Prognostic Value of Cytokines for Ischemic Heart Disease in Patients with Hypertension Stage II

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Abstract

Aim of the study is to determine the predictive value with respect to the development of coronary heart disease (CHD) of inflammatory activity, in patients with hypertension (HT) stage II.

Methods: We examined 180 patients (men and women) with documented HT stage II. All surveyed people were divided into two groups: the first group consisted of 130 primary HT patients stage II without CHD, the average age of 56.5 ± 0.5 years; a second comparison group – 50 patients with CHD combined with HT II stage, average age of 58.1 ± 0.8 years.

Results: The results of the ROC-analysis showed significantly higher (AUC = 0.87) (95% CI AUC 0,812-0,915) predictive value ratio of IL-1β / IL-10 in the development of coronary artery disease in hypertensive patients, with an optimal distribution of the threshold of > 1.7 sensitivity was 64.0 % and specificity - 94.6 %. The high sensitivity (90.0%), to the development of coronary artery disease in hypertensive patients was significantly (AUC = 0,87) hs-CRP found at the point of separation of> 4.7 mg / L specificity was 72.3%.

Keywords: ischemic heart disease, hypertension, prediction, inflammatory activity

Introduction

Coronary heart disease (CHD) is one of the most common and dangerous pathologies, it is considered the most common cause of sudden death [1]. One of the urgent problems of modern cardiology is atherosclerosis (AS) [2]. One of the risk factors for the development of the AS can act hypertension [3]. The emergence of an imbalance of cytokine system contributes to the development of vascular disorders, which are the basis of atherogenesis, which leads eventually to the formation and destabilization of atherosclerotic plaques and the development of cardiovascular complications. There exists the need to create a system for early detection of cardiovascular risk in this connection is constantly searching for biomarkers, the determination of which would be more likely to obtain information about the formation of cardiovascular disease in the preclinical stage [4].

Material and methods

The study is based on a survey of 180 full machining patients (51 men and 129 women) with documented II stage HT with grade 2-3.

Criteria for inclusion in the study: patients' age 40 to 65 years; HT stage II with grade 2-3.

Criteria for exclusion from the study: verified of CHD; heart failure (HF) III-IV degree of NYHA; hormonally active disease; kidney disease; symptomatic arterial hypertension; diseases of the central nervous system (CNS); oncological diseases; clinically significant disease, according to researchers, may directly or indirectly affect the quality of research; the refusal of the patient from the study.

The patients were divided into two groups: the first group consisted of 130 primary hypertensive patients stage II without coronary artery disease, the average age of $56,5 \pm 0,5$ years; a second comparison group - 50 patients with HT II stage, verified with the CHD, the average age of $58,1 \pm 0,8$ years.

The patient groups were comparable in age, the average systolic (SBP) and diastolic blood pressure (DBP), as well as the average duration of HT in both groups.

Coronaroventriculography (CG) being accessed by the method of M. Judkins.

The level of Interleukin-1β, Interleukin-10 and hs-CRP in blood plasma was determined by ELISA method using standard sets IL-1β-ELISA-best "," IL-10-ELISA-best "and" hs-CRP ELISA-best " (Vector-best, Russia) according to the method described in the application instruction for the test systems. The analysis was performed using "SUNRISE TS" (Austria) immunoassay analyzer.

Statistical analysis of the results

Statistical analysis was performed using the application PSPP (version 0.7.9, the license GNU GPL). The adequacy of mathematical models was evaluated by the method of constructing and analyzing the curves of operating characteristics (ROC - Receiver Operating Characteristic curve), with the calculated area under the ROC-curve (AUC - Area under the ROC curve)) and its 95% confidence interval, sensitivity (Se), specificity (Sp), the likelihood ratio for positive (+LR) and negative (-LR) results. The cut-off point was found using the J-Youden index. [5]. In order to compare AUC method was used overlapping confidence intervals.

Results

In order to determine the diagnostic value of coronaroventriculography ROC-analysis was used to calculate the data set, we used two groups of hypertensive patients without coronary artery disease (n = 130) and ischemic heart disease combined with HT (n = 50). According to our data it was coronaroventriculography Se 92,3% and Sp 91,9% at AUC = 0,92 (95% CI 0,836-0,970), positive likelihood ratio = 11,38 and negative likelihood ratio = 0,084. This method of diagnosis of CHD has been selected as the standard.

Identification of possible markers of immune-inflammatory response in relation to the development of coronary artery disease in patients with HT stage II using ROC-analysis was determined by their diagnostic value, the results are presented in Table. 1.

Table 1. Predictive value of markers in relation to the development of coronary artery disease in patients with stage II hypertension (n = 180)

The indicator unit	Indicators						
	Cut off	Se, %	Sp, %	AUC	95%DI AUC	+LR	–LR
IL-1β, pg/ml	>5,2	84,0%	65,4%	0,80	0,735–0,857	2,43	0,24
IL-10, pg/ml	<2,9	42,0%	82,3%	0,62	0,546–0,692	2,37	0,70
IL-1β/IL-10	>1,7	64,0%	94,6%	0,87	0,812–0,915	11,89	0,38
hs-CRP, mg / l	>4,7	90,0%	72,3%	0,87	0,809–0,913	3,25	0,14

The level of IL-1β significantly (AUC = 0,80) had at the optimum point distribution > 5.2 pg / ml (sensitivity 84.0% and specificity of 65.4%, for the development of coronary artery disease in patients with HT stage II. The optimum point for separation the level of IL-10 significantly (AUC = 62), according to the

ROC-analysis was <2.9 pg / ml (sensitivity 42.0% and specificity - 82.3%. The results of the ROC-analysis showed significantly higher (AUC = 0.87) (95% CI AUC 0,812-0,915) predictive value ratio of IL-1β / IL-10 in the development of coronary artery disease in hypertensive patients, with an optimal distribution of the threshold of > 1.7 sensitivity was 64.0 % and specificity - 94.6 %. The high sensitivity (90.0%), to the development of coronary artery disease in hypertensive patients was significantly (AUC = 0,87) hs-CRP found at the point of separation of> 4.7 mg / L specificity was 72.3%.

The highest AUC had levels of IL-1β / IL-10 and hs-CRP. Just for these indicators was the intersection with the 95% CI AUC coronaroventriculography, respectively CG AUC = 0,92 (95% CI 0,836-0,970) vs IL-1β / IL-10 AUC = 0,87 (95% CI 0,812-0,915) and vs hs-CRP AUC = 0.87 (95% 0,809-0,913).

Discussion

In scientific studies revealed that the inflammatory mediators involved in the processes of formation are related to the formation of the AS and coronary artery disease. The idea that inflammatory processes are involved in the pathogenesis of coronary heart disease is not new, but markers of inflammation as a component of the current state of the disease are poorly understood. In the study of mechanisms of pathogenesis HT in recent years, more attention is paid to research of endothelial function, in violation of the antioxidant defense system may be the cause of immune disorders [6].

Therefore, interested in the possibility of the use of inflammatory activity as a marker for coronary artery disease in hypertensive patients. Today hs-CRP is the most studied inflammatory markers [7, 8]. We assume that the higher level of inflammatory markers in patients with hypertension, more active are the local and systemic inflammation in the coronary arteries, which can lead to the development of coronary artery disease.

Non-specific indicators of inflammatory activity condition may be useful to detect latent flowing coronary heart disease in patients with hypertension, as well as evaluate the effectiveness of therapy, which requires further study.

Conclusions

1. Assessment of the severity of immune-inflammatory response by the ratio of IL-1β / IL-10 may have predictive value with respect to the development of coronary artery disease in hypertensive patients.

2. To increase the sensitivity and specificity of the model prediction of CHD in hypertensive patients need to develop indicators of combinative using independent predictors that require further scientific research.

Ethical Declaration. The study was approved by the local ethics committee of State Institute «Zaporizhzhia Medical Academy of Postgraduate Education of Ministry of Health of Ukraine». The study was carried out in conformity with the Declaration of Helsinki.

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