

## The prevalence of the metabolic syndrome components and their combinations in men and women with acute ischemic syndromes

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**Key words:** metabolic syndrome components; acute ischemic syndromes.

**Summary.** During the last decade, it has been shown that the metabolic syndrome and its different components – arterial hypertension (AH), abdominal obesity (AO), diabetes mellitus (DM), atherogenic hypertriglyceridemia (HTG), and/or low concentration of high-density lipoprotein cholesterol (HDL-C) – increase the risk of cardiovascular diseases. There is increasing evidence that the incidence of the metabolic syndrome and the distribution of its components in combinations in the general male and female population differ. The aim of our study was to determine the incidence of the metabolic syndrome in men and women with acute ischemic syndromes and to evaluate the distribution of the metabolic syndrome component combinations in the presence of the metabolic syndrome.

**Contingent and methods.** The study included 2756 patients (1670 males and 1086 females) with acute ischemic syndromes (1997 with myocardial infarction and 759 with unstable angina pectoris), in whom all five components of the metabolic syndrome were assessed. Women were significantly older than men (68.1±9.5 vs. 60.2±11.8 years,  $P<0.001$ ). The metabolic syndrome was found (according to modified NCEP III) in 1641 (59.5%) patients (in 70.2% of females and in 52.6% of males,  $P<0.001$ ). The most common components in both men and women were AH and AO (94.0% vs. 95.9% and 86.4% vs. 84.5%, respectively). HTG was significantly more common in men than in women (80.0% vs. 73.0%,  $P<0.001$ ), while decreased HDL-C concentration was more common in women (82.8% and 59.2%,  $P<0.001$ ). The DM component, detected in more than one-third of patients with acute ischemic syndromes, was significantly more common in women than in men (39.2% vs. 33.1%,  $P<0.05$ ). Combinations of three components were significantly more common in men than in women, while combinations of four–five components were more common in women (55.6% vs. 41.4%,  $P<0.001$ ; and 58.6% vs. 44.4%,  $P<0.01$ ). The most common combination of three components in men was AH+AO+HTG and in women – AH+AO+low HDL-C; the most common combination of four components in both men and women was AH+AO+HTG+low HDL-C.

**Conclusion.** In the metabolic syndrome, the differences between the components of atherogenic dyslipidemia in patients with acute ischemic syndromes were related to the patients' gender: men significantly more frequently had increased TG concentration and women – decreased HDL-C concentration; this is the problem to be addressed in further studies of dyslipidemia.

### Introduction

During the last decade, a number of clinical and epidemiological studies have analyzed the pathogenesis, clinical course, and the risk of unfavorable outcomes of the metabolic syndrome (MS) consisting of the main risk factors of ischemic heart disease (IHD) – arterial hypertension (AH), abdominal obesity (AO), diabetes mellitus (DM), and atherogenic dyslipidemia (1). Numerous studies have showed that separate components of MS are associated with increased risk of IHD, and that a rise in the number of MS compo-

nents increases the incidence of cardiovascular events following myocardial infarction (MI) (2–4). There is growing evidence that the determination of MS component combinations is important in the evaluation of the risk of IHD. It has been shown that the combination of DM, AH, and AO increases the risk of first MI by 50% (5). So far, there has been no unanimous opinion concerning the incidence of MS and the distribution of its components in male and female population and in patients with cardiovascular diseases (6–8).

The aim of our study was to determine the inci-

dence of MS in men and women with acute ischemic syndromes (AIS) and to evaluate the distribution of MS component combinations in the presence of MS.

### Contingent and methods

The study included 3530 patients who had AIS during 2000–2005 and were treated at the Department of Cardiology, Hospital of Kaunas University of Medicine. The following case history data were analyzed: clinical examination, IHD risk factors, components of MS, ECG, two-dimensional echocardiography, coronary angiography, biochemical blood tests, as well as the administered interventional or pharmacological treatment. The information was stored and analyzed in a computer database. A total of 2756 patients who had all five components of MS (1670 males and 1086 females; mean age,  $63 \pm 11$  years) were selected for the study. MS was diagnosed in 1641 (59.5%) patients (878 males and 763 females).

MI diagnosis was based on the angina syndrome, characteristic newly developed ischemic signs in the ECG, and elevated troponin I concentration. Unstable angina pectoris (UAP) was diagnosed in the presence of newly developed ischemic changes in the ECG without elevated of troponin I levels. MS was diagnosed based on the criteria set in the National Cholesterol Education Program (NCEP III, 2003). MS was diagnosed in the presence of three and more MS criteria: AH, when systolic blood pressure was  $\geq 130$  mm Hg or diastolic blood pressure was  $\geq 85$  mm Hg during the inpatient treatment or when the patient used hypotensive drugs prior to developing AIS; AO, when waist circumference in men was  $\geq 102$  cm and in women was  $\geq 88$  cm; hypertriglyceridemia (HTG), when fasting triglyceride concentration was  $\geq 1.7$  mmol/L; decreased concentration of high-density lipoprotein

cholesterol (HDL-C) was  $< 1.03$  mmol/L in men and  $< 1.29$  mmol/L in women, and DM history. Hyperglycemia ( $\geq 6.1$  mmol/L) detected on hospitalization without diagnosed DM before AIS was not considered a component of MS.

Differences between men and women were tested using chi-square test for categorical variables. A  $P$  value of  $\leq 0.05$  was considered significant. Computations were carried out using SPSS, version 12.0.

### Results

The metabolic syndrome was significantly more common in women than in men (70.2% vs. 52.6%,  $P < 0.001$ ) (Fig. 1).

### Characteristics of patients with MS

Women with MS and AIS were significantly older as compared to men (mean age,  $68.1 \pm 9.5$  and  $60.2 \pm 11.8$  years, respectively;  $P < 0.001$ ) (Table 1). The number of women aged  $\geq 65$  years doubled that of men of the same age (67.7% vs. 32.1%,  $P < 0.001$ ).

The majority of the patients had MI, and one-third of the patients had UAP. One-fifth of the patients with AIS had previous MI. One-half of men and women with AIS had  $\geq 70\%$  stenosis of two-three coronary arteries (CAs) in the presence of MS. Myocardial revascularization was performed in 49.8% of men and 40.1% of women ( $P < 0.01$ ) during hospital phase of AIS. Decreased left ventricular function (ejection fraction  $< 40\%$ ) was detected in similar number of men and women (in 15.1% vs. 12.3%).

### Characteristics of metabolic syndrome components

In the presence of MS, the most common MS component among men and women with AIS was AH

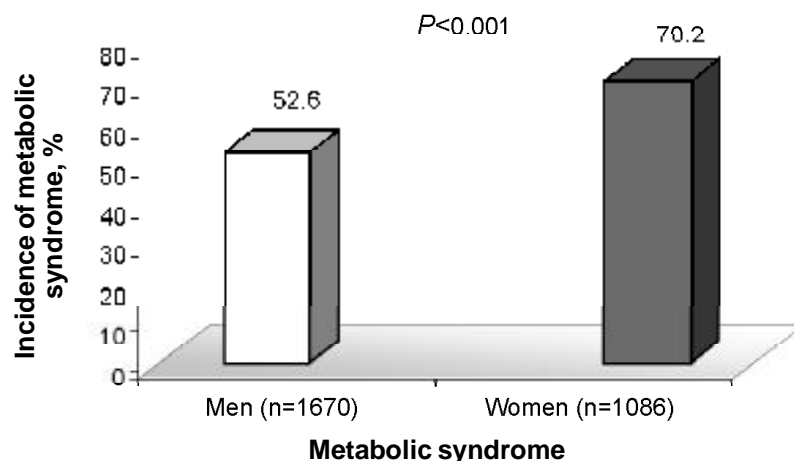


Fig. 1. The incidence of the metabolic syndrome in men and women with acute ischemic syndromes

**Table 1. Characteristics of the contingent with acute ischemic syndromes and metabolic syndrome (n=1641)**

Characteristic		Men (n=878)		Women (n=763)		P
		n	%	n	%	
Mean age, years		60.2±11.3		68.1±9.5		<0.001
Age ≥65 years		282	32.1	516	67.7	<0.001
Previous myocardial infarction		208	23.7	153	20.1	NS
Q-wave myocardial infarction		362	41.2	281	36.8	NS
Non-Q-wave myocardial infarction		281	32.0	231	30.3	NS
Unstable angina pectoris		235	26.8	251	32.9	<0.01
Persistent atrial fibrillation		45	5.1	44	5.8	NS
Paroxysmal atrial fibrillation		57	6.5	55	7.2	NS
Non-fatal fibrillation		28	3.2	27	3.5	NS
Underwent coronary angiography		696	79.3	529	69.3	<0.001
CA stenosis ≥70%	one	256	36.8	173	32.7	NS
	two-three	370	53.2	268	50.7	NS
CA stenosis <70%		50	7.2	59	11.2	<0.05
CA without stenoses		20	2.9	29	5.5	<0.05
Percutaneous transluminal coronary angioplasty		293	33.4	206	27.0	<0.01
Coronary artery bypass surgery		124	14.1	100	13.1	NS
Left ventricular hypertrophy		391/665	58.8	335/418	80.1	<0.001
Left ventricular ejection fraction <40%		128/847	15.1	91/737	12.3	NS

CA – coronary artery; NS – not significant.

(94.0% vs. 95.9%); the majority of men and women also had AO (86.4% and 84.5%, respectively) (Fig. 2).

HTG was detected in more than three-fourths of the patients with MS, and it was significantly more common in men than in women (80.2% vs. 73.0%,  $P<0.001$ ), while reduced HDL-C concentration was significantly more common in women than in men (82.8% vs. 59.5%,  $P<0.001$ ) in all age groups. DM was found significantly more frequently in women than in men (39.2% vs. 33.1%,  $P<0.05$ ). There was no significant difference in the incidence of DM between men and women within age groups.

Combinations of three MS components were more common in men than in women (55.6% vs. 41.4%,  $P<0.001$ ), while combinations of four components were significantly more common in women than in men (41.7% vs. 35.6%,  $P<0.05$ ) (Fig. 3).

Five-component combinations were also significantly more common in women than in men (16.9% vs. 8.8%,  $P<0.01$ ).

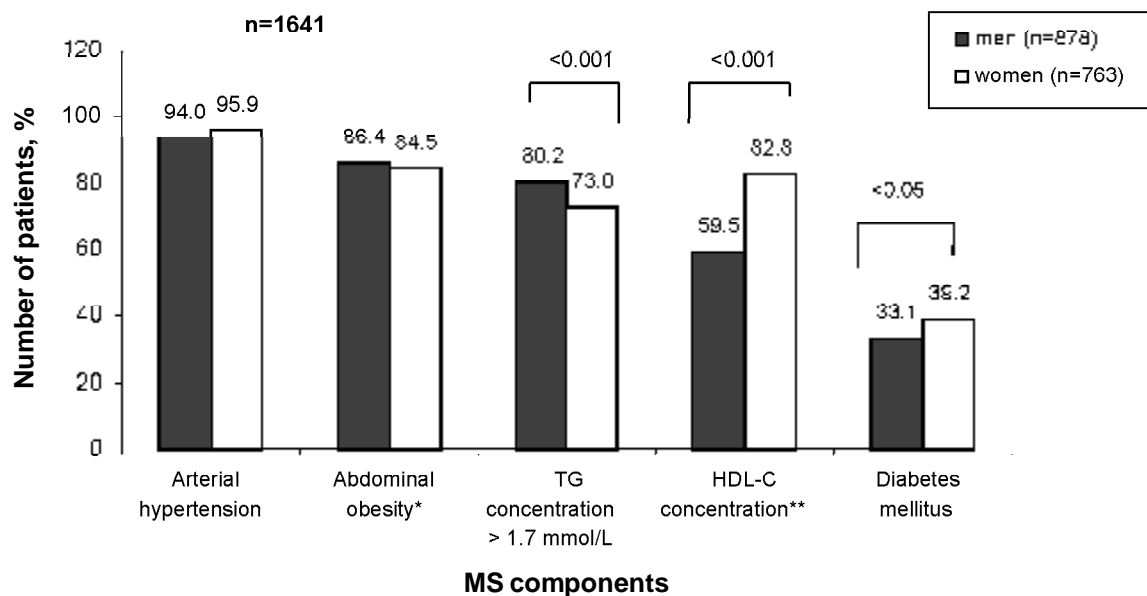
In total, 16 different combinations were determined, each containing from three to five MS components (Table 2). We found that the most common combination of three components in men was AH+AO+HTG and that in women – AH+AO+low HDL-C (25.4% vs. 14.0%).

The most common four-component combination was AH+AO+HTG+low HDL-C, and it occurred more commonly in women than in men (27.3% vs. 20.6%,  $P<0.01$ ).

### Discussion

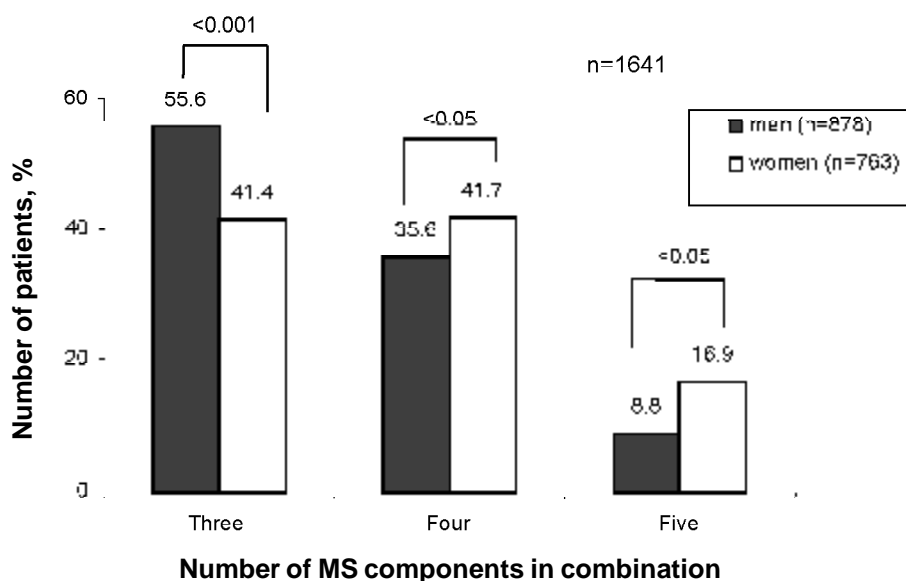
From the modern viewpoint, MS with its five major IHD risk factors – increased insulin resistance, AH, AO, HTG, and reduced HDL-C concentration – in combinations of three or more components undoubtedly conditions the development of atherosclerotic changes in arteries, the development of IHD, and ischemic sequelae.

Many studies show that in addition to the main



**Fig. 2. The incidence of the metabolic syndrome components in men and women with acute ischemic syndromes and metabolic syndrome**

\*Waist circumference: men  $\geq 102$  cm, women  $\geq 88$  cm. \*\*Men  $< 1.03$  mmol/L, women  $< 1.29$  mmol/L. MS – metabolic syndrome; TG – triglycerides; HDL-C – high-density lipoprotein cholesterol.



**Fig. 3. The frequency of the metabolic syndrome combinations with different number of components in men and women with acute ischemic syndromes and metabolic syndrome**

MS – metabolic syndrome.

components of MS, there are other components playing an equally important role in the development of IHD. Such components are age, smoking, lifestyle peculiarities, gender, genetic factors, low-density lipoprotein cholesterol  $\beta$  phenotype, reduction of endothelial function, increased activity of C-reactive protein, fibrinogen, lipoprotein ( $\alpha$ ), homocysteine, low-density lipoprotein cholesterol, uric acid, VII factor,

interleukin-6, and plasminogen activator inhibitor and they are associated with pathogenesis of MS components. The incidence of factors that are MS components, the interrelationship between these factors, the sequence of their development, their association with other important IHD risk factors, and their impact on the development of IHD have been analyzed in a number of clinical and epidemiological studies (2, 6–8).

**Table 2. The frequency of various metabolic syndrome component combinations in men and women with acute ischemic syndromes and metabolic syndrome**

Components of the metabolic syndrome	Men (n=878)		Women (n=763)		P
	n	%	n	%	
<b>3 components (n=804)</b>	55.6%		41.4%		<0.001
AH+DM+AO	27	3.1	23	3.0	<0.05
AH+DM+HDL-C	16	1.8	18	2.4	<0.001
AH+DM+TG	22	2.5	13	1.7	NS
DM+AO+HDL-C	6	0.7	3	0.4	NS
DM+AO+TG	5	0.6	0		<0.05
AO+TG+HDL-C	27	3.1	20	2.6	NS
AH+AO+HDL-C	97	11.0	107	14.0	<0.001
AH+AO+TG	223	25.4	68	8.9	<0.001
AH+HDL-C+TG	59	6.7	61	8.0	NS
DM+HDL-C+TG	6	0.7	3	0.4	NS
<b>4 components (n=631)</b>	35.6%		41.7%		<0.05
AH+DM+AO+HDL-C	28	3.2	55	7.2	<0.001
AH+DM+AO+TG	79	9.0	27	3.5	<0.001
DM+AO+HDL-C+TG	9.0	1.0	5	0.7	NS
AH+AO+HDL-C+TG	181	20.6	208	27.3	<0.01
AH+DM+TG+HDL-C	16	1.8	23	3.0	NS
<b>5 components (n=206)</b>	8.8%		16.9%		<0.001
AH+AO+DM+TG+HDL-C	77	8.8	129	16.9	<0.001

AH – arterial hypertension; AO – abdominal obesity (waist circumference: men  $\geq 102$  cm, women  $\geq 88$  cm); TG – triglyceride concentration  $\geq 1.7$  mmol/L; HDL-C – high-density lipoprotein cholesterol concentration (men  $< 1.03$  mmol/L, women  $< 1.29$  mmol/L); DM – diabetes mellitus; NS – not significant.

According to literature data, during the last decade, there has been an increasing incidence of MS and morbidity from cardiovascular diseases in industrialized countries, countries of the former Eastern block, and in Southern and Southeast Asia. It has been contended that the increasing incidence of MS components results in the increasing morbidity from IHD (9, 10). MS is detected in 20–40% of the general population and in 30–65% of people with IHD (11–14).

MS is more common in men than in women (10, 15). The results of a 10-year study performed in Italy showed that in 5898 men and 11354 women aged 35–69 years and with no history of cardiovascular diseases, MS was detected in 34.6% of men and 21.2% of women (6). However, other researchers claim that MS is more common in women than in men or that its incidence is more or less equally distributed between both sexes. In the NHANES III study that included 8814 people aged  $\geq 20$  years, MS was found in a similar percentage of male and female subjects (24% vs. 24.4%) (16). According to the findings of a screening performed in 2001–2002 in Kaunas (Lithuania), MS was detected in 19.4% of men and in 26.3% of women, and in 34.2% of men and 39.7% of women

with IHD (17). According to Feinberg *et al.*, in patients with AIS, MS was also found more common in women than in men (18). Our findings showed that MS was diagnosed in more than one-half of patients with AIS, and it was significantly more common in women than in men (70.2% vs. 52.6%,  $P < 0.001$ ). Higher incidence of MS among women may have been caused by the fact that women with AIS tended to be older than men with the same condition.

During the last decade, much attention has been paid not only to the prevalence of MS but also to the impact that characteristics of MS components, their number, and combinations exert on the prediction of the cardiovascular risk in the general population and in patients with IHD. According to the findings of the PROCAM study, in 40–65-year-old men with DM, there is an 8-fold risk of developing MI within 4 years in those with DM and AH and 19-fold risk in those with DM, AH, and dyslipidemia (19).

Literature quotes that more than one-half of patients with IHD and MS have three MS components, more than one-third of such patients have four MS components, and around 10–15% – five MS components (20–22). According to the findings of our study,

three components were detected in one-half of the studied population and they were more frequently detected in men than in women (55.6% vs. 41.4%,  $P<0.0001$ ), whereas four or five components were more common in women than in men (41.7% vs. 35.6%,  $P<0.05$ ; 16.9% vs. 8.8%,  $P<0.01$ ).

The study of the general population in Poland, involving 2329 subjects aged 18–90 years, found that 22.9% of the population studied had MS. The most common MS components were AH and HTG (58.3% vs. 50.1%), while AO, low HDL-C, and elevated blood glucose levels were less common (28.0%, 22.3%, and 15.0%, respectively) (23). Anderson *et al.* found that the most common components in patients with IHD were AH, AO, and low HDL-C, while elevated triglyceride concentration and DM were less common (76.0%, 58.0%, 71.0%, 52.0%, and 40.0%, respectively) (24).

According to our findings, AH and AO in the presence of MS were detected in nearly all patients with AIS; the majority of such patients had atherogenic dyslipidemia, and one-third of them had DM. There was no significant difference in the incidence of AH and AO between males and females (94.0% and 95.9%; 86.4% and 84.5%, respectively). HTG was more common in men than in women (80.2% vs. 73.0%,  $P<0.001$ ), while low HDL-C and DM were more common in women than in men (82.8% and 59.5%,  $P<0.001$ ; 39.2% and 33.1%, respectively;  $P<0.05$ ).

Last year it was found that the most common combination of three components in healthy men and women was AH+AO+HTG (9.2% vs. 5.3%), and the most common combination of four components was AH+AO+HTG+low HDL-C (6.4% vs. 4.5%) (6, 25). In our study, the combination AH+AO+HTG in the presence of AIS and MS was more common in men than in women (25.4% vs. 8.9%,  $P<0.001$ ), while in women the most common combination was AH+AO+low HDL-C, and this combination was more common in women than in men (14.0% vs. 11.0%,  $P<0.001$ ). The combination of four components –

AH+AO+low HDL-C+HTG – occurred most frequently both in men and in women (27.3% vs. 20.6%). The incidence of the five-component combination was twice as common in women than in men (16.9% vs. 8.8%). We did not find any literature data presenting the distribution of MS components in different combinations in men and women with AIS. Therefore, no comparison could have been performed.

The determination of differences in the incidence of MS and the components of atherogenic dyslipidemia between men and women with AIS is an issue to be dealt with in further studies, as is the determination of the impact of these factors on cardiovascular risk.

### Conclusions

1. In the majority of men and women with acute ischemic syndromes and the metabolic syndrome, the most common components were arterial hypertension and abdominal obesity (94.0% and 95.9%, respectively; 86.4% and 84.5%, respectively); hypertriglyceridemia ( $\geq 1.7$  mmol/L) was significantly more common in men than in women (80.2% vs. 73.0%,  $P<0.001$ ), while low blood levels of HDL-C were more common in women than in men (82.8% vs. 59.2%,  $P<0.001$ ).

2. Diabetes mellitus was detected in more than one-third of the patients with acute ischemic syndromes, and it was significantly more common in women than in men (39.2% vs. 33.1%,  $P<0.05$ ).

3. Combinations of three components were significantly more common in men, while combinations of four and five components were more common in women than in men (55.6% and 41.4%,  $P<0.001$ ; 41.7% and 35.6%,  $P<0.05$ ; 16.9% and 8.8%,  $P<0.01$ , respectively).

4. The most common combination of three components in men was arterial hypertension + abdominal obesity + hypertriglyceridemia, and in women – arterial hypertension + abdominal obesity + low levels of HDL-C; the most common combination of four components both in men and women was arterial hypertension + abdominal obesity + hypertriglyceridemia + low levels of HDL-C.

### Metabolinio sindromo komponentų ir jų derinių dažnumas tarp vyrų ir moterų, susirgusių ūminiais išeminiais sindromais

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**Raktažodžiai:** metabolinis sindromas, ūminiai išeminiai sindromai.

**Santrauka.** Per pastarąjį dešimtmetį pateikiama vis daugiau įrodymų, kad metabolinis sindromas bei atskiri jo komponentai (rizikos veiksniai): arterinė hipertenzija, pilvinis nutukimas, cukrinis diabetas ir aterogeninė dislipidemija, trigliceridai (trigliceridų koncentracijos padidėjimas ar (ir) didelio tankio lipidų koncentracijos sumažėjimas) didina širdies ir kraujagyslių ligų riziką. Daugėja įrodymų, kad metabolinio sindromo dažnumas bei jų komponentų pasiskirstymas bendrojoje populiacijoje yra skirtingas.

**Darbo tikslas** – nustatyti metabolinio sindromo dažnumą tarp vyrų ir moterų, susirgusių ūminiais išeminiiais sindromais, ir įvertinti komponentų pasiskirstymą deriniuose.

**Tirtųjų kontingentas ir tyrimo metodika.** Į studiją atrinkti 2756 ligoniai (1670 vyrų ir 1086 moterys), susirgę ūminiu išeminiu sindromu (miokardo infarktu – 1997, nestabiliąja krūtinės angina – 759), kuriems buvo įvertinti visi penki metabolinio sindromo komponentai. Moterys buvo reikšmingai vyresnės už vyrus ( $68,1 \pm 9,5$  metų ir  $60,2 \pm 11,8$  metų,  $p < 0,001$ ). Metabolinis sindromas nustatytas (NCEP III) daugiau kaip pusei (59,5 proc.) susirgusiųjų (70,2 proc. – moterų ir 52,6 proc. – vyrų,  $p < 0,0001$ ). Dažniausi komponentai tiek vyrams, tiek moterims buvo arterinė hipertenzija ir pilvinis nutukimas (94,0 proc. ir 95,9 proc.; 86,4 proc. ir 84,5 proc.). Hipertrigliceridemija reikšmingai dažniau buvo vyrams nei moterims (80,2 proc. ir 73,0 proc.,  $p < 0,001$ ). Cukrinio diabeto komponentas, nustatytas daugiau kaip trečdaliui susirgusiųjų ūminiu išeminiu sindromu, buvo reikšmingai dažnesnis moterims nei vyrams (39,2 proc. ir 33,1 proc.,  $p < 0,05$ ). Trys komponentai reikšmingai dažniau buvo vyrams nei moterims, o keturi penki – moterims (55,6 proc. ir 41,4 proc.,  $p < 0,001$ ; 58,6 proc. ir 44,4 proc.,  $p < 0,01$ ). Dažniausias trijų komponentų derinys vyrams buvo arterinė hipertenzija+pilvinis nutukimas+trigliceridai, moterims – arterinė hipertenzija+pilvinis nutukimas+didelio tankio lipidų koncentracija, o dažniausiai pasikartojantis keturių komponentų derinys vyrams ir moterims buvo arterinė hipertenzija+pilvinis nutukimas+trigliceridai+didelio tankio lipidų koncentracijos sumažėjimas.

**Išvada.** Susirgusiųjų ūminiu išeminiu sindromu, esant metaboliniam sindromui, aterogeninės dislipidemijos komponentų skirtumai susiję su lytimi: vyrams – reikšmingai dažniau nustatytas trigliceridų koncentracijos padidėjimas, o moterims – didelio tankio lipidų koncentracijos sumažėjimas yra viena iš tolesnių dislipidemijos tyrimų problemų.

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