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Clinical significance of 24-hour blood pressure monitoring in patients with ankylosing spondylitis

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The aim of the study was to determine the clinical significance of 24-hour ambulatory blood pressure monitoring (ABPM) in patients with ankylosing spondylitis (AS).

Methods. A cross-sectional, single-center study included 47 men with a confirmed diagnosis of AS, aged 18 to 60 years (mean age 42.51 ± 6.04 years), with a mean disease duration of 17.26 ± 9.03 years. All patients were divided into two groups depending on the presence of hypertension based on office blood pressure (BP) measurement. AS activity was assessed using BASDAI and ASDAS–CRP indices. ABPM was performed in all patients.

Results. Low AS activity was observed in 2 (4.3 %) patients, moderate in 20 (42.6 %), and high in 25 (53.2 %). A normal circadian BP profile ("dipper" type) was found in 16 (34 %) patients, while impaired circadian BP regulation was observed in 31 (66 %). No significant differences were identified between the two groups regarding the prevalence of abnormal BP profiles ($p = 0.547$). The duration of AS was significantly longer in patients with arterial hypertension (AH) (both previously diagnosed and newly detected by ABPM) compared with those without AH according to ABPM data ($p = 0.035$). Masked AH, as revealed by ABPM, was found in 10 (43.5 %) patients from

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the second group; among them, 5 (50%) also had an impaired circadian BP profile.

Conclusion. Arterial hypertension in patients with spondyloarthritis may remain subclinical. Nearly half of the patients who denied having AH were found to have masked hypertension, and half of them exhibited abnormal circadian BP profiles. These findings underscore the necessity of ABPM for the early detection of hypertension in patients with AS.

Keywords: spondyloarthritis, ankylosing spondylitis, arterial hypertension, masked arterial hypertension, circadian blood pressure profile, cardiovascular comorbidity.

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Introduction

Cardiovascular diseases (CVD) have been the leading cause of mortality worldwide for many years [1].

The development of CVD is promoted by risk factors (RF), which are classified into non-modifiable (sex, age, race, genetics, etc.) and modifiable ones (smoking, physical inactivity, arterial hypertension (AH), dyslipidemia, obesity, diabetes mellitus, etc.) [2].

A pooled analysis of data from 112 cohort studies conducted in 34 countries including 1,518,028 participants demonstrated that modifiable RF account for about 50% of CVD burden in the general population. Among them, AH is the most significant [2].

Among patients with rheumatic diseases (RD), CVD also rank first in the structure of mortality, while the risk of their development substantially exceeds that in the general population [3]. This is explained by the higher prevalence of traditional RF as well as factors associated with chronic inflammation itself [4].

According to the largest cross-sectional observational study of comorbidities and RF in patients with spondyloarthritis (SpA) (COMOSPA), cardiovascular RF are highly prevalent in this group, with AH being the most common [5].

Ankylosing spondylitis (AS) is a chronic inflammatory disease from the SpA group, characterized by obligatory involvement of the sacroiliac joints and/or spine, potentially progressing to ankylosis, with frequent involvement of entheses and peripheral joints [6]. The disease mainly affects young, working-age individuals, gradually leading to disability. The development of AH and, consequently, the acceleration of CVD reduce working capacity and significantly impair quality of life in this patient population.

Diagnosis of AH includes office blood pressure (BP) measurement and ambulatory blood pressure monitoring (ABPM).

Depending on the circadian BP profile, patients with AH can be divided into four groups. A normal profile is the "dipper" type, characterized by a 10–20% decrease in nocturnal BP compared with daytime values. Other profiles — non-dipper, night-picker, and over-dipper — are associated with an increased risk of cardiovascular complications [7].

ABPM also allows for the detection of masked hypertension (MH), which is diagnosed in patients with normal BP values measured in a clinical setting but elevated BP outside the clinic. MH was first described more than 20 years ago and immediately became a subject of scientific interest [8]. Over the years, it has been shown that the risk of complications in MH is higher than in normotensive individuals and comparable to the risk of fatal cardiovascular events in manifest AH [9].

In the general population, the prevalence of MH is 8.5–16.6% [10]. In RA it reaches 38.7% [11]. However, no such studies have been conducted in patients with AS, and thus the value of ABPM in this population remains undefined.

The aim of the study was to determine the clinical significance of 24-hour ABPM in patients with ankylosing AS.

Methods

A cross-sectional single-center study included 47 men with a confirmed diagnosis of AS (according to the New York criteria, 1984 [12]) who were treated in the rheumatology department of the Saratov Regional Clinical Hospital. The mean age of patients

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was 42.51 ± 6.04 years, and the mean duration of AS was 17.26 ± 9.03 years. Low AS activity was observed in 2 patients (4.3%), moderate in 20 patients (42.5%), and high in 25 patients (53.2%).

All patients were divided into two groups depending on the presence of AH: Group 1 included patients with established AH (n = 24, 51.1%), and Group 2 included patients in whom hypertension had not been previously diagnosed based on office BP measurement (n = 23, 48.9%). Patients in Group 1 were receiving adequate antihypertensive therapy at a stable dose for at least two weeks, maintaining BP within target values. The groups were comparable in age and AS activity (p > 0.05).

AS activity was assessed using the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and ASDAS–CRP (Ankylosing Spondylitis Disease Activity Score) [12]. ABPM was performed using the BPLab device (LLC "Petr Telegin," Russia).

Exclusion criteria were the presence of other RD besides AS, thyroid dysfunction, previous myocardial infarction or stroke, as well as any comorbid pathology in the acute phase.

The main limitation of the study was the relatively small sample size, which did not allow us to establish associations between AS severity and the frequency of MH, as well as gender differences. The study had no sources of funding.

Statistical analysis

Statistical analysis was performed using StatTech v.4.8.11 software (developer – StatTech LLC, Russia).

Quantitative variables were assessed for normality using the Shapiro–Wilk test.

Quantitative variables with distributions consistent with normality were described using arithmetic means (M) and standard deviations (SD). The boundaries of the 95% confidence interval (95% CI) were provided as a measure of representativeness for mean values.

If the distribution of quantitative variables deviated from normality, the data were described using the median (Me) and lower and upper quartiles (Q1–Q3).

Categorical data were described using absolute values and percentages. The 95% CI for proportions was calculated using the Clopper–Pearson method.

Comparison of two groups for a quantitative variable with normally distributed data and equal variances was performed using Student's t-test; in the case of unequal variances, Welch's t-test was applied.

Comparison of two groups for a quantitative variable with a non-normal distribution was carried out using the Mann–Whitney U-test.

Comparison of proportions in 2×2 contingency tables was performed using Fisher's exact test (when the minimum expected frequency was less than 10). As a quantitative measure of effect when comparing relative indicators, odds ratios (OR) with 95% CI were calculated. In cases of zero cell frequencies in contingency tables, the odds ratio was calculated with the Haldane–Anscombe correction.

Comparison of proportions in multi-way contingency tables was carried out using Pearson's χ^2 test.

Differences were considered statistically significant at p < 0.05.

All participants were thoroughly informed and provided written informed consent. All procedures were approved by the Ethics Committee of Saratov State Medical University named after V.I. Razumovsky, Ministry of Health of Russia.

Results

The characteristics of the examined patients are presented in Table 1. The groups did not differ in terms

Table 1. **Clinical characteristics of patients with AS depending on the presence of AH**

Parameters	Group 1 (AS + AH), n=24	Group 2 (AS with no AH), n=23	p
Age, M (SD)	44.08 (6.68)	40.87 (4.92)	0.068
Disease duration, M (SD)	19.96 (8.93)	14.43 (8.43)	0.035*
CRP, Me [IQR]	7.35 [3.30; 24.50]	15.00 [3.90; 28.65]	0.595
Low activity, abs. (%)	0 (0.0%)	2 (8.7%)	0.310
Moderate activity, abs. (%)	10 (41.7%)	10 (43.5%)	
High activity, abs. (%)	14 (58.3%)	11 (47.8%)	
Continuous NSAID therapy	23 (95.8%)	22 (95.7%)	1.000
DMARD thearapy	10 (43.5%)	10 (41.7%)	1.000
Biologic agents therapy	9 (37.5%)	4 (17.4%)	0.193
GC use	18 (75%)	13 (56.5%)	0.227

Note. * — the differences are statistically significant (p<0.05)

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Table 2. **ABPM parameters in patients with AS depending on the initial presence of AH**

Parameters	Group 1 (AS + AH), n=24	Group 2 (AS with no AH), n=23	p
Mean daytime SBP, M (SD), mmHg	133.96 (12.50)	125.74 (15.17)	0.048*
Mean daytime DBP, M (SD), mmHg	85.67 (8.11)	84.78 (11.18)	0.759
Mean nighttime SBP, M (SD), mmHg	125.33 (17.86)	113.30 (16.86)	0.022*
Mean nighttime DBP, M (SD), mmHg	78.21 (12.07)	75.52 (10.89)	0.428
Impaired circadian BP profile	17 (70.8%)	14 (60.9%)	0.547
Mean heart rate, M (SD), bpm	72.79 (11.60)	71.91 (10.06)	0.783

Note. * — the differences are statistically significant ($p<0.05$)

of age or AS activity; however, patients in Group 1 had a longer disease duration ($p < 0.035$).

No significant differences were found between the groups in terms of C-reactive protein (CRP) levels or AS activity. The number of patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs) on a regular basis, as well as those on disease-modifying antirheumatic drugs (DMARDs) or biologic agents, also did not differ significantly between the groups.

The results of ambulatory blood pressure monitoring (ABPM) in the examined patients are presented in Table 2.

According to ABPM, a normal circadian BP profile ("dipper" type) was identified in 16 patients (34%), while an abnormal circadian BP profile was observed in 31 patients (66%). Among these, the "non-dipper" profile was found in 22 patients (71%), the "over-dipper" profile in 3 patients (9.7%), and the "night-picker" profile in 6 patients (19.3%). There were no significant differences between the two groups in the frequency of abnormal circadian BP profiles ($p = 0.547$).

Mean systolic BP (SBP) was significantly higher in Group 1 during both daytime ($p = 0.048$) and nighttime ($p = 0.022$). No significant differences between the groups were observed in mean diastolic BP (DBP), either during the day ($p = 0.759$) or at night ($p = 0.428$).

MH according to ABPM data was detected in 10 patients (43.5%) in Group 2, of whom 5 patients (50%) had an abnormal circadian BP profile.

Discussion

The increased prevalence of CVDs in patients with RDs may be explained by a combination of traditional RFs with inflammation, oxidative stress, and the use of DMARDs, biologic agents, glucocorticoids (GCs), and NSAIDs [4, 13].

In the search for an association between CRP levels and the development of AH, a cohort of 20,525 female health professionals in the United States aged over 45 years with normotension at baseline was followed for a mean of 7.8 years, with incident hypertension cases recorded. In adjusted models, an increase in baseline CRP by 1 SD was associated with an adjusted relative risk of developing AH of 1.14, suggesting that enhanced inflammation clearly preceded the clinical manifestation of elevated blood pressure [14]. The fact that AH appears to be associated with autoimmune inflammation underscores the need to investigate its coexistence with various RDs.

In the present study, it was found that patients with longer disease duration of AS more frequently had AH, while nearly every second patient with AS who denied having hypertension was found to have MH. This likely makes a significant contribution to the increased incidence of CVD in this patient population.

The prevalence of MH in AS is considerably higher than in the general population and higher than in patients with rheumatoid arthritis (Table 3).

Table 3. **Frequency of MH in different population groups**

Group	Frequency of MH
General population, n=7700	8.5–16.6%
Patients with RA, n=31	38.7%
Patients with AS, n=23	43.5%

Thus, there is a strong tendency toward studying the BP profile in patients with RDs, and the results obtained highlight the problem of underdiagnosis of AH as one of the key contributors to the elevated CVD risk in this nosological group.

It is noteworthy that AH is a modifiable RF and therefore may serve as a successful target for interventions aimed at preventing CVD and mortality. Consequently, performing ABPM in patients with AS is essential for the timely detection and management of AH.

Conclusion

SpA are a group of diseases with a proven cardiovascular risk. AH in patients with AS may remain subclinical. Almost half of the patients who denied having AH were found to have MH, and among them, half had an abnormal circadian blood pressure profile. This highlights the necessity of ABPM for the early detection of hypertension in patients with AS, since timely diagnosis will allow optimization of therapy and thereby delay the development of CVD in this population.

Further studies are needed to clarify the role of MH in cardiovascular risk stratification not only in patients with AS but also in those with other RDs.

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