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Early Predictors of Cognitive Decline and Stroke

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Abstract: *Background* Insulin resistance can affect multiple tissues and organs, from the classic "triumvirate" (myocyte, adipocyte, and hepatocyte) to possible effects on organs such as the central nervous system. This review explores shared pathophysiological mechanisms between MCI and MS and establishes a hypothesis of a possible MCI role in the development of IR and the appearance of MS. *Objective* The objective of the study was to investigate new biomarkers for early diagnosis of MS, cognitive decline as a follow-up and stroke. A cardiological, neuropsychological and neurological study was conducted among 75 Bulgarian participants. All data and samples derived from the University Hospital of Pleven. Beta amyloid in the blood, procalcitonin (PCT), NT-proBNP as predictors of cognitive impairment in patients with MS were identified. *Methods* Clinical, anthropometric, biochemical, neuropsychological, cognitive and statistical data processing. Plasma amyloid beta (Aβ) levels, procalcitonin, NT-proBNP in MS were investigated in participants with MS and in healthy controls. RESULTS In the present study, an inverse relation between NT-proBNP and diastolic blood pressure, waist circumference, triglycerides, HDL- and LDL cholesterol was found. Plasma levels of Aβ42 and Aβ40 were found to be reduced in MetS participants. Regression analysis showed a positive relationship between NT-proBNP and systolic blood pressure ($p < 0.001$) and fasting blood glucose ($p < 0.05$). *Conclusions* There was a positive association between PCT levels, decreased levels of Aβ42 and Aβ40, as well as elevated NT-proBNP and cognitive impairment in people with MS and stroke. A concentration of NT-proBNP of 60 pg / ml or greater could be an indicator of metabolic abnormalities and early cognitive decline. Large-scale studies and longer follow-up periods will be necessary to establish a direct and accurate causal relationship between MS and MCI pathologies.

Keywords: Metabolic syndrome, Cognitive decline, Healthcare engineering

Introduction

Metabolic syndrome (MetS), a risk factor for many vascular conditions, may be a prodromal manifestation of vascular cognitive impairment. Diagnosing early stages of cerebrovascular pathology can lead to prevention and delay of the progression of pathological conditions such as vascular cognitive impairment. It can be said that MetS, which is considered as risk factor for the development of diabetes, hypertension, dyslipidemia, and coronary artery disease can also act as an important risk factor for the development of dementia.

Dementia is among the leading causes of disability in developed societies, affecting approximately 6% of the population aged 65 and older, and its prevalence increases exponentially with age: 40–70% at the age of 95 years and over suffer from dementia. The vascular and vascular-related factors that have been associated with dementia and cognitivedecline included high blood pressure (BP) and hypertension, total cholesterol and other lipid parameters, diabetes and insulin resistance, body mass index (BMI) and obesity,and the metabolic syndrome (MetS).

Metabolic-Cognitive Syndrome: Is This Understanding Useful?

It is suggested that possibly the metabolic-hormonal changes which occur over the course of MetS may be detrimental for neuronal cells and are resultantly responsible for development of dementia. The current level of understanding suggests that the concept of Metabolic Cognitive Syndrome (MCS) provides an important window for primary prevention of dementia (Panza et al., 2006). Changing the modifiable risk factors can reduce the incidence of dementia and also possibly delay the onset of dementia. There are strong links between obesity, insulin resistance, and components of the metabolic syndrome. Chronic low-grade inflammation has been implicated in the pathophysiology of these three intertwined entities. Procalcitoninpolypeptide, is the precursor of calcitonin hormone produced by neuroendocrine C-cells of the thyroid and K-cells of the lung,encoded from the calcitonin chromosome 11.

Procalcitonin is best known as a biomarker of infection and severe systemic inflammation. Recent studies show that adipose tissue is capable of expressing and secreting procalcitonin. This makes Procalcitonin a potential biomarker for obesity-related low-grade inflammation. There are no data addressing the significance of variation in plasma procalcitonin levels in the general population. So far, procalcitonin level in the normal population has been studied only in a small sample, and only an association of procalcitonin with sex was acknowledged. We hypothesize that plasma procalcitonin may be associated with measures of obesity, insulin resistance, and metabolic risk factors.

Method

Data were statistically processed using variation and regression analyses. To analyze data, parametric and non-parametric methods were applied, and the value of chi-square was used for analyses of qualitative variables. Evaluation of statistical reliability for the groups studied was made according to the p-value for the meaning of chi-square, and differences were considered significant at $p<0.05$. Statistical studying of dependences between variables to a great extent depends on the way the variables are measured. When studying the statistical dependence between two qualitative variables, it is convenient to present data in a table reflecting mutual connection of the characteristics. In this table, the categories of the first variable (subdivisions, varieties) are 42 entered along the rows), and the categories of the other variable are entered down the columns. In the points where the rows and columns cross, the frequencies (numbers) of the respective combinations of categories of the variables.

The sums of those are figures that are called borderline (marginal) frequencies. Relative frequencies, expressed in per cent, are calculated by dividing the frequencies of cells by dividing the borderline frequencies in the respective row in the excerpt, and the figures obtained are multiplied by 100 (percent along the rows). Looking for statistical dependence between the variable implies whether the relationship between the variables is a natural characteristics of the population, a sample of which is selected, or this relationship is the result from the influence of accidental factors, i.e. the latter relationship is found in the actual sample but it is not characteristic of the population. It makes sense to take this into consideration only if the population sample investigated has been collected at random, and the population has been strictly defined. That would mean that each person on a population, that is well-differentiated from the environment should have an equal chance to be in the sample selected. To find the statistical dependence between two variables measured in qualitative scales, the chi-square criterion is used. This allows to ascertain the hypothesis that the variables forming the rows and the columns are independent, without defining the extent and tendency in the dependence.

From data about the sample, as presented in a table, the respective value of the chi-square statistics and its empirical level of significance (p-value) is calculated. If this empirical level is lower than 0.05 (this being the most common level of dependence a researcher chooses) then the hypothesis of lack of dependence between the characteristics in the population, from which the samples is selected, is rejected. In this case, a hypothesis is proposed for the presence of statistically significant dependence (alternative hypothesis).

The chi-square criterion (Fischer's exact test) make it possible to only answer the question regarding the presence or absence of dependence. When the two variables are qualitative, it is impossible to conclude whether the dependence is positive or negative. The chi-square value shows whether the difference between the percentages expected and those found is big enough to allow the assumption that it exists (presents regularly) in the whole population, or it is too small, which implies that there is no significant relationship between the variables in this population. When $p<0.05$, this means that the differences established in the percentages are regular, and not due to the influence of accidental factors.

Logistic Regression Analysis

Regression analysis is applied to describe the dependence between one dependent variable and one or more independent variables. In the "case-control epidemiological studies, odds ratio is used as a measure for the degree of dependence between one risk factor and a certain disease. The risk factor can be a quantitative or a qualitative variable, but the simplest situation is that in which the factor also has two characteristics: presence of the factor, coded as "1", and absence of the factor, coded as "0". Under such circumstances, the linear regression analysis is not applicable. When the dependent variable is discrete, i.e. when it can have most commonly, two values, then the standard method for analysis is the logistic regression analysis. It makes it possible to study the individual impact of each factor. In addition, logistic regression analysis may help to find the most appropriate and cost-effective, as well as the most acceptable biomedical model, which can describe the relationship between the outcome of a disease and a multitude of independent variables (factors). In this study, most of the potential risk factors were qualitative and their characteristics were coded in a relevant manner. The odds ratio is used as an approximate measure for risk regarding the outcome of the disease, depending on a certain risk factor or a certain group of risk factors.

Results and Discussion

Heart rate was 77.53/min for oncology patients and 81.24/min for other people in the study. Systolic (SBP) blood pressure, diastolic (DBP) blood pressure and BMI were measured. The 67 serum samples of patients with different tumors were evaluated for CBC. We also collected 31 serum samples from 31 patients without cancer as controls in April 2018. The number of women was 17and the number of men was 14. The following CBC parameters were analyzed: red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelet count (PLT), mean white blood cell count (WBC), and leukocyte differential count.

One way ANOVA test was performed on ECGs by splitting the participants into four groups:

1) men with cancer
2) men without cancer
3) women with cancer
4) women without cancer.

Multiple comparison test of means was used to obtain the differences between every two groups. Multiple logistic regression analysis was implemented to estimate OR of cancer. The box plots for one way ANOVA test of pulse pressure (Figure 1) showed that the difference between persons with and without MS is more significant for women. The ANOVA F-statistic was 3.683 with p-value 0.0145 and the hypothesis that the all groups' means were equal had to be rejected.

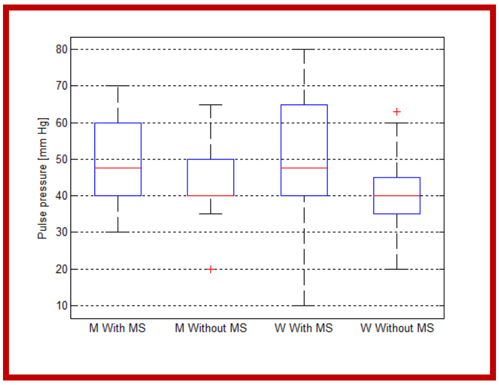

Figure 1: Box plots for one way ANOVA test of pulse pressure for groups: Men with MS, Men without MS, Women with MS and Women without MS

The multiple comparison tests indicated statistically significant difference in the PP mean values between groups of women with and without MS (Table 1). A considerable difference in means between groups of men without MS and women without MS was obtained (Table 1). Some difference in means was observed between groups of men with and without MS (Table 1). The difference in means between groups of men with MS and women with MS was very small (Table 1).

Table 1. Table of multiple comparison test for men and women with and without MS.

First group	Second group	Lower boundary of the CI	Difference between means	Upper boundary of the CI
Men with MS	Men without MS	-6.303	4.001	14.323
Men with MS	Women with MS	-10.866	-0.033	10.801
Men without MS	Women without MS	-2.565	5.085	12.736
Women with MS	Women without MS	0.788	9.128	17.464

MODEL 1

The results indicated that the increasing of OR with increasing of PP for men was similar to that for women when the men's APO B/APO A1 ratio was with about 0.1 greater. The obtained model showed that for increase of PP with 5 mm Hg it was expected about 1.2314 times increase in the odds ratio of MS and for increase of APO B/APO A1 ratio with 0.1 it was expected about 1.6363 times increase in the odds ratio.

MODEL 2: WC, HDL-CHOL, GLU, TG

In the second model-- in addition to PP-- four dichotomous variables were included and the model was adjusted for gender. The dichotomous variables were composed using the following components of MS: waist (WC), HDL cholesterol, blood glucose (Glu) and serum triglycerides (Tg). Each dichotomous variable received value 1 if the criterion for corresponding component in NCEP-ATP III definition was met. The p-value for overall model fit statistic was less than 1×10-6. The p-values of regression coefficients were 0.0001 for WC>102/88 cm (men/women), 0.0302 for HDL<1.03/1.3 mmol/l (men/women), 0.0097 for Glu>6 mmol/l and 0.0002 for Tg>1.7 mmol/l.

The p-value of regression coefficient for PP was 0.0061. These p-values showed that all model variables contribute significantly to the odds ratio of MS. This model was used to study the relation between the odds ratio of MS and the value of pulse pressure when only one of the other MS components met criterion (Figure 4) The results demonstrated when only HDL-cholesterol or blood glucose met criterion the odds ratio was less than 1 even for PP up to 80 mm Hg (Figure 4).

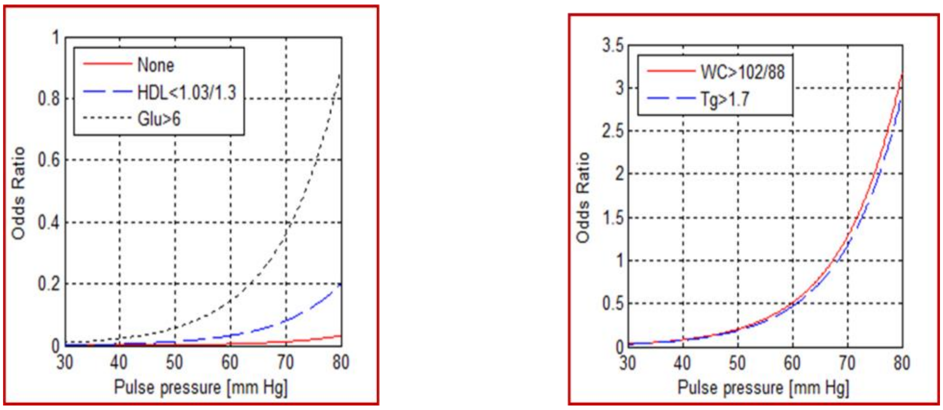

Figure 2. Odds ratio as function of PP when only one of the MS components was met criterion.

When waist or triglycerides met criterion the odds ratio was more than 1 for wide PP. The models for waist and triglycerides were very similar. The obtained model showed that for increase of PP with 5 mm Hg it was expected about 1.5787 times increase in the odds ratio of MS. In the second model in addition to PP four dichotomous variables were included and the model was adjusted for gender. The dichotomous variables were composed using the following components of MS – waist (WC), HDL cholesterol, blood glucose (Glu) and serum triglycerides (Tg).

The MCS model could also help us to explain the complex relationship between metabolic disorders and cognitive disturbances and the boundaries between normal and pathological conditions, with a better understanding of clinical and neuropathological features of these metabolic-based cognitive disorders. At present, there is gross lack of data in terms of association of MetS and cognitive decline. There is an urgent need to study this association in community samples. Understanding the progress from MetS to overt NCDs and development of dementia can also help in identifying other associated risk and protective factors for development of dementia.

Conclusion

There was a positive association between PCT levels, decreased levels of Aβ42 and Aβ40, as well as elevated NT-proBNP and cognitive impairment in people with MS and stroke. A concentration of NT-proBNP of 60 pg / ml or greater could be an indicator of metabolic abnormalities and early cognitive decline. Large-scale studies and longer follow-up periods will be necessary to establish a direct and accurate causal relationship between MS and MCI pathologies.

Scientific Ethics Declaration

The author declares that the scientific ethical and legal responsibility of this article published in EPSTEM Journal belongs to the author.

Acknowledgements or Notes

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References

Alberti, K. G. M. M., & Zimmet, P. Z. (1998). Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic Medicine*, *15*(7), 539-553.

Grodstein, F. (2007). Cardiovascular risk factors and cognitive function. *Alzheimer's & Dementia*, *3*(2), S16-S22.

Grundy, S. M., Brewer Jr, H. B., Cleeman, J. I., Smith Jr, S. C., & Lenfant, C. (2004). Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*, *109*(3), 433-438.

Luis, C. A., Loewenstein, D. A., Acevedo, A., Barker, W. W., & Duara, R. (2003). Mild cognitive impairment: directions for future research. *Neurology*, *61*(4), 438-444.

Frisardi, V., Panza, F., Seripa, D., Imbimbo, B. P., Vendemiale, G., Pilotto, A., & Solfrizzi, V. (2010). Nutraceutical properties of Mediterranean diet and cognitive decline: possible underlying mechanisms. *Journal of Alzheimer's Disease*, *22*(3), 715-740.

Panza, F., Capurso, C., D'Introno, A., Colacicco, A. M., Capurso, A., & Solfrizzi, V. (2006). Prevalence rates of mild cognitive impairment subtypes and progression to dementia. *Journal of the American Geriatrics Society*, *54*(9), 1474-1475.

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