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DIAGNOSTIC VALUE OF SERUM INTERLEUKINS IN ELDERLY PATIENTS WITH METABOLIC SYNDROME ASSOCIATED WITH ARTERIAL HYPERTENSION

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Abstract: This study assessed serum cytokine patterns in elderly patients with metabolic syndrome and arterial hypertension. The study included 86 patients aged 60–75 years with metabolic syndrome and grade II–III primary hypertension and 35 age-matched controls. Serum concentrations of several interleukins were determined using an enzyme-linked immunosorbent assay. Patients demonstrated increased proinflammatory cytokines, particularly IL-8, IL-1β, IL-6, IL-2, TNF-α, and interferon-γ, accompanied by reduced IL-4 and IL-10 levels. IL-8 showed the highest diagnostic association with metabolic syndrome and hypertension, with an odds ratio of 7.281 and a 95% confidence interval of 6.864–7.825.

Keywords: metabolic syndrome; arterial hypertension; serum cytokines; interleukins; IL-8.

ДИАГНОСТИЧЕСКАЯ ЗНАЧИМОСТЬ СЫВОРОТОЧНЫХ ИНТЕРЛЕЙКИНОВ У ПОЖИЛЫХ ПАЦИЕНТОВ С МЕТАБОЛИЧЕСКИМ СИНДРОМОМ, АССОЦИИРОВАННЫМ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Аннотация: В исследовании оценен сывороточный цитокиновый профиль у пожилых пациентов с метаболическим синдромом и артериальной гипертензией. Обследованы 86 пациентов в возрасте 60–75 лет с метаболическим синдромом и первичной артериальной гипертензией II–III

степени и 35 лиц контрольной группы сопоставимого возраста. Концентрацию сывороточных интерлейкинов определяли методом иммуноферментного анализа. У пациентов выявлено повышение провоспалительных цитокинов, особенно IL-8, IL-1β, IL-6, IL-2, TNF-α и интерферона-γ, одновременно со снижением уровней IL-4 и IL-10. Наиболее выраженная диагностическая связь установлена для IL-8: отношение шансов составило 7,281 при 95% доверительном интервале 6,864–7,825.

Ключевые слова: метаболический синдром; артериальная гипертензия; сывороточные цитокины; интерлейкины; IL-8.

Introduction: Metabolic syndrome is a common age-associated condition characterized by several cardiovascular and metabolic abnormalities. Its combination with arterial hypertension is particularly important in older adults because metabolic, vascular, and inflammatory mechanisms may accelerate cardiovascular remodeling and increase adverse outcomes. The systemic immune response has increasingly been considered an important component of these processes. Cytokines participate in communication between immune cells and vascular tissues, regulate inflammation, and may influence endothelial function and vascular tone. An imbalance between proinflammatory and anti-inflammatory mediators can therefore reflect persistent immune activation accompanying metabolic and cardiovascular disorders. IL-1β, IL-2, IL-6, IL-8, TNF-α, interferon-γ, IL-4, and IL-10 are of particular interest because altered production may characterize different directions of inflammatory regulation. However, the diagnostic value of individual cytokines in elderly patients with simultaneous metabolic syndrome and arterial hypertension requires quantitative assessment rather than subjective interpretation. The source study examined serum interleukins in patients aged 60–75 years and compared them with age-matched individuals without metabolic syndrome or hypertension. Determination of odds ratios and confidence intervals allowed identification of cytokines with the strongest statistical association with the combined pathology. This approach may help define informative immunological markers and improve objective differentiation of

elderly patients with metabolic syndrome and hypertension from individuals without these conditions for risk assessment and monitoring.

Aim of the study: To determine the diagnostic significance of serum interleukins in elderly patients with metabolic syndrome and grade II–III primary arterial hypertension and to identify cytokines showing the strongest statistical association with the combined metabolic and cardiovascular condition.

Materials and methods. The study was performed in clinical inpatient conditions and included 86 patients aged 60–75 years with verified metabolic syndrome and primary arterial hypertension of grade II–III. The control group consisted of 35 individuals of comparable age and sex who had neither metabolic syndrome nor arterial hypertension. Diagnosis of metabolic syndrome and hypertension followed recommendations of the Russian Research Society of Cardiology and International Diabetes Federation criteria. Central obesity was considered the principal component, with at least two additional abnormalities: fasting hyperglycemia or previously diagnosed type 2 diabetes, arterial hypertension, reduced high-density lipoprotein cholesterol, or increased triglycerides. Patients were excluded when they had experienced stroke, malignant tumors, acute myocardial infarction, or renal failure during the preceding six months. Serum cytokines were measured by enzyme-linked immunosorbent assay using the Protein Contour reagent system. The investigated cytokine spectrum included IL-1β, IL-2, IL-6, IL-8, TNF-α, interferon-γ, interferon-α, IL-4, IL-10, and IL-18. Diagnostic informativeness was evaluated by calculating odds ratios according to the standard cross-product formula, with corresponding confidence intervals. Only statistically significant odds ratios were considered informative. Statistical processing was performed using Statistica 6.0 and the Wilcoxon nonparametric test. Discriminant analysis was subsequently applied to classify elderly patients with metabolic syndrome and hypertension versus age-matched controls according to serum interleukin concentrations. The quality of classification was assessed using Mahalanobis distance. Cytokine assessment was standardized.

Results. Serum cytokine analysis demonstrated a pronounced imbalance between proinflammatory and anti-inflammatory mediators in elderly patients with metabolic syndrome and arterial hypertension. Compared with controls, IL-1β increased from 10.3±1.2 to 72.4±2.8 pg/ml, IL-2 from 15.8±1.9 to 64.7±2.4 pg/ml, and IL-6 from 63.7±3.3 to 204.5±3.6 pg/ml; all differences were significant at $p<0.001$. The most marked proinflammatory change was observed for IL-8, which increased from 5.0±1.6 to 49.6±3.1 pg/ml, representing an approximately tenfold elevation ($p<0.001$). TNF-α increased from 6.8±1.7 to 14.8±1.3 pg/ml, while interferon-γ increased from 13.4±1.1 to 28.2±1.5 pg/ml, both $p<0.001$. In contrast, anti-inflammatory IL-4 decreased from 4.4±0.3 to 1.1±0.1 pg/ml and IL-10 from 19.5±1.2 to 5.2±0.3 pg/ml ($p<0.001$). The odds-ratio analysis showed the strongest association for IL-8, OR=7.281, 95% CI 6.864–7.825, $p<0.0001$. Significant associations were also obtained for IL-1β, OR=4.965, IL-4, OR=4.287, IL-10, OR=3.642, IL-2, OR=2.754, IL-6, OR=2.082, IL-18, OR=1.856, interferon-α, OR=1.765, TNF-α, OR=1.828, and interferon-γ, OR=1.603. Discriminant analysis showed 8.7% of controls were incorrectly classified as patients, while 8.2% of patients were incorrectly assigned to the control class. Thus, serum interleukin profiles provided high classification accuracy for distinguishing the two groups. IL-8, IL-1β, IL-4, and IL-10 were identified as leading diagnostic markers. Mahalanobis-distance classification further confirmed separation between the study and control groups based on the measured serum cytokine concentrations. Interferon-γ was the only listed variable noted as producing erroneous classification and was not recommended as an isolated clinical classifier.

Conclusions: Elderly patients with metabolic syndrome and arterial hypertension demonstrated a clear systemic cytokine imbalance characterized by increased proinflammatory and reduced anti-inflammatory mediator concentrations. IL-8 showed the strongest statistical association with the combined pathology, followed by IL-1β, IL-4, and IL-10. The high odds ratios and narrow confidence intervals indicate substantial diagnostic informativeness of these cytokines. Discriminant analysis based on serum interleukins provided high classification accuracy, with

misclassification rates of 8.7% among controls and 8.2% among patients. These findings support serum cytokine profiling as a promising adjunctive approach for objective identification of metabolic syndrome with hypertension in older adults in clinical practice.

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