STRATIFICATION OF AMBULATORY BLOOD PRESSURE MONITORING FINDINGS BY CLUSTER ANALYSIS IN PATIENTS WITH ARTERIAL HYPERTENSION, OBESITY AND ALBUMINURIA

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The aim of the investigation was to study the characteristics of ambulatory blood pressure monitoring (ABPM) indices in the combination of arterial hypertension (AH) with obesity and albuminuria using cluster analysis.

Material and Methods. The study involved 70 AH patients randomly chosen, aged from 23 to 71 years (mean age — 47.9 years). ABPM was performed before antihypertensive therapy administration. We estimated body mass index and albuminuria level. ABPM indices were stratified into clusters.

Results. Clusters with normal heart rate prevailed in patients with normal weight and overweight, I degree obesity in all AH varuants. Hypertensive clusters with tachycardia were found to prevail in patients with II–III degree obesity. AH structure changed with body mass increase. In overweight and I degree obesity there grows the occurrence of systolic-diastolic AH clusters. In II–III degree obesity the clusters of systolic-diastolic and isolated diastolic AH were revealed less frequently than in normal body weight, while isolated systolic AH clusters were found more frequently. Their occurrence increased in patients with a high albuminuria level as well.

Conclusion. ABPM data can be grouped into clusters, and their own pathogenic mechanisms of AH maintenance and regulation seem to prevail in each cluster. In overweight and I degree obesity patients the occurrence of systolic-diastolic AH increases. With obesity degree increase there is the tendency for heart rate rise, and hemodynamic AH variants are redistributed towards the increase of isolated systolic AH, which is likely to be due to the increase in AH severity with vascular wall remodeling progression. Isolated systolic AH prevalence is increasing not only in II–III degree obesity, but also in high albuminuria supporting the significance of systolic AH in albuminuria development. No interaction between albuminuria and heart rate was revealed.

Key words: arterial hypertension; obesity; albuminuria; ambulatory blood pressure monitoring.

Arterial hypertension (AH) and obesity are recognized pandemic of the XXI century. Among 142 million Russian population, about 42 million suffer from AH (AH incidence among men — 39%, among women — 41%) [1]. 55% of Russians have overweight, and among them 22% suffer from obesity [2]. Obesity is a trigger of cardiovascular diseases and an independent risk factor of cardiovascular complications. Obese people are known to have threefold AH risk compared to those with normal body mass [3]. AH causes target lesions, namely, kidneys, heart, vessels, kidneys being affected most frequently — in 36.9% of AH patients [4].

Hypertensive changes of daily AP profile with increased mean values are risk factors of renal disorders with more frequent micro- and macroalbuminuria [5]. Albumin urinary excretion over 10 mg/d is one of the most accurate diagnostic and prognostic markers of renal diseases; the value over 300 mg/d means a severe renal disorder. In addition, albuminuria characterizes not only renal diseases, its clinical value being wider. Being a local renal marker of generalized endothelial dysfunctions, albuminuria appears as an independent risk factor of cardiovascular complications including fatal ones. If AH and obesity are combined, albuminuria is revealed twice as more frequently than on the average in polyclinic population [6].

Currently, in clinical practice, standard method of AP assessment in AH patients is ambulatory blood pressure monitoring (ABPM). There is no unified ABPM evaluation scheme, conventionally there are interpreted average AP daily and nightly indices, the degree of nightly AP decrease, pressure load, AP variability. Current information technology horizon including mathematical data bulk processing enables to analyze in ABPM a variety of indices. However, their complete and adequate interpretation is quite a task even for experts in this field [7]. By means of cluster analysis it is possible to stratify multidimensional ABPM indices into groups clustered by common features.

The aim of the investigation was to study the

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characteristics of ambulatory blood pressure monitoring indices in the combination of arterial hypertension with obesity and albuminuria using cluster analysis.

Material and Methods. The study involved 70 AH patients randomly chosen, aged from 23 to 71 years (mean age — 47.9 years); among them 39 males (55.71%) and 31 females (44.29%). The study complies with the declaration of Helsinki (adopted in June, 1964 (Helsinki, Finland) and revised in October, 2000 (Edinburg, Scotland)) and was performed following approval by the ethic committee of Nizhny Novgorod State Medical Academy (Russia). Written informed consent was obtained from every patient.

All patients, before hypotensive therapy administration, in the outpatient setting underwent ABPM on a daily AP monitor TM-2421 (AD Company, Japan). The measurements were taken using a combined auscultatory oscillometric method. According to data processing and interpretation program we determined hypotension level. Mean AP values showed 56 patients (80%) to have I degree AH, 12 patients (17.14%) — II degree AH, 2 patients (2.86%) — III degree AH.

By means of statistical analysis program Statgraphics Plus 5.0 we stratified ABPM values into groups united by common features. As a stratification method we used cluster analysis. Varda algorithm was applied. We took into consideration the following indices: systolic AP (SAP), diastolic AP (DAP), pulse pressure (APp=SAP–DAP), mean pressure (APm=DAP+1/3 APp), AP structural point (SPAP=DAP/SAP), heart rate (HR). According to 2D-diagrams and dendrograms, we determined visually the number of different AH clusters and their percentage ratio. Based on these data, the clusters were grouped. There were formed 8 groups: clusters of normal and borderline AP, isolated systolic AH (ISAH), isolated diastolic AH (IDAH) and systolic-diastolic AH (SDAH) with HR under 80 per minute and four groups of similar clusters with HR over 80 per minute.

Body mass index (BMI) was calculated in every patient according to the formula BMI=body mass (kg)/height (m^2). In accordance with BMI obesity classification (WHO, 1997), 9 patients (12.86%) were revealed to have normal body mass (BMI — 18.5–24.9), 31 (44.28%) — overweight (BMI — 25.0–29.9), 14 (20%) — I degree obesity (BMI — 30.0–34.9), and 16 (22.86%) — II–III degree obesity (BMI⩾35). All patients had abdominal obesity.

52 patients were diagnosed albuminuria, among them 21 patients (40.38%) were found to have increased albumin urinary excretion (10–29 mg/d), 31 (59.62%) — high albuminuria (30–299 mg/d). Albuminuria was classified based on National Guidelines for Chronic Kidney Disease.

Results and Discussion. Standard assessment of ABPM indices accepted in clinical practice and realized using daily AP monitor software is based on the averaging of SAP and DAP measured within 24 hours. In this way SAP and DAP arithmetic mean values are calculated in diurnal and night hours. By mean square deviation we calculated SAP and DAP variability, and by percentage ratio of average daily and average nightly AP levels — SAP and DAP diurnal rhythm, by time percentage of critical AP increase — hypertension time index. As the result, we had a set of indices, each of which indicates only one characteristic of SAP or DAP and does not permit detailed description of AP level in a patient. In fact, every measurement can be presented as a point in multidimensional space of attributes and characterized more completely. The analysis of data obtained after ABPM stratification showed that within 24 hours AH structure is heterogeneous, and AP measurement in any patient can be grouped into clusters. Optimal number of clusters ranges from 3 to 8, in each of which peculiar pathogenic mechanism of AP maintenance prevails.

The analysis of percentage ration of AP clusters in AH patients with different body mass types (Table 1) showed that in general, clusters with normal HR prevail in patients with normal body mass and overweight, as well as with I degree obesity in all AH variants. The exception is ISAH in patients with normal body mass, with tachycardia prevailing (8.73% versus 4.77%) that can be explained by sympathetic nervous system activation due to their higher physical activity in diurnal hours. Hypertensive clusters with tachycardia prevail in patients with II–III degree obesity. In

Table 1

Occurrence of AP clusters in hypertensive patients with different body mass (n=70), %

Body mass	Observation period	Normal and borderline AP		ISAH		IDAH		SDAH	
		HR<80	HR>80	HR<80	HR>80	HR<80	HR>80	HR<80	HR>80
Normal (n=9)	Day	15.85	6.84	3.03	8.73	8.61	5.86	13.89	16.98
	Night	10.07	0	1.74	0	2.79	0.97	3.72	0.92
	24-h	25.92	6.84	4.77	8.73	11.4	6.83	17.61	17.9
Overweight (n=31)	Day	15.72	5.85	9.77	5.17	5.7	3.4	15.05	18.08
	Night	7.35	0.82	1.14	0	1.54	0	9.67	0.74
	24-h	23.07	6.67	10.91	5.17	7.24	3.4	24.72	18.82
I degree obesity (n=14)	Day	9.56	2.61	4.37	4.15	7.02	4.82	24.74	19.58
	Night	13.52	0	0.72	0.75	3.31	0	3.75	1.1
	24-h	23.08	2.61	5.09	4.9	10.33	4.82	28.49	20.68
II–III degree obesity (n=16)	Day	18.75	9.12	7.44	11.24	5.78	8.78	9.4	11.04
	Night	7.97	0	1.8	0.92	0	0	5.82	1.94
	24-h	26.72	9.12	9.24	12.16	5.78	8.78	15.22	12.98

Table 2

Occurrence of AP clusters in patients with albuminuria (n=52), %

Albuminuria	Observation period	Normal and borderline AP		ISAH		IDAH		SDAH	
		HR<80	HR>80	HR<80	HR>80	HR<80	HR>80	HR<80	HR>80
Increased: 10–29 mg/d (n=21)	Day	12.71	8.7	5.14	5.19	5.01	8.36	15.32	18.68
	Night	9.62	1.08	0.34	0.54	0.42	0.49	7.1	1.3
	24-h	22.33	9.78	5.48	5.73	5.43	8.85	22.42	19.98
High: ⩾30 mg/d (n=31)	Day	15.44	4.74	7.45	8.93	7.86	3.31	19.25	14.21
	Night	7.43	0	2.26	0	1.6	0	6.55	0.97
	24-h	22.87	4.74	9.71	8.93	9.46	3.31	25.8	15.18

this group of patients in ISAH, clusters with tachycardia occur 1.3 times as frequent than in those with normal HR (12.16 versus 9.24%), in IDAH — 1.5 times as frequent (8.78 versus 5.78%), in SDAH in diurnal hours — 1.2 times as frequent (11.04 versus 9.4%).

Body weight gain results in AH structure changing. The patients with overweight and degree I obesity the occurrence of SDAH increases — respectively, by 1.2 and 1.4 times (43.54 and 49.17% versus 35.51% in patients with normal body mass). However, further body weight gain and obesity, a part of this AH type decreases up to 28.2%. SAH and IDAH clusters at II–III degree obesity are revealed 1.3 times as less frequently compared to normal body mass (28.2 versus 35.51% and 14.56 versus 18.23%), and ISAH clusters — 1.6 times as frequent (21.4 versus 13.5%).

The data we received indicate the tendency for HR and systolic AP increase in obesity, and are consistent with the findings of the investigations concerned with the study of sympathetic nervous system activity, which give evidence that plasma noradrenaline concentration in obese patients is higher than in subjects with normal body mass [8].

AH pathogenesis in abdominal obesity is known to be extremely complicated; and insulin resistance and compensatory hyperinsulinemia, sympathetic nervous system activation and rennin-angiotensin-aldosterone system, sodium and water retention have an essential role. The increase in minute volume of the left ventricular and total peripheral resistance is accompanied by SDAH.

When ISAH develops, there is of particular concern the great vessel wall remodeling with further decrease of vascular compliance and the loss of ability to quench pulse wave oscillations related to cardiac cycle phases. Therefore, ISAH is regarded as both a risk factor and a marker of target lesions [9]. The increase in the occurrence of ISAH clusters in II–III degree obesity patients we have demonstrated in this study indicates more severe AH in this group due to vascular wall remodeling. Endothelial dysfunction marked by albuminuria plays a key role in the development of this process.

Calculated percentage ratio of AP clusters in albuminuria (Table 2) showed the patients with a very high albuminuria level to have ISAH clusters 1.7 times as frequent than those with a high level (18.64 versus 11.21%), and IDAH and SDAH clusters — less frequently (12.77 versus 14.28 and 40.98% versus 42.4%, respectively). The above said indicates that in albuminuria development SAP level is essential. The relationship of ISAH and albuminuria has been demonstrated by a great number of studies. For instance, GUBBIO survey involving 1567 subjects with no diabetes mellitus [10] showed the risk of albuminuria development is 4.95 times as high in case of ISAH. The same study has demonstrated that it is AP increase, especially systolic, that is the most important in microalbuminuria determinant population. Our findings are consistent with the results of these studies.

Total number of clusters with tachycardia in patients with a high albuminuria level was 32.16%, and with an increased level — 44.34% that indicates the lack of relationship of tachycardia and albuminuria severity. Since tachycardia, being a sign of sympathicotonia, does not reflect the presence of endothelial dysfunction, the findings appear to be consistent.

Conclusion. Arterial hypertension structure within 24 hours is heterogeneous. ABPM data can be grouped into clusters, and their own pathogenic mechanisms of AH maintenance and regulation seem to prevail in each cluster. In overweight and I degree obesity patients the occurrence of systolic-diastolic AH increases due to the increase in minute volume of the left ventricular and total peripheral resistance against the background of sympathetic nervous system activation and rennin-angiotensin-aldosterone system. With obesity degree increase there is the tendency for heart rate rise, and hemodynamic AH variants are redistributed towards the increase of isolated systolic arterial hypertension, which is likely to be due to the increase in arterial hypertension severity with vascular wall remodeling progression. Isolated systolic arterial hypertension prevalence is increasing not only in II–III degree obesity, but also in high albuminuria supporting the significance of systolic AH in albuminuria development. No interaction between albuminuria and heart rate was revealed.

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References

1. Sorokin E.V., Karpov Yu.A. Kombinirovannaya antigipertenzivnaya terapiya — klyuch k povysheniyu effektivnosti serdechno-sosudistoy profilaktiki [Combined antihypertensive therapy is the key to improve the efficiency of cardiovascular prevention]. *Rus Med Z — Russian Medical Journal* 2012; 25: 1304–1308.

2. Shilov A.M., Dulaeva M.S., Osiya A.O., Abdullaeva A.T. Osobennosti lecheniya arterial'noy gipertonii pri ozhirenii kak faktora riska KhSN [The aspects of arterial hypertension treatment in obesity as a risk factor of chronic heart failure]. *Rus Med Z — Russian Medical Journal* 2012; 14: 672–677.

3. Astashkin E.I., Glezer M.G. *Ozhirenie i arterial'naya gipertoniya* [Obesity and arterial hypertension]. *Problemy zhenskogo zdorov'ya — Women health aspects* 2008; 4(3): 23–33.

4. Gorostidi M., Prieto M.A., Marin R., et al. Renal insufficiency is the most prevalent target-organ disease in primary care attended essential hypertension. *AHJ* 2005; 18(5, Pt 2).

5. Giaconi S., Levanti C., Fommei E., Innocenti F., Seghieri G., Palla L., et al. Microalbuminuria and casual and ambulatory blood pressure monitoring in normotensives and in patients with borderline and mild essential hypertension. *Am J Hypertens* 1989; 2(4): 259–261.

6. Böhm M., Thoenes M., Danchin W., Bramlage P., La Puerta P., Volpe M. Association of cardiovascular risk factors with microalbuminuria in hypertensive individuals: the i-SEARCH global study. *J Hypertens* 2007; 25(11): 2317–2324.

7. Pshenitsyn A.I., Mazur N.A. *Sutochnoe monitorirovanie arterial'nogo davleniya* [Ambulatory blood pressure monitoring]. Moscow: Medpraktika-M; 2007; 216 p.

8. Triosi R.L., Weiss S.T., Parker D.R., Sparrow D, Young J.B., Landsberg L. Relation of obesity and diet to sympathetic nervous system activity. *Hypertension* 1991; 17(5): 669–677.

9. Klinicheskie razbory. *Vnutrennie bolezni* [Clinical discussions. Internal diseases]. Pod red. Mukhina N.A. [Mukhin N.A. (editor)]. Moscow: Litterra; 2005; 608 p.

10. Mukhin A.V., Fomin V.V., Moiseev S.V., Saginova E.A. Mikroal'buminuriya — integral'nyy marker kardiorenal'nykh vzaimootnosheniy pri arterial'noy gipertonii [Microalbuminuria is an integral marker of cardiorenal relations in arterial hypertension]. *Consilium Medicum* 2007; 9(5): 13–19.