

# Interleukin-22 Level and Vascular Remodeling in Patients with Hypertension in Associated with Abdominal Obesity

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## Abstract

The purpose of the study was to estimate the interleukin-22 (IL-22) level in the blood serum of hypertensive patients with abdominal obesity (AO), depending on common carotid arteries (CCA) remodeling presence.

Ninety-five subjects: 83 hypertensive patients and 12 healthy controls were examined. The patients were divided into two groups, depending on the presence of AO followed by the division of patients into subgroups depending on the intima-media thickness (IMT). For all patients, the following anthropometric parameters were measured: weight, height, waist circumferences (WC), hip circumferences (HC); the body mass index (BMI) and the waist-to-hip ratio (WC/HC) were calculated. The serum IL-22 level was determined in the patients by means of the Bender Medsystems® Human IL-22 Platinum ELISA kit by immunoassay method. Additionally, the patients underwent an ultrasound examination of carotid arteries.

The study revealed that the CCA IMT in hypertensive patients with and without AO compared to the control group were significant differences.

Serum IL-22 levels in hypertensive patients with AO having  $IMT \geq 0.9$  mm was statistically higher as compared with patients having  $IMT < 0.9$  mm.

The IL-22 levels in hypertensive patients without AO having  $IMT < 0.9$  mm and having  $IMT \geq 0.9$  mm were significantly exceeds cytokine level in the control group.

The obtained results may indicate that the blood serum IL-22 level is associated with a greater degree of vascular wall damage in hypertensive patient both with and without AO.

Higher IL-22 levels in the groups of hypertensive patients both with and without AO, with normal IMT compared with the control group, probably indicate that elevated blood serum IL-22 content can promote an early affection of the vascular endothelium.

**Keywords:** interleukin-22, abdominal obesity, vascular remodeling

## 1. Introduction

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality of middle-aged and elderly patients in most countries of the world [5]. According to the World Health Organization (WHO) about 17.5 million people die from CVD every year [6]. One of the most frequent CVD is essential hypertension (EH), which rarely occurs in isolation and often clusters with metabolic risk factors, such as dyslipidaemia, glucose intolerance and obesity [5]. Presence of abdominal obesity (AO) increases the risk of the development of hypertension, and predisposes to rapid development of hypertension-associated target organ damage, which has additional adverse prognostic significance.

One of the typical early target organ damage in patients with EH is arterial remodeling. In recent times, increasing attention is paid to the problem of remodeling the heart and blood vessels in EH. This is due to the fact that structural and functional changes that occur in case of high blood pressure (BP) are not only compensatory responses, but also an independent factor in the further progression of the disease [3, 9].

The unifying mechanism of these pathological conditions associated with EH is immune inflammation, mediators of which are pro-inflammatory cytokines, and which is engaged not only in obesity, dyslipidemia, but also in disruptions of the blood vessels architectonics [2, 7, 4]. In recent years, the role of interleukins has been actively studied in this context. Thus, the biological effects of interleukin-22 (IL-22), a member of the IL-10 family having proinflammatory properties, have been studied. The IL-22 effects are various, including participation in many physiological and pathophysiological processes, specifically inflammation, tissue regeneration, etc. [1]. However, its importance in the pathogenesis of a cardiovascular pathology remains insufficiently studied; therefore, it is reasonable to determine and analyze the IL-22 effects on the remodeling of elastic type arteries, such as common carotid arteries (CCA) in hypertensive patients with concomitant obesity.

**The aim of the study** was to estimate the IL-22 levels in the blood serum of EH patients with AO, depending on CCA remodeling presence.

## 2. Materials and methods

Ninety-five subjects: 83 hypertensive patients and 12 healthy controls were examined. The patients were divided into two groups, depending on the presence of AO, which was diagnosed at a waist circumference (WC) of more than 102 cm for men and more than 88 cm for women [10]. Group 1 included the patients with EH and AO (n = 43); Group 2 included the patients with EH (n = 40); the control group consisted of the healthy subjects (n = 12). The age of patients in Group 1, among whom there were 9 (21%) men and 34 (79%) women, ranged from 42 to 78 years; the median was 58.0 years. The age of the examined subjects enrolled to Group 2, among whom there were 23 (57.5%) men and 17 (42.5%) women, ranged from 42 to 78 years; the median was 66.0 years. Four (33.3%) men and 8 (66.7%) women were enrolled to the control group. The age of the subjects in this group ranged from 41 to 60 years; the median was 52.5 years. The body weight of the EH patients with and without AO was 88.0 (76.0; 100.0) kg and 75.0 (63.0; 80.0) kg, respectively.

For all patients, the following anthropometric parameters were measured: weight, height, waist circumferences (WC), hip circumferences (HC); the body mass index (BMI) and the waist-to-hip ratio (WC/HC) were calculated. The serum IL-22 level was determined in the patients by means of the Bender Medsystems® Human IL-22 Platinum ELISA kit by immunoassay method.

Additionally, the patients underwent an ultrasound examination of carotid arteries. The intima-media thickness (IMT) was measured using the technique of P. Pignoli in the middle third of the CCA on the posterior wall as the distance between the characteristic echoic area formed by the intima-lumen interface and the media-adventitia interface in a cross sectional plane [8].

Statistical analysis of the data was performed using nonparametric statistical methods. In the samples with nonparametric data distribution, the results are presented as Me (Q25; Q75) where Me is the median (50th percentile), Q25 and Q75 are the 25th and 75th percentiles, respectively. To compare the results, the Mann-Whitney test was used. The Spearman's rank correlation coefficient was used to estimate the degree of dependence. The null hypothesis was discarded at the statistical significance of  $p < 0.05$ .

## 3. Results and discussion

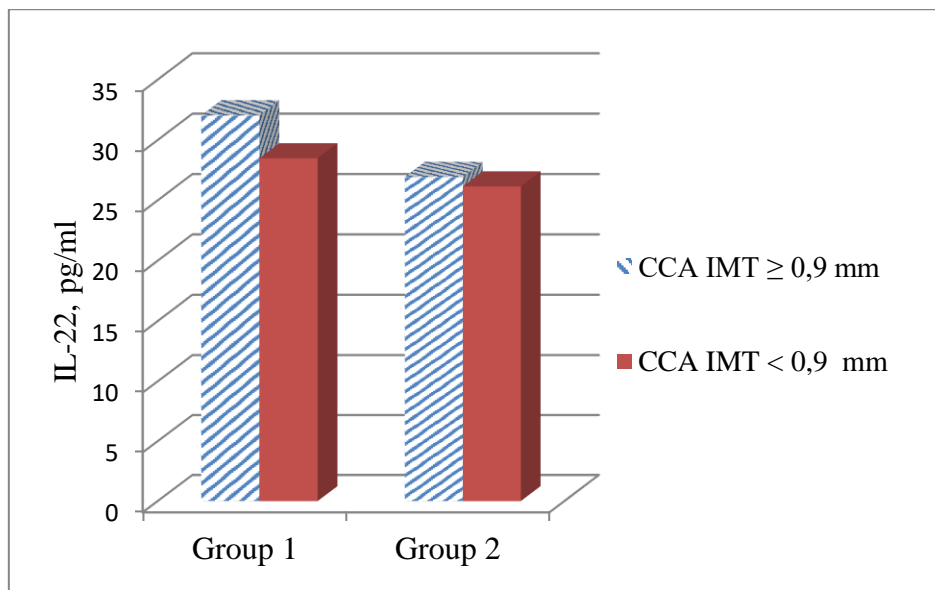
The study revealed that in the control group the common carotid arteries intima-media thickness was 0.71 (0.69; 0.78) mm, in the group of EH patients – 1.00 (0.91; 1.10) mm, in patients with EH in combination with abdominal obesity – 1.10 (0.95; 1.40) mm. There were significant differences between the common carotid arteries intima-media thickness in EH patients with and without abdominal obesity compared to the control group ( $p < 0.05$ ), as well as between Groups 1 and 2 ( $p < 0.05$ ).

Serum IL-22 levels in EH patients with abdominal obesity having intima-media thickness  $\geq 0.9$  mm was statistically higher (32.05 (28.64; 51.64) pg/ml) as

compared with patients having intima-media thickness  $< 0.9$  mm (28.49 (26.81; 32.26) pg/ml;  $p < 0.05$ ).

The IL-22 levels in the EH patients without abdominal obesity having intima-media thickness  $< 0.9$  mm were 26.16 (23.01; 30.44) pg/ml and having intima-media thickness  $\geq 0.9$  mm were 26.95 (23.21; 29.61) pg/ml, which significantly exceeds cytokine level in the control group – 19.91 (18.77; 20.15) pg/ml ( $p < 0.05$  in both cases) (Fig. 1).

Figure 1.  
Serum level of IL-22 in patient's groups



Note: Group 1 – hypertensive patients with abdominal obesity;  
Group 2 – hypertensive patients without abdominal obesity.

The obtained results may indicate that the blood serum IL-22 level is associated with a greater degree of vascular wall damage in EH patient both with and without abdominal obesity. A positive correlation relationship was established between the serum IL-22 level and intima-media thickness in EH with abdominal obesity ( $R=0.67$ ;  $p < 0.05$ ) and without abdominal obesity ( $R=0.39$ ;  $p < 0.05$ ). Higher IL-22 levels in the groups of EH patients both with and without abdominal obesity, with normal intima-media thickness compared with the control group, probably indicate that elevated blood serum IL-22 content can promote an early affection of the vascular endothelium.

## Conclusion

Common carotid arteries remodeling in essential hypertension patients in combination with abdominal obesity is associated with an increased blood level of the proinflammatory cytokine interleukin-22 ( $p < 0.05$ ).

The positive correlation established between interleukin-22 and the intima-media thickness in essential hypertension with abdominal obesity ( $R=0.67$ ), ( $p<0.05$ ) and without abdominal obesity ( $R=0.39$ ), ( $p<0.05$ ) may indicate that interleukin-22 can take part in the structural and functional changes in the vascular wall.

The increase in interleukin-22 serum levels is the most significant in patients with comorbid course of essential hypertension and abdominal obesity, which allows consider this cytokine as a biomarker of vascular damage; and one of the factors that significantly enhance this process is abdominal obesity.

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**Received: April 15, 2019; Published: May 8, 2019**