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Global cardio – metabolic risk in patients with cognitive dysfunction

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Summary

Aim. The authors explored the metabolic profile of patients with cognitive dysfunctions by means of levels of lipoproteins, glycaemia and hypertension.

Research Design and Methods. In a prospective, randomised manner, we studied 100 persons – 44 without cognitive dysfunctions, 56 with cognitive dysfunction. Patients were grouped according to ICD-10 criteria of dementia and STMS cut-off levels.

Results. We found independent risk factors of dementia, which are HDL cholesterol (p=0.03), hyperglycaemia(p=0.008), dyslipidemia atherogenic (p=0.0017), metabolic syndrome (p=0.03) and age (p=0.001). We confirmed also correlations of glucose levels with CT changes, and age, fasting glucose, HDL levels with STMS results.

Conclusions. Cardiometabolic syndrome seems to be a risk factor of dementia.

metabolic syndrome / dementia

INTRODUCTION

To assess classical cardiovascular risk, such factors like older age, male gender, smoking, diabetes, hypertension, abnormal lipid profile in the form of elevated LDL and lower HDL cholesterol should be taken into account. These factors, together with the metabolic syndrome, form a so-called global cardio-metabolic risk [1, 2].

The aim of this study is to determine the global cardiometabolic risk in patients with impaired cognitive functions.

MATERIAL AND METHODS

Characteristics of patients

In this prospective study 100 patients were enrolled, selected at random from December 2010 to March 2011 from the in patients Second Department of Psychiatry in the Institute of Neurology and Psychiatry in Warsaw.

The characteristics of patients taken into account were: age, sex, presence of hypertension, diabetes, dyslipidemia, laboratory parameters: fasting plasma glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides. Division of patients into those with proficient cognitive processes and cognitive disorders (MCI, dementia) was done using the ICD-10 criteria and STMS - Short Test of Mental Status.

In this study we used the Berlin criteria for metabolic syndrome (IDF, 2005), by which the following criteria must be met: central obesity (waist circumference exceeding 80 cm in women and 94 cm in men) with at least two of the following factors coexisting: level of triglycerides above 150 mg/dl or treatment for this disorder, a decrease of HDL below 40 mg/dl in men and below 50 mg/dl in women or treatment of this disorder, blood pressure above 135/85 mmHg or treatment of high blood pressure, fasting plasma glucose above 100 mg/dl or treated type 2 diabetes.

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Hypercholesterolaemia was defined as total cholesterol level above 190 mg/dl and LDL cholesterol above 115 mg/dl.

Atherogenic dyslipidemia was defined as triglyceride level above 150 mg/dl and a decrease in HDL cholesterol below 40 mg/dl in men and below 46 mg/dl in women.

For each patient, head computer tomography was performed, taking into account parameters such as: changes in focal outbreaks, atrophy, leukoaraiosis, ventricular system enlargement, widening of the space fluid, calcification in the carotid arteries.

Division of the studied population

The studied population was selected according to the criterion of the presence of cognitive impairments consistent with the cut-off points STMS. STMS scale is a scale evaluating the following parameters: orientation, attention, learning, arithmetic, abstract thinking, general news, play after postponement . This scale is considered to be a screening test for the presence of dementia, which is suggested by a figure of less than 30 points. However, any such result should be confirmed by additional tests and in-depth diagnostics. The maximum score possible to obtain in the STMS scale is 38 [3, 4]. The Polish version of STMS was examined in a study conducted in 2009 among 400 participants (100 healthy subjects, 100 subjects with mild cognitive impairment, 100 persons with mild dementia and 100 persons with moderate dementia). It was found to have sufficient sensitivity (68-87%) and specificity (80-89%) in the assessment of cognitive functions. Specified cut-off levels for each subgroup: 30.4±4.2 points for group without cognitive deficits, 27.9±4.8 points for mild cognitive impairment group, 21.6±5.0 points for patients with of mild dementia and 15.0±4.6 for patients with moderate dementia [5].

In the study, patients were divided into 2 groups: Group 1 – patients with impaired cognition with a score below 30 points STMS (56%), Group 2 – patients with no cognitive impairments with a score above 30 points STMS (44%). ICD-10 criteria for presence/absence of dementia were also used.

THE RESULTS

Patients differed from each other in terms of age – patients in Group 1 were significantly older (p=0.0006). Patients differed significantly in terms of prevalence of fasting hyperglycaemia (p=0.02). The highest concentration of glucose (111.4±31.4 mg%) could be observed among patients with impaired cognitive functions. HDL was significantly higher among patients without cognitive impairment, these patients did not have atherogenic dyslipidemia. Patients from both groups differed in terms of metabolic syndrome – it occurred significantly more frequently among those in Group 1.

Table 1. Characteristic of the variables in study groups

Feature	GROUP 1 n=56 (56%)	GROUP 2 n=44 (44%)	Level of p
Gender (Male)	18 (32.1)	11 (25)	0.54
Age (years)	78.6±7.8	73.1±7.2	0.0006
Metabolic syndrome	20 (35.7)	7 (15.9)	0.004
Hypertension	37 (66.1)	23 (52.3)	0.24
Diabetes	6 (10.7)	2 (4.5)	0.6
Abnormal lipid profile	15 (26.8)	16 (36.3)	0.41
Glycaemia	111.4±31.4	95.5±22	0.0036
Fasting hyperglycaemia	27 (4)	9 (20)	0.02
Total cholesterol	181.9±39.1	193.6±37.7	0.13
TG	101.7±42.2	112.9±49.6	0.35
LDL	107.7±27.3	109.9±36.3	0.87
HDL	52.1±16.2	62.5±12.7	0.037
Hypercholesterolemia	15 (26.8)	8 (18.2)	0.46
Dyslipidemia arterogenic	8 (14.3)	0 (0)	0.009
Changes in CT	36 (64.3)	22 (50)	0.15
Focal	22 (39.3)	13 (29.5)	0.31
Ischemic changes	17 (30.4)	12 (27.3)	0.73
Hypodense focus	25 (44.6)	13 (29.5)	0.12
Atrophy	16 (28.6)	4 (9.1)	0.016
leukoaraiosis	11 (19.6)	4 (9.1)	0.14
Enlarged ventricular system	16 (28.6)	11 (25)	0.69
Enlarged fluid spaces	9 (16.1)	11 (25)	0.27
Calcification in the a. cervical	13 (23.2)	6 (13.6)	0.22

Group 1 Patients with cognitive dysfunction (56%)
Group 2 Patients without cognitive dysfunction (44%)

The analysis in the form of logistic regression showed that independent risk factors for dementia are: the levels of HDL cholesterol (p=0.036,

OR=1.061, <0.99, 1.13>), dyslipidemia atherogenic (p=0.0017, OR=1,05, <0.9 - 1.1>) and glucose levels (p=0.008, OR=0.97, <0.95, 0.99>. In the study, computed tomography showed the relationship between changes in brain and plasma glucose (p=0.01, OR=0.97, <0.95, 0.99>).

Table 2. Study of the laboratory-clinical variables, cognitive dysfunction and morphological changes in Computer Tomography

Feature	P	Cognitive dysfunction	p	Morphological changes in CT
Gender	0.21	0.54 (0.2–1.44)	0.45	1.41 (0.56–3.58)
Age	**0.001**	**0.9 (0.84–0.95)**	0.6	0.98 (0.93–1.04)
Hypertension	0.69	0.82 (0.31–2.14)	0.98	1.01 (0.37–2.69)
Metabolic syndrome	**0.03**	**0.34 (0.12–0.91)**	**0.03**	**0.25 (0.068–0.95)**
Total cholesterol	0.23	1 (0.99–1.02)	0.98	0.99 (0.98–1.01)
HDL	**0.03**	**1.06 (0.99–1.13)**	0.4	1.02 (0.97–1.07)
LDL	0.85	1 (0.97–1.02)	0.22	1.01 (0.99–1.03)
TG	0.28	1 (0.99–1.01)	0.66	1 (0.99–1.01)
Hypercholesterolemia	0.31	1.64 (0.61– 4.39)	0.26	0.58 (0.22–1.51)
Arterogenic dyslipidemia	**0.0017**	1.05 (0.9–1.1)	0.78	0.81 (0.18–3.68)
Glycaemia	**0.01**	**0.97 (0.95–0.99)**	**0.03**	**0.97 (0.95–0.99)**

HDL – High Density Lipoproteins; LDL – Low Density Lipoproteins; TG-Triglicerides

Scoring on a scale KTSP correlates inversely with age and fasting glucose levels, as well as in direct proportion to the levels of HDL.

Patients did not differ significantly among themselves in the incidence of hypertension, as well as the number and type of medication.

Table 3. Correlation between punctuation in STMS and laboratory parameters

Correlation between punctuations in STMS and:	R Spearman	p level
Age	-0.47	0.000001
Glycaemia	-0.33	0.0024
Total cholesterol	0.15	0.18
Triglycerides	0.16	0.14
LDL	0.01	0.93
HDL	0.32	0.05

HDL – High Density Lipoproteins; LDL – Low Density Lipoproteins

Table 4. Characteristics of groups for selected medications commonly used in patients with metabolic syndrome

Medicaments:	GROUP 1 n=56 (56%)	GROUP 2 n=44 (44%)	p level
Metformine	2(3.6)	1(2.3)	0.91
Gliklazyde	3(5.4)	1(2.3)	0.79
Glimepiride	0(0)	1(2.3)	0.84
Statinsć	15(26.8)	15(34.1)	0.53
Valsartan	0(0)	1(2.3)	0.84
Losartan	2(3.6)	1(2.3)	0.91
Enarapryl	5(8.9)	3(6.8)	0.86
Imidapryl	0(0)	1(2.3)	0.84
Chinapryl	3(5.4)	0(0)	0.65
Ramipryl	8(14.3)	3(6.8)	0.52
Captopryl	1(1.8)	1(2.3)	0.97
Peryndopryl	1(1.7)	0(0)	0.88
Nitrendypine	0(0)	1(2.3)	0.85
Lacidypina	1(1.8)	0(0)	0.88
Amlodypine	13(23.2)	14(31.8)	0.47
Atenolol	11(19.6)	5(11.4)	0.48
Carwedilol	1(1.8)	0(0)	0.88
Bisoprolol	9(16.1)	3(6.8)	0.43
Pindolol	0(0)	1(2.3)	0.84
Metoprolol	5(8.9)	3ć(6.8)	0.86

DISCUSSION

The metabolic syndrome and all its components increase the cardiometabolic risk [6]. Increasingly, this problem is widely recognised, examining the impact of central obesity, hyperglycaemia, hypertriglyceridaemia, hypertension and decrease in HDL cholesterol in other chronic diseases, including dementia [7].

It is estimated that the metabolic syndrome occurs in more than 50% of patients with ischaemic stroke [8]. Parameters such as age, height, inflammatory markers, alcohol consumption affect the occurrence of multiple silent infarcts, those found in computed tomography as leukoaraiosis, which are proven risk factors for VaD [9, 10]. It was also shown that the presence of these factors influences the occurrence of memory impairment in older women and men [11, 12].

The impact of the metabolic syndrome in vascular dementia and adverse cardiac events is associated mainly with thrombotic action. Endothelial inflammation, which is formed primarily in response to hypertriglyceridaemia, hyperglycaemia, activation of the renin – angiotensin – aldosterone system, generates excess of lipoprotein cholesterol through the production of inflammatory cytokines, acute phase proteins – in this particular fibrinogen [13, 14]. Another component of impaired fibrinolysis is prothrombotic action through an imbalance between endogenous factors involving tissue plasminogen activator deficiency and excess of its inhibitor type 1, which occurs in virtually every atherothrombotic vessel amended [15, 16]. An important factor is the change in the structure and function of platelets, that occurs particularly intensively in patients with diabetes and hypertension, leading to their aggregation and adhesion to the damaged endothelium [17].

Many studies have demonstrated the relationship between metabolic syndrome and Alzheimer's disease [18]. It has been proven that high cholesterol, especially LDL, increases the activity of the enzyme ß-secretase, which is putting away the amyloid in the brains of patients with Alzheimer's disease, and γ-secretase, which catalyses the reaction of formation of the precursor protein – APP [19, 20].

In our study, we have demonstrated that the presence of the metabolic syndrome is significantly associated with the occurrence of cognitive disorders. A special role is played here by particular parameters, such as low HDL and high glucose levels.

It is known that high HDL cholesterol level above 60 mg/dL, is a protective factor for coronary heart disease. This protection is mainly based on the return transport of cholesterol from the vessel walls, as well as the antioxidant in LDL cholesterol [21]. The test results are in line with earlier ones and confirmed the studies indicating that both the low level of HDL as well as hyperglycaemia are independent risk factors for dementia [22, 23, 24, 25, 26]. Some reports about the atherogenic impact of dyslipidemia as well as hypercholesterolemia on cognitive dysfunctions can also be found in literature [27].

CONCLUSIONS

1. In line with previous research findings, the survey has confirmed that the components of cardiometabolic risk increase the risk of developing cognitive impairment.
2. Among the important risk factors special attention must be paid to HDL cholesterol and glucose levels.
3. The concentration of glucose (and the presence of type 2 diabetes) is part of the pathomechanisms of cognitive impairment.

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