

Integrative assessment of candidate gene polymorphisms distribution by forming a gene modification index in arterial hypertension with and without obesity: a new perspective in cardiology management

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The concept of evolutionary accumulation of candidate gene polymorphisms in the realization of the hypertensive phenotype becomes promising in understanding of arterial hypertension (AH). A large amount of data about genetic polymorphisms in population have been accumulated and perspective approaches to their integrative assessment are being formulated for practical management.

The purpose of the research was to analyze and compare the proportion of modified candidate genes (CG) in the group of hypertensive patients with and without obesity with the group of non-hypertensive patients by calculating the gene modification index (GMI) for the assessment of possible usage of genetic stratification in the management of AH.

Methods: 106 patients with AH and obesity (age 46.2 [24–72], m/f 79/27), (group 1), 96 hypertensive patients without obesity (age 48.3 [26–75], m/f 72/24), (group 2) and 98 non-hypertensive patients (age 41.6 [26–69], m/f 39/59), (group 3) (ESC/ISH 2018, WHO 1997) were examined. The analysis of polymorphisms of the following CG by PCR was performed: ADD1: 1378, AGT: 704, AGT: 521, AGTR1: 1166, AGTR2: 1675, CYP11B2: –344, GNB3: 825, NOS3: –786, NOS3: 894. The GMI which represents the percentage of “pathological” genotypes was formed and calculated by the formula: $GMI = (N/13.5) \times 100$, where N is the sum of points of present GP (“pathological” homozygous was 1,5 points, heterozygous – 1 point, “normal” genotype – 0 points); 13.5 – maximum number of points. The GMI

from 0 to 20% was considered as low genetic risk (GR), from 21 to 40% – moderate GR, from 41 to 70% – high GR, from 71 to 100% – very high GR.

Results: In patients with AH and obesity, a low GR was in 4 (3.8%), in the group of hypertensive patients without obesity – 13 (13.5%), in normotensive patients – in 81 (82.7%) ($p_{1-3} = 0.0001$, $p_{2-3} = 0.0001$, $p_{1-2} = 0.02$). Moderate GR was observed in 21 (19.8%) patients of the 1st group, in 25 (26%) patients of the 2nd group and in 12 (12.2%) patients of the 3rd group ($p_{1-3} = 0.07$, $p_{2-3} = 0.01$, $p_{1-2} = 0.02$). 54 (50.9%) patients of group 1, 41 (42.7%) patients of group 2 and 5 (5.1%) of patients of group 3 had a high GR ($p_{1-3} = 0.0001$, $p_{2-3} = 0.0001$, $p_{1-2} = 0.08$); a very high GR was in 27 (25.5%) patients of the 1st group, in 17 (17.8%) of the 2nd group and was absent in the patients of the 3rd group ($p_{1-3} = 0.0001$, $p_{2-3} = 0.0001$, $p_{1-2} = 0.02$). The average GMI in group 1 was 66.2% [CI 95%, 20–78], in group 2 – 56.4% [CI 95%, 18–72], in group 3 – 22% [CI 95% 5–41], ($p_{1-3} = 0.0001$, $p_{2-3} = 0.0001$, $p_{1-2} = 0.04$).

Conclusions: It was revealed a strong significant predominance of the proportion of modified CG in hypertensive patients with and without obesity compared with non-hypertensive patients. There was a moderate significant difference between hypertensive patients, depending on the presence of obesity. Evaluation of GMI is a perspective direction in the diagnosis and prevention of AH and can be used in practical management.