

# The circadian characteristics of arterial blood pressure in patients with acid-related diseases and arterial hypertension

## Abstract

**Background:** At present the comorbidity of arterial hypertension (AH) and acid-related diseases (ARD) still is of undoubted interest because of their high incidence and social importance.

**Aim:** The aim of our study was to present the circadian characteristics of arterial blood pressure (ABP) in patients with AH, associated with ARD.

**Materials and Methods:** a total of 69 males aged 25 to 45 years were included into a study. Among them 44 patients had associated course of AH and ARD, 25 patients suffered with isolated AH. 24-hours blood pressure (BP) monitoring and esophagogastroduodenoscopy were performed to verify the diagnosis.

**Results and Discussion:** Patients with associated course of AH and ARD were found to have the specific features in circadian BP profile. The co morbid patients were characterized with significant lower hypertensive indices, excessive night BP decrease and significant increase in morning speed of systolic and diastolic BP rise, which is considered to be negative for further clinical outcomes.

**Conclusion:** The co morbidity of ARD and AH can exacerbate the clinical course of AH and increase the cardiovascular risks in patients with associative diseases.

**Keywords:** arterial hypertension, acid-related diseases, co morbidity, circadian characteristics of blood pressure monitoring

Volume 3 Issue 2 - 2018

KhlinoVA OV,<sup>1</sup> Tuev AV,<sup>1</sup> Shishkina EA,<sup>2</sup> Spasenkov GN,<sup>2</sup> Kalashnikova TR,<sup>1</sup> Naumov SA<sup>2</sup><sup>1</sup>Department of Hospital Therapy, Federal State Budgetary Educational Institution of Higher Education, Russia<sup>2</sup>The State Budgetary Healthcare Establishment of the Perm Krai "Clinical Cardiological Clinic, Russia

**Correspondence:** KhlinoVA OV, Department of Hospital Therapy, Federal State Budgetary Educational Institution of Higher Education "Perm State Medical University named after academician E.A. Wagner" of the Ministry of Health of the Russian Federation, 614990, Perm, ul. Petropavlovskaya, 26, Email olgakhlynova@mail.ru

**Received:** December 04, 2017 | **Published:** May 04, 2018

## Abbreviations

CVS, cardiovascular system; ARD, acid-related diseases; DU, duodenal ulcer; GERD, gastroesophageal reflux disease; VNS, visceral nervous system; EFGDS, esophagogastroduodenoscopy; SBP systolic blood pressure; DBP, diastolic blood pressure

## Relevance of the problem

In modern medicine, an individual approach to the patient dictates the need for a multifaceted study of the clinical picture of underlying, concomitant and transmitted diseases, as well as their comprehensive diagnosis and rational treatment.<sup>1</sup> To date, at the stage of outpatient and inpatient care, patients with multiple diseases are more the rule than the exception. Various nosologies increasingly acquire the status of co morbidity, changing the classical clinical picture of each of the concomitant diseases, continuing to worsen the quality of life of the patient.<sup>2</sup> This is why the problem of the associated disease course continues to be important both for science and for practical health care.<sup>3</sup> The steady increases in the number of patients who have a combined pathology can be associated with both an increase and aging of the population and a negative impact of the socioeconomic characteristics of society. Obviously, nosological synthropy becomes particularly relevant in relation to widespread and socially significant diseases. In the conditions of daily clinical practice, the practitioner increasingly meets with patients who have combinations of peptic ulcer (duodenal ulcer) (DU) and coronary heart disease, diabetes mellitus and pulmonary tuberculosis, bronchial asthma and duodenal

ulcer, AH and acid-related diseases (ARD).<sup>2,4</sup> AH is the most common chronic non-infectious disease of the adult population and the most frequent pathology of the cardiovascular system (CVS).<sup>5,6</sup> The prevalence of hypertension in economically developed countries reaches 25%. In turn, ARD, including gastroesophageal reflux disease (GERD) and DU, to date also have a high prevalence in the population, a tendency to increase and are the most common among diseases of the gastrointestinal tract.<sup>7,8</sup> Thus, AH and ARD remain the main nosological forms of modern cardiology and gastroenterology. Already by virtue of their prevalence, these diseases would have to meet quite often together, having in addition a certain common mechanism of formation. The proximity of the location with the heart, the generality of the innervations, are capable of provoking arrhythmias, imitating coronary heart disease when the stomach is overfilled, the pathology of the esophagus by the type of viscerovisceral reflexes. The pathology of the upper gastrointestinal tract can lead to functional disorders of the CVS that arise mediated through the autonomic/visceral nervous system (VNS).<sup>9,10</sup> Taking into account the above mentioned positions, it can be assumed that the combined course of AH and ARD which is found, according to various data, from 11.6% to 50%.<sup>4,6,8</sup> is not just random, but can have pathogenetic and etiological patterns. Moreover, mutual weaning is not excluded when combining these nosologies. The comorbidity of ARD and AH can aggravate the development of the underlying pathological process and lead to the disruption of adaptive mechanisms. In this respect, further studies of the pathogenetic relationship of ARD and AH on the basis of the structural and functional characteristics of the heart, heart

rate variability, daily BP profile are important.<sup>11</sup> However, despite the great social significance and fairly frequent joint flow of AH and ARD the peculiarities of such a combination remain single, poorly understood, and at times and contradictory.<sup>11</sup> It should be noted that in most studies, as a rule, individual aspects of the problem are considered, and a single opinion on the features of the daily profile of BP in patients with AH in combination with various variants of RCC is absent. These circumstances determined the relevance and expediency of the present work. The purpose of this study was to study the chronobiological features of the daily profile of AD in patients with AH in combination with various clinico-endoscopic variants of the ARD.

## Materials and methods

A total of 69 men aged  $35.37 \pm 10.34$  years were examined. A group of patients with co morbid course of ARD and AH was represented by 44 patients, 21 of whom had association of DU and AH, and 23 had a combination of GERD and AH. The comparison group consisted of 25 patients with AH without concomitant diseases. All groups were comparable in age, sex, length of service AG, GERD and DU. All the studies were conducted prior to the appointment of patients with drug therapy, or against the abolition of previously prescribed drug therapy for AH and GERD for at least 72 hours. In accordance with the purpose and objectives of the study in the selection of patients the following inclusion criteria were determined: male sex; age of the patient is from 18 years; compliance with the diagnostic criteria of each nosological form: AH stage I or II stage, risk 1-3, GERD and / or DU; ability to cancel previously prescribed therapy for up to 72 hours; written consent of the patients was obtained to participate in the study. The exclusion criteria from the study were: non-compliance with the inclusion criteria; symptomatic nature of hypertension; coronary heart disease; presence of an artificial pacemaker; noncoronogenic forms of myocardial damage; heart defects of any etiology; chronic heart failure of III and IV functional classes according to NYHA; an indication of an acute history of cerebral blood flow disorder; signs of acute or exacerbation of chronic infections or parasitic disease; malignant neoplasms; pathology of the endocrine glands; presence of bronchial obstructive diseases; the presence of concomitant diseases of the digestive system, including cholelithiasis, viral hepatitis, ulcerative colitis. During the clinical examination of the patients, a survey and examination according to the traditional scheme were conducted. To verify the diagnosis of AH, generally accepted recommendations were used.<sup>12-14</sup> In accordance with the requirements of the Committee of Experts of the VNOK12, the patients underwent a comprehensive examination, including a clinical analysis of blood and urine, a biochemical blood test, instrumental methods of investigation (measurement of blood pressure by the method of NS Korotkov, ECG, chest X-ray, ultrasound examination of the heart, abdominal organs and kidneys).<sup>15</sup>

During the 24-hour monitoring of BP, a device of the Cardiotekhnika-04-AD system (INKART, St. Petersburg) was used. The signal was recorded and processed in accordance with generally accepted requirements. Registration of BP was performed by two methods - oscillometric and auscultatory (according to Korotkov) with an interval of 15 minutes during the day and 30 minutes during sleep. The duration of the monitoring was 24-25 hours.<sup>8</sup> For the analysis of the daily profile of BP, the following groups of indices were used: average values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) for time intervals: 24 hours (SBP<sub>24</sub>, DBP<sub>24</sub>), wakeful period

(SBP<sub>w</sub>, DBP<sub>w</sub>), sleep period (SBP<sub>s</sub>, DBP<sub>s</sub>); "Pressure load" was estimated from the time index (TI) as the percentage of time during which the values of BP were above the threshold values of 140/90mm of mercury column in the afternoon and 120/80mm of mercury column for the night, and an area index (AI) for SBP and DBP. Within 2-4 hours after awakening, the increase in BP was studied in comparison with the night clock - the morning rise in BP (MR BP) for SBP and DBP and speed of the morning rise in BP (SMR). To verify the diagnosis of the ARD, esophagogastroduodenoscopy (EFGDS) was performed using flexible endoscopes (Olympus GIF F apparatus, Japan). The state of the mucous membrane of the esophagus, stomach, duodenum, endoscopic criteria for the stage of DU, as well as the size, localization of the ulcerative defect, and the activity of periulcerous inflammation were assessed. In the process of verifying GERD, according to the clinical and pathogenetic classification of GERD for Ya S Zimmerman,<sup>16</sup> endoscopically positive (reflux-esophagitis) (EP GERD) and isolated endoscopically negative forms of the disease (EN GERD) were isolated. The severity of esophagitis was diagnosed in accordance with the Savary-Miller classification (1977) in the modification of Ivashkin VT, Trukhmanova AS.<sup>7</sup> the presence of complications of GERD, hernia of the esophageal aperture of the diaphragm (GVPD). With EN GERD, fluoroscopy of the esophagus and stomach with barium in the Trendelenburg position was additionally performed. The statistical analysis of the material was carried out using the program STATISTICA 6.0. To describe the obtained data, the mean (M) and standard deviation ( $\sigma$ ) values were used. To select methods of statistical processing of results, the nature of the distribution of characteristics was previously studied. To compare the two independent samples, the non-parametric U method, the Mann-Whitney test, was used to estimate the differences between the two samples in terms of the level of the quantitative trait and to identify differences between small sample sizes. To determine the existence of differences between groups by qualitative characteristics, we used the criterion  $\phi^*$  - angular Fisher transform (Fisher). The correlation analysis was carried out using the rank correlation coefficient  $r_s$  of Spearman. The null hypothesis was rejected with a significance of the level of statistical significance  $p < 0.05$ .<sup>17</sup>

## Results and discussion

One of the stages of our study was a comparative analysis of the mean values of blood pressure, the "pressure load" index, the daily profile of blood pressure, morning dynamics and BP variability in patients with isolated hypertension and with AH and ARD combination. It should be noted that 24 - hour BP monitoring rightfully takes the place of one of the largest achievements in cardiology, closely correlates with target organ damage and has great prognostic significance for the development of cardiovascular complications.<sup>12,13</sup> Our survey made it possible to distinguish specific features of circadian characteristics of blood pressure in patients with association ARD and AH ( $n = 44$ ). It was found that for them, in general, a lower hypertonic load is characteristic in comparison with patients of the isolated AH group ( $n = 25$ ), which was expressed in significantly lower mean values of DBP in daytime and night hours ( $91.68 \pm 6.89$ mm of mercury column compared with  $99.76 \pm 12.27$ mm of mercury column, ( $p = 0.002$ ), and  $82.68 \pm 11.68$ mm of mercury column against  $88.24 \pm 19.51$ mm of mercury column respectively ( $p = 0.004$ ), as well as IV AD and IP AD during all monitoring periods, both for SBP and for DBP. It would seem that a more "mild" course of hypertension and better tolerability of hypertension in patients with a combination of AH and ARD could

be a predictor of lower complications in this category of patients, compared with the group of isolated hypertension. Nevertheless, when performing a comparative analysis of indicators characterizing the circadian rhythm of blood pressure in patients with isolated hypertension and patients with combined pathology, we obtained a statistically significant difference in the rate of SB UAS, which was greater in the group of patients AH + ARD ( $31.16 \pm 33.92$  mm of mercury column / hour vs.  $17.95 \pm 15.66$  mm of mercury column / hour,  $p=0.005$ ). It should be noted that the parameters of the speed of DPP were also significantly higher in the group of combined course of AH and ARD ( $24.92 \pm 25.19$  mm of mercury column / h versus  $13.12 \pm 9.88$  mm of mercury column,  $p=0.048$ ). At the same time, it is now known that the large magnitude and rate of BP rise in the morning are independent risk factors for left ventricular myocardial hypertrophy and may trigger a cascade of adverse cardiovascular events. Moreover, it is believed that patients with excessive blood pressure lowering at night are significantly more likely than in other groups to have ischemic complications that patients with coronary pathology require caution in the use of prolonged antihypertensive drugs due to aggravation of absolute or relative nocturnal hypotension, and, consequently, myocardial ischemia.<sup>14</sup> We also noted that when the combination of hypertension and ARD occurs, the structure of the circadian BP rhythm changes. So, if in patients with isolated hypertension the normal variant - "Dippers" (44%) prevails in the structure of circadian BP, this value was 59% in patients with co morbid course of AH and ARD. The number of individuals with the type of "Over Dippers" was observed in 27% (AH + DU) and 16% (with isolated AH) for SBP, and DBP - 61% versus 24% ( $p=0.002$ ). At the same time, in the group with syntropy, there was a lack of a daily profile of the type "Nightpeakers" for SBP and a reliable increase in the daily profile of "Over Dippers" for DBP (61% versus 24%,  $p=0.002$ ).

It was established that the values of the SMR BP for SBP and DBP were significantly higher in the group of patients with a combination of AH and DU in the exacerbation stage ( $n=8$ ) compared to the group of patients with AH in whom DU was in remission ( $n=13$ ) ( $41.4 \pm 44.16$  mm of mercury column / hour vs.  $13.05 \pm 0.92$  mm of mercury column / h,  $p=0.02$  and  $41.36 \pm 31.14$  mm of mercury column / hour versus  $12 \pm 4.27$  mm of mercury column / hour,  $p=0.0003$ , respectively). The mean values of SBP and DBP at night were significantly lower in the group of patients with AH and DU at the stage of exacerbation ( $n=8$ ) compared with the group of patients with AH and DU in remission ( $n = 13$ ) ( $119.44 \pm 8.01$  mm of mercury column vs.  $128.41 \pm 6.28$  mm of mercury column, ( $p=0.006$ ), and  $73.77 \pm 9.57$  mm of mercury column. Against  $82.33 \pm 7.49$  mm of mercury column. respectively ( $p=0.001$ ). The values of TI and AI of BP during all monitoring periods, both for SBP and for DBP, were also significantly lower in the group of patients with combination of AH and DU of duodenum in the stage of exacerbation ( $p<0.05$ ). We also studied the parameters of during the 24-hour monitoring of BP in patients with associated course of AH and GERD, depending on various clinical endoscopic variants of GERD. It turned out that the SMR of SBP in the group of patients with a combination of AH and EP GERD was significantly higher in comparison with patients who had a combined course of AH and EN GERD ( $53 \pm 0.12$  mm Hg / hour vs.  $47.06 \pm 14.77$  mm Hg / h,  $p=0.027$ ). The presence of EP GERD in patients with AH was characterized by a significant decrease in mean SBP values ( $116.37 \pm 6.16$  mm Hg vs.  $125.6 \pm 10.79$  mm of mercury column,  $p=0.002$ ) and DBP ( $75.12 \pm 11.34$  mm of mercury column

vs.  $85.93 \pm 10.66$  mm of mercury column,  $p=0.033$ ) at night compared with the AH and EN GERD group. The mean daily values of TI DBP and AI DBP during all monitoring periods, as well as TI SBP and AI SBP in day and night in the group of patients with combination of AH and EP GERD were significantly lower in comparison with the group of patients with association of AH and EN GERD ( $p<0.05$ ). Thus, based on the results obtained, it can be concluded that the daily profile of blood pressure in the combination of AH and ARD has its own distinctive features. In patients with this nosological syndrome, there is a significant decrease in the mean values of diastolic blood pressure, BP time indices and BP area indices for both systolic BP and diastolic BP during all monitoring periods. At the same time, the rate of morning rise in systolic and diastolic BP in patients with this comorbidity is significantly higher than in isolated AH. Patients with co morbid course of AH and ARD ( $n=44$ ), in view of their excessive night time BP decrease, as well as a significant increase SMR SBP, have a higher risk of cardiovascular disasters compared with the group of patients with isolated AH ( $n=25$ ). The highest risk of cardiovascular events is to be expected in patients with AH and DU in the acute stage, as well as with association of hypertension and reflux esophagitis. The significant correlation between the parameters of during the 24-hour monitoring of BP and clinico-endoscopic ARD variants is indicated by the effect of the degree of endoscopic changes in the esophagus mucosa and duodenum on the course of hypertension when it is combined with the ARD, which in turn can affect the prognosis of the disease as a whole. Thus, when trying to predict the course of hypertension with its combination with the ARD, it is necessary to rely on the endoscopic picture of the disease, since the severity of endoscopic changes in the mucosa of the esophagogastroduodenal zone correlates with the manifestations of hypertension.<sup>18–19</sup>

## Conclusion

Proceeding from the foregoing, it follows that the association of AH and ARD, taking into account its high prevalence, requires further research to disclose and explain both the pathogenetic features of the course and the methods of optimal drug therapy for this category of patients. Also taking into account the peculiarities of the daily profile of blood pressure in patients with AH associated with ARD in our study, it becomes clear that the management of this category of patients requires a more careful selection of antihypertensive drugs, dose adjustment and dosing regimen should be performed taking into account the degree of endoscopic changes in the mucosa of duodenum and esophagus.

## Acknowledgements

None.

## Conflict of interest

Author declares there is no conflict of interest.

## References

1. Belyalov FI. Twelve co-morbidity theses. *Klin Med (Mosk)*. 2009;87(12):69–71.
2. Krylov AA. To the problem of combining diseases. Krylov AA, editor. *Clinical medicine*. 2000;1:56–68.
3. Kuzmina AYU. The state of the cardiovascular system in the pathology of the upper part of the gastrointestinal tract. In: Kuzmina AYU, editor. *The attending physician*. 2004;4:12–15.

4. Lazebnik LB. Genesis of polymorbidity. In: Lazebnik LB, Drozdov VN, editors. *Clinical gerontology*. Taylor & Francis. 2001;2:3–5.
5. Rebrova OYu. *Statistical analysis of medical data*. Application of application programs STATISTICA. In: Rebrova OYu, editor. Moscow: MediaSfera. 2003. p. 312.
6. Smirnov IuV, Oslopov VN, Bilich IL, et al. The epidemiological aspects of combined arterial hypertension and peptic ulcer. *Ter Arkh*. 1990;62(2):48–50.
7. Ivashkin VT, Mayev IV, Trukhmanov AS, et al. Diagnostics and treatment of gastroesophageal reflux disease: clinical guidelines of the Russian gastroenterological association. *Ross z gastroenterol gepatol koloproktol*. 2017; 27(4):75–95.
8. Lazebnik LB, Masharova AA, Bordin DS, et al. Multicentre study Epidemiology of gastroesophageal reflux disease in Russia (MEGRE): first results. *Eksp Klin Gastroenterol*. 2009;(6):4–12.
9. Golovskoy BV. The state of central vegetative regulation in patients with peptic ulcer. In: Golovskoi BV, Malygina AP, editors. Modern problems of diagnosis and treatment of diseases of the digestive system. *Collection of scientific works*. 1978;17–20.
10. Golovskoy BV. Peripheral autonomic syndromes in gastroenterological diseases. In: Golovskoi BV, Khovaeva YaB, editors. *GastroBulletin*. 2000;1(2):19–4.
11. Kitaeva EA. Heart rate variability in patients with arterial hypertension in combination with acid-dependent diseases. In: Kitaeva EA, et al. editors. *Perm medical journal*. 2010;27(5):26–32.
12. Russian Medical Society for Arterial Hypertension (RIOH), All-Russian Scientific Society of Cardiology (VNOK). Diagnosis and treatment of hypertension. Russian recommendations (the third revision). *Cardiovascular therapy and prevention*. 2008;7(6), 2–32.
13. Kobalava JD. *Monitoring of blood pressure: methodological aspects and clinical significance*. In: Kobalava ZhD, Kotovskaya YuV, editors. 1999. p. 234.
14. Provotorov VM. Features of daily variability of blood pressure and heart rhythm in patients with essential hypertension. In: Provotorov VM, et al. editors. *Herald of arrhythmology*. 2000;3:3–8.
15. Ivanov SYu. *Combined daily monitoring of electrocardiograms and arterial pressure: methodological possibilities and clinical advantages*. In: Ivanov SYu, Kireenkov IS, editors. 2006. p.128.
16. Zimmerman YaS. *Clinical gastroenterology*. In: Zimmermann YaS, editor. Moscow: GEOTAR-Media. 2009. p. 416.
17. Belyalov FI. Twelve co-morbidity theses. *Klin Med (Mosk)*. 2009;87(12):69-71.
18. Tuev AV. Peculiarities of cardiac rhythm variability in patients with associated GERD. In: Tuev AV, et al, editors. *Experimental and Clinical Gastroenterology*. 2016;6(130):9–13.
19. Uspensky YuP. *The problem of combined pathology in the clinic of gastroenterology*. In: Uspensky YuP, editor. *Gastroenterology of St. Petersburg*. 2005;3(4):33–36.