosynthesis of PAI-1, whose normal sources include the liver and endothelial cells, is significantly increased in adipocytes and exceeds its concentration in other tissues [32].

CONCLUSIONS

1. Overweight and obesity, particularly visceral obesity, are associated with renal dysfunction and elevated markers of inflammation in patients with ischaemic heart disease, DM and metabolic syndrome.
2. Renal dysfunction correlates with elevated serum uric acid.
3. Elevated uric acid markedly increases markers of inflammation in patients with metabolic syndrome.
4. Markers of inflammation in patients with ischaemic heart disease, DM and metabolic syndrome correlate with prothrombotic factors, such as elevated fibrinogen or platelet count.
5. Uric acid should be considered an important link in the pathogenesis of metabolic syndrome between renal dysfunction and pro-inflammatory and prothrombotic state.

Conflict of interest: *none declared*

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Kwas moczowy jako ogniwo łączące upośledzenie czynności nerek i stan zapalny oraz stan prozakrzepowy u osób z zespołem metabolicznym i chorobą niedokrwienną serca

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Streszczenie

Wstęp: Od dawna wiadomo, że podwyższone stężenie kwasu moczowego wiąże się z chorobami układu sercowo-naczyniowego, a szczególnie często występuje u osób z chorobami nerek, zespołem metabolicznym i cukrzycą. Zespół metaboliczny stymuluje w organizmie odpowiedź prozapalną i prozakrzepową.

Cel: Celem pracy była ocena zależności między funkcją nerek, stężeniem kwasu moczowego i wskaźnikami stanu zapalnego i prozakrzepowego u pacjentów z cukrzycą i zespołem metabolicznym.

Metody: Do badania włączono 91 chorych: 58 mężczyzn i 33 kobiety w wieku 57,6 ± 10,3 roku, z cukrzycą i zespołem metabolicznym. Badaną grupę wyselekcjonowano ze znacznie większej liczby chorych przyjętych w celu wykonania planowego badania koronarograficznego w latach 2006–2009. Zbierano dokładny wywiad z uwzględnieniem czynników ryzyka miażdżycy, takich jak: nadciśnienie, zaburzenia lipidowe, cukrzyca, palenie tytoniu, obecność chorób układu sercowo-naczyniowego w wywiadzie rodzinnym. U wszystkich chorych na czczo pobierano krew z żyły obwodowej. Oceniano następujące parametry: morfologię krwi pełnej, stężenie w surowicy krwi: mocznika, kreatyniny, ASPAT, ALAT, CRP, fibrynogenu, kwasu moczowego, cholesterolu całkowitego, cholesterolu LDL i HDL, triglicerydów, stężenia glukozy na czczo, HbA_{1c}, GFR, zawartość białka w moczu. Dokonywano pomiaru wskaźnika masy ciała (BMI) oraz wskaźnika talia/biodra (WHR).

Wyniki: Wykazano następujące istotne statystycznie korelacje: masa ciała *v*. kreatynina ($r = 0,291$; $p = 0,009$), WHR *v*. kreatynina ($r = 0,672$; $p < 0,001$), WHR *v*. GFR ($r = –0,706$; $p < 0,001$), WHR *v*. kwas moczowy ($r = 0,295$; $p = 0,05$), BMI *v*. CRP ($r = 0,231$; $p = 0,031$), WHR *v*. CRP ($r = 0,236$; $p = 0,024$), kreatynina *v*. kwas moczowy ($r = 0,362$; $p < 0,001$), GFR *v*. kwas moczowy ($r = –0,341$; $p = 0,001$), kwas moczowy *v*. CRP ($r = 0,251$; $p = 0,016$), CRP *v*. fibrynogen ($r = 0,420$; $p < 0,001$), CRP *v*. liczba płytek ($r = 0,282$; $p = 0,04$), HbA_{1c} *v*. płytki ($r = 0,263$; $p = 0,012$). Analiza regresji wielokrotnej wykazała, że istotnym, niezależnym czynnikiem wpływającym na stężenie kwasu moczowego są WHR, GFR i CRP.

Wnioski: Nadwaga i otyłość, zwłaszcza w postaci trzewnej, wiążą się z upośledzeniem czynności nerek i podwyższonymi wskaźnikami stanu zapalnego u osób z chorobą niedokrwienną serca oraz cukrzycą i zespołem metabolicznym. Upośledzenie czynności nerek koreluje z podwyższonym stężeniem kwasu moczowego w surowicy krwi. Podwyższenie stężenia kwasu moczowego w znaczący sposób powoduje wzrost wskaźników stanu zapalnego u chorych z zespołem metabolicznym. U osób z chorobą niedokrwienną serca oraz cukrzycą i zespołem metabolicznym wskaźniki stanu zapalnego korelują z czynnikami prozakrzepowymi, takimi jak podwyższone stężenie fibrynogenu oraz stężenie płytek krwi. Kwas moczowy należy brać pod uwagę jako ważne ogniwo w patogenezie zespołu metabolicznego łączące zaburzenia czynności nerek ze stanem prozapalnym i prozakrzepowym.

Słowa kluczowe: zespół metaboliczny, cukrzyca, kwas moczowy, zapalenie, stan prozakrzepowy

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