ISSN 1607-419X
ISSN 2411-8524 (Online)
УДК 616.12-008.331-073.7

Hypertension — a significant risk factor for recurrent stroke in patients with atrial fibrillation

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Received 11 August 2015;
accepted 26 January 2016.

Abstract

Objective. The purpose of research was to study the indicators of daily monitoring of blood pressure (ABPM) in post-stroke patients with atrial fibrillation (AF) and their relationship to mortality. **Design and methods.** We included 350 stroke survivors with non-valvular AF. The patients were divided into 3 groups according to the stroke severity assessed by NIHSS (National Institutes of Health Stroke Scale). All patients underwent ABPM at baseline, at 3-and 6-month follow-up. **Results.** By the time of stroke onset, 72% of patients have already had AF, in 28% patient AF was newly verified. Systolic (SBP) and diastolic blood pressure (DBP) was significantly ($p < 0.05$) higher in patients with paroxysmal AF ($n = 109$), they had significantly ($p < 0.05$) lower degree of blood pressure (BP) decrease at baseline, 3 and 6 months. At 6 months, the group of patients with paroxysmal AF included 96 people, 13 patients (3.7%) died: 4 (2.6%) in group I; 3 (2.5%) — in group II, and 6 (7.7%) in group III. In the subgroup of died patients, there was a significant correlation ($r = 0.56$, $p < 0.05$) between insufficient nocturnal BP decline and the incidence of paroxysmal AF. **Conclusions.** Our findings suggest an independent contribution of the abnormal daily BP profile to the increased frequency of night AF episodes and its association with high mortality in post-stroke patients.

Key words: hypertension, atrial fibrillation, cardioembolic stroke

For citation: Davydkin IL, Zolotovskaya IA. Arterial hypertension — a significant risk factor for recurrent stroke in patients with atrial fibrillation. Arterial'naya Gipertenziya = Arterial Hypertension. 2016;22(1):32–40. ***doi: 10.18705/1607-419X-2016-22-1-32-40.***

Прогностическое значение суточного мониторирования артериального давления у пациентов с фибрилляцией предсердий, перенесших кардиоэмболический инсульт

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Статья поступила в редакцию 11.08.15 и принята к печати 26.01.16.

Резюме

Цель исследования — изучение показателей суточного мониторирования артериального давления (СМАД) у пациентов с фибрилляцией предсердий (ФП), перенесших инсульт, и оценка взаимосвязи с показателями смертности. **Материалы и методы.** В исследование включено 350 больных с ФП неклапанного генеза, перенесших инсульт. Пациенты разделены на 3 группы в соответствии с показателями критерия тяжести инсульта по шкале оценки степени выраженности неврологической симптоматики (National Institutes of Health Stroke Scale, NIHSS). СМАД проводилось трижды: на момент включения, через 3 и через 6 месяцев. **Результаты.** В остром периоде инсульта у 72% больных диагноз ФП имел место в анамнезе, у 28% — был верифицирован впервые. У всех пациентов с пароксизмальной ФП (n = 109) показатели систолического (САД) и диастолического артериального давления (ДАД) были существенно выше ($p < 0,05$), чем в целом по группе; отмечена более низкая степень снижения артериального давления исходно ($p < 0,05$), через 3 и 6 месяцев на фоне антигипертензивной коррекции лекарственными средствами. За 6 месяцев группа пациентов с пароксизмальной ФП составила 96 человек, умерло 13 больных (3,7%): в группе I — 4 (2,6%); в группе II — 3 (2,5%); в группе III — 6 (7,7%). Анализ показателей СМАД группы умерших больных выявил значимую корреляцию ($r = 0,56$, $p < 0,05$) между недостаточным уровнем ночного снижения САД и ДАД и частотой развития пароксизмов у пациентов с ФП. **Выводы.** Полученные данные свидетельствуют о существенном самостоятельном вкладе неблагоприятного суточного профиля АД в увеличение частоты ночных эпизодов ФП и его тесной взаимосвязи с высоким уровнем смертности у пациентов с ФП, перенесших мозговой инсульт.

Ключевые слова: артериальная гипертензия, фибрилляция предсердий, кардиоэмболический инсульт

Для цитирования: Давыдкин И.Л., Золотовская И.А. Прогностическое значение суточного мониторирования артериального давления у пациентов с фибрилляцией предсердий, перенесших кардиоэмболический инсульт. Артериальная гипертензия. 2016;22 (1):32–40. ***doi: 10.18705/1607-419X-2016-22-1-32-40.***

Introduction

Arterial hypertension (HTN) is associated with the high cardiovascular risk and is the main risk factor of an acute cerebrovascular accident (ACVA). High stroke morbidity and mortality is not only a health care issue, it also implies notable social and economic losses for the society. Currently, effective medical technologies for the reduction of stroke mortality including repeated stroke are highly required. Target organ damage (heart, kidneys, brain) in HTN leads to the enhancement of functional insufficiency, decompensation and possible development of an acute cardiovascular event. HTN is shown to contribute to the development of the cardioembolic ischemic stroke (CS) in patients with nonvalvular atrial fibrillation (AF) [1]. A number of studies demonstrated that HTN combined with AF leads to the increased risk of thrombus formation in the left atrial appendage, often causing strokes, especially in elderly persons [2]. In post-stroke patients with AF, HTN is a contributing factor for both the neurologic aggravation and recurrent stroke. According to 2013 ESH/ESC Guidelines for the management of HTN there is a robust relationship between HTN, adequate antihypertensive therapy and AF [3]. HTN control should be considered as one of the main approaches for the cardioembolic stroke prevention in patients with AF. It should also be noted that HTN is an independent risk factor of both AF onset and induction of more frequent AF paroxysms.

The most important novel approaches to prevent the first and recurrent ACVA is antihypertensive medication treatment in patients with persistent and paroxysmal forms of AF in clinical practice. This issue should be considered with regard to the possible elimination of the adverse impact of elevated blood pressure (BP) as the most adverse factor in relation to both AF progression and increased risk of acute thromboembolic events. The relationship between ACVA development, BP changes over time, and relapses of AF attacks has been insufficiently studied so far. AF is an independent risk factor of ischemic stroke development since it increases the likelihood of stroke in patients with AF compared to the subjects without AF. This was demonstrated in large-scale epidemiologic studies [4, 5].

Direct association between AF incidence and the age is found in the population studies [6]. The results of the previous studies showed that advanced age, male gender, HTN, coronary heart disease, heart failure, obstructive sleep apnea as well as increased body mass index, and smoking are the main risk factors of AF development [7, 8]. Structural, morphological and functional changes in the myocardium in AF were described, especially changes related to fibrosis and apoptosis of atrial myocytes [9]. Electron microscopy showed mitochondrial changes, glycogen accumulation, deficiency of myofibrils, nuclear chromatin redistribution, and reduction of the sarcoplasmic reticulum in the structures of myocardiocytes with the increasing duration of AF history [10]; i. e., there is a morphologic substrate promoting AF "maintenance"; therefore, the likelihood of the repeated cerebral accident in post-stroke patients is extremely high.

For the better understanding of cerebrovascular diseases, investigation of the mechanisms leading to stroke development as well as studies aimed at the discovery of clinical and laboratory syndromes with prognostic value regarding possible secondary stroke prevention. Further studies of the relationships between the risk factors of acute cerebrovascular events and their possible correction are required. Adequate follow-up is a necessary mechanism for the stabilization of cerebral hemodynamics, especially in early rehabilitation period when compensation of the neurological impairment can be achieved. Regulation of BP level can lead to the reduction of one of the key stroke risk factors. In addition, it is the way to reduce mortality due to the high risk of recurrent ACVA in hypertensive patients with AF.

Objective of the study is to analyze the indices of the daily BP monitoring (DBPM) in patients with AF and history of CS and to assess their association with mortality rates.

Design and methods

Altogether 350 patients (227 females and 123 males) with nonvalvular AF who suffered CS in the carotid system were enrolled in the study not later than 20 days after the discharge from a primary or regional vascular center. In all patients HTN duration was 11.9 (7.3, 15.4) years. The age of the patients was 65.5 (62.0, 73.0) years old.

In addition, 336 patients (96%) had comorbidities: 184 (54.8%) — diabetes mellitus, 23 (6.8%) — rheumatoid arthritis, 55 (16.4%) — chronic kidney disease, 74 (22.0%) — coronary heart disease. Exclusion criteria were the following: age under 45 years old, valvular AF, oncological diseases, rheumatic heart diseases, severe comorbidity — class III–IV chronic heart failure, grade 2–3 chronic respiratory insufficiency, stage 4–5 chronic kidney disease, thyroid disorders. Patients were enrolled when written consent was obtained.

The patients were divided into 3 groups according to the criteria of stroke severity (assessment according to the National Institutes of Health Stroke Scale, NIHSS) at discharge after specialized care was provided: 0–6 points — group I (n = 153, 43.7%); 7–12 points — group II (n = 119, 34.0%); more than 13 points — group III (n = 78, 22.3%). The scale enables to carry out an unbiased assessment of the results of diagnostic and treatment measures in acute stroke, and it is also a very accurate and prognostically valuable tool for both practical and research purposes.

All patients underwent a complex clinical and instrumental examination at the beginning of monitoring (V1) and after 3 (V2) and 6 (V3) months of monitoring. For objective assessment of changes in neurological status and functional disorders, and the efficiency of rehabilitation measures, the Rankin scale and the Barthel index were used. Cognitive functions were assessed using the Mini-Mental State Examination (MMSE). HTN type, time of onset, duration, and 24-hour variation were assessed using the DBPM with a preliminary series of control measurements (device Corol (x)plore, Meditech LTD, Hungary). For accuracy check, each patient underwent a series of consecutive BP measurements in automatic mode at 15-minute intervals in the waking hours and 30-minute intervals at the nighttime. According to the results of office BP monitoring, systolic BP (SBP) ≥ 140 mm Hg and diastolic BP (DBP) ≥ 90 mm Hg were considered as threshold values. The following parameters of the DBPM were assessed: average daily SBP and DBP, SBP and DBP variability (SBPV and DBPV). The levels of 140/90 mm Hg in the daytime and 130/80 mm Hg in the nighttime were considered as threshold BP levels. For the circadian rhythm assessment, daily index of SBP and DBP was used. It reflects the nocturnal BP fall in relation to the daytime BP: velocity of the morning BP surge, degree of nocturnal BP fall. According to the degree of nocturnal SBP and DBP fall, the following groups were formed: 1) "dippers" — subjects with the nocturnal BP fall of 10–20% (normal); 2) "non-dippers" — subjects with the variations in the daily BP profile of less than 10%, 3) "over-dippers" — subjects with the degree of nocturnal BP fall of more than 20%, and 4) "night-peakers" — subjects with the nocturnal BP rise (< 0%).

During the entire follow-up patients or people submitting information about the patients kept diaries of well-being assessment, BP and pulse self-control. In patients with paroxysmal AF, in self-control diaries the frequency and duration of AF paroxysms were registered separately. The paroxysmal form of AF was diagnosed if the following criteria were met:

• AF terminated spontaneously or after an intervention and lasted ≤ 7 days from the onset;

• episodes repeated with various frequency.

The obtained data were processed using the standard program Microsoft Excel and statistical program package Statistica for Windows 6.0.

Table 1

DISTRIBUTION OF THE PATIENTS WITH ATRIAL FIBRILLATION DEPENDING ON THE DURATION OF DIAGNOSED ATRIAL FIBRILLATION

AF diagnosis	Groups of patients						Total	
	I (n = 153)		II (n = 119)		III (n = 78)			
	n	%	n	%	n	%	n	%
Before CS	122	34.8	93	26.6	37	10.6	252	72.0
In acute CS	31	8.9	26	7.4	41	11.7	98	28.0
Total	153	43.7	119	34.0	78	22.3	350	100.0

Note: AF — atrial fibrillation; CS — cardioembolic stroke.

The values of quantitative parameters with normal distribution are given as median and root mean square deviation (M ± SD). For the analysis, descriptive statistics was used with the parametric test (Student t-test) implementation. Description of the parameters with distribution differing from the normal one is given as Me [Q25; Q75] where Me is median, Q25 and Q75 are the 25th and 75th quartiles, respectively. For group comparison, methods of nonparametric statistics were used — Mann–Whitney rank test for related groups and Wilcoxon test for unrelated groups. For the analysis of the relationship between the quantitative parameters, Spearman's rank correlation coefficient (R) was used. Differences between the studied parameters were considered statistically significant at p-level < 0.05.

Results

In 252 subjects (72.0%) enrolled in the study the duration of AF was 1–10 years. In the total group the duration of AF was 51.3 (38.7, 68.4) months. In 28.0% AF was diagnosed for the first time in the acute period of ACVA (Table 1). Distribution of the patients with AF by groups, according to the duration of AF was diagnosed is presented.

Interestingly, in group III (patients with severe neurological impairment) AF was undiagnosed earlier in 41 patients (almost 11,7% of all examined subjects and more than 52.6% of patients in group III), whereas in group I the rate was much lower — 31 patients (more than 8.9% of all examined subjects and more than 20.3% in group I).

Only 72% of patients with verified AF diagnosis were admitted to the hospital, and in 28% of all patients AF was diagnosed for the first time in the acute period of stroke (Table 1). A considerable number of patients showed marked neurological impairment: 16.3 ± 1.9 points according to NIHSS at admission, and 14.3 ± 1.5 points at discharge. Paroxysmal AF was diagnosed in 109 (31.1%) of patients, all the cases were diagnosed for the first time at admission or during hospital admission by an ambulance team. The maximum number of paroxysmal AF cases occurred in group III (41.0%); in groups I and II (patients with less severe neurological impairment) the proportion of such patients was notably lower — 32.0 and 23.5%, respectively (Table 2).

Reaching target BP levels in patients with the history of ACVA is a controversial issue, that is

Table 2

DISTRIBUTION OF THE PATIENTS ACCORDING TO THE ATRIAL FIBRILLATION TYPE

AF	Groups of patients						Total	
	I (n = 153)		II (n = 119)		III (n = 78)			
	n	%	n	%	n	%	n	%
Permanent	104	29.7	91	26.0	46	13.2	241	68.9
Paroxysmal	49	14.0	28	8.0	32	9.1	109	31.1
Total	153	43.7	119	34.0	78	22.3	350	100.0

Note: AF — atrial fibrillation.

Table 3

DISTRIBUTION OF THE PATIENTS ACCORDING TO THEIR BLOOD PRESSURE LEVEL AT BASELINE

BP, mm Hg	Groups of patients						Total	
	I (n = 153)		II (n = 119)		III (n = 78)			
	n	%	n	%	n	%	n	%
SBP ≤ 130 mm Hg	26	7.4	22	6.3	9	2.6	37	10.6
SBP 131–145 mm Hg	51	14.6	29	8.3	12	3.4	42	12.0
SBP > 145 mm Hg	76	21.7	68	19.4	57	16.3	201	57.4
Total	153	43.7	119	34.0	78	22.3	350	100.0

Note: BP – blood pressure; SBP — systolic blood pressure.

Table 4

PARAMETERS OF 24-HOUR BLOOD PRESSURE MONITORING (M ± m)

BP parameter	V_1	V_2	V_3
SBP, mm Hg			
24-hour	162.8 ± 12.8	146.9 ± 13.7*	136.4 ± 12.4**
Daytime	164.1 ± 13.1	149.1 ± 11.8*	139.9 ± 12.8**
Nighttime	156.8 ± 15.2	143.9 ± 14.5*	129.4 ± 13.1**
DBP, mm Hg			
24-hour	101.8 ± 4.2	97.5 ± 8.3*	88.9 ± 6.4**
Daytime	102.7 ± 5.3	99.3 ± 5.1*	90.4 ± 6.7**
Nighttime	99.4 ± 7.6	92.1 ± 6.3*	87.2 ± 7.4*†
NF SBP, %	3.7 ± 9.8	4.5 ± 6.1	7.8 ± 5.1
NF DBP, %	5.5 ± 8.6	7.1 ± 4.3	9.9 ± 7.8
SBP variability, day	17.8 ± 5.9	15.8 ± 4.3	13.0 ± 5.1*†
SBP variability, night	15.5 ± 3.8	14.0 ± 5.7	12.7 ± 6.3*†
DBP variability, day	14.1 ± 3.2	12.0 ± 3.4*	10.2 ± 4.5*†
DBP variability, night	13.3 ± 3.8	12.2 ± 2.8*	9.2 ± 2.7*†

Note: V_1 visit 1; V_2 — visit 2 after 3 month; V_3 — visit 3 after 6 month; BP – blood pressure; SBP — systolic blood pressure; DBP — diastolic blood pressure; NF — nocturnal fall; * — $p < 0.05$; ** — $p < 0.01$; † — $p < 0.05$ compared after 3 months.

also evidenced in 2013 ESH/ESC Guidelines for the management of arterial hypertension. In our study, follow-up during the early rehabilitation period after the stroke was carried out in the patients with central hemodynamic instability. It had an additional unfavourable effect in addition to the heart rhythm disturbances. At the present time there are certain difficulties in the interpretation of both office and home BP measurements in patients with AF mainly due to high variability level of SBP and DBP during repeated control measurements and simultaneous measurements in both upper extremities. At the beginning of the study we divided the patients according to their SBP level in order to reveal subjects with a good response to the antihypertensive therapy, including the period of in-patient care. Baseline BP readings are shown in Table 3. It turned out that, at the time of enrollment, in the majority of patients (57.4%) the office SBP level was over 145 mm Hg. We believe that this fact cannot be interpreted only as the poor level of HTN control, since all the patients received antihypertensive medication with the regular drug dose control. We suggest that the cerebral blood flow decompensation causes substantial BP variability both in the acute phase and in the early rehabilitation period. During the first 12 weeks continuous BP monitoring and BP diaries fare required in order to timely adjust antihypertensive therapy. Physicians responsible for the management of the patient with AF and the history of ACVA should pay attention to this fact.

Table 4 shows the dynamic of the DMBP parameters over a period of 6 months. At enrollment (V1) average SBP level was 162.8 ± 12.8 mm Hg, DBP level — 101.8 ± 4.2 mm Hg, and nocturnal fall (NF) of BP was extremely low which can be considered as one of unfavorable prognostic parameters. Significant decrease of the following parameters is found: average daily, average daytime SBP and DBP after 3 months ($p < 0.01$ and $p < 0.001$ respectively). After 6 months of follow-up, the decrease of average daily SBP and average daily DBP occurred. It evidenced the efficiency of rehabilitation measures in general, including antihypertensive therapy.

The analysis of BP effect in patients with paroxysmal AF and BP impact on the frequency of BP paroxysms was carried out. The BP parameters in patients with paroxysmal AF (109, 103 and 96 patients, respectively) were analyzed including patients who died during the follow-up period. Among the patients with AF, in each group SBP and DBP were significantly higher ($p < 0.05$) than in the group in general; BP

Table 5

PARAMETERS OF THE 24-HOUR BLOOD PRESSURE MONITORING IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION (M ± m)

BP, mm Hg	Groups of patients (n = 109/103/96)								
	I group (n = 49/47/45)			II group (n = 28/28/25)			III group (n = 32/28/26)		
	V_1	V_2	V_3	V_1	V_2	V_3	V_1	V_2	V_3
SBP, 24h	168.8 ± 10.1	156.7 ± 9.2*	145.3 ± 8.5*	174.1 ± 11.3	155.8 ± 10.6*	146.1 ± 7.2*	175.3 ± 9.7	156.4 ± 8.3*	148.7 ± 9.3*
SBP, day	172.1 ± 12.4	157.1 ± 9.8	147.2 ± 8.1	174.9 ± 13.1	156.9 ± 9.9*	151.8 ± 9.5*	176.5 ± 11.2	157.3 ± 8.4*	150.6 ± 11.3*
SBP, night	159.8 ± 12.3	149.9 ± 11.5*	144.4 ± 10.7**†	169.1 ± 10.5	147.1 ± 8.5*	145.2 ± 10.3**†	172.6 ± 9.4	153.7 ± 9.5*	146.6 ± 8.4**†
DBP, 24h	101.8 ± 4.1	99.4 ± 6.2*	94.1 ± 7.4*	102.3 ± 5.7	100.1 ± 5.3*	94.8 ± 7.2*	103.3 ± 6.1	101.8 ± 7.2*	95.7 ± 8.7**†
DBP, day	102.9 ± 5.8	99.8 ± 5.3*	95.2 ± 4.8*	103.8 ± 4.4	100.8 ± 8.2*	95.2 ± 3.7*	103.8 ± 6.4	102.4 ± 8.5*	96.4 ± 7.6*
DBP, night	99.9 ± 7.8	96.1 ± 5.7**	92.7 ± 6.3**	101.2 ± 8.3	96.1 ± 5.1**	90.8 ± 5.1**	100.9 ± 7.4	97.3 ± 7.8**	91.9 ± 6.6*†
NF SBP, %	3.6 ± 8.7	3.9 ± 2.8	4.8 ± 2.2*	2.9 ± 7.5	3.1 ± 2.9	4.9 ± 3.2*	2.4 ± 8.1	2.8 ± 1.9	3.8 ± 3.1*
NF DBP, %	5.5 ± 7.1	6.0 ± 4.9	6.2 ± 4.9*	5.1 ± 6.8	6.2 ± 3.7	7.0 ± 5.4*	5.0 ± 4.2	6.1 ± 3.1	6.8 ± 4.3*
SBP variability, day	19.3 ± 4.3	17.5 ± 4.5	16.9 ± 3.5	20.1 ± 4.1	16.2 ± 4.2	14.3 ± 4.2*†	20.7 ± 4.6	17.3 ± 4.1	14.6 ± 4.1*†
SBP variability, night	16.8 ± 4.2	16.0 ± 4.6	16.7 ± 5.1*	18.2 ± 4.0	16.4 ± 4.6*	15.3 ± 4.4*†	18.5 ± 4.2	17.8 ± 4.1	15.1 ± 4.1*†
DBP variability, day	15.5 ± 4.1	14.0 ± 3.4	14.8 ± 4.5*	14.6 ± 4.5	13.5 ± 3.9	12.6 ± 4.7*†	15.3 ± 4.1	14.7 ± 3.4	13.1 ± 3.3*†
DBP variability, night	14.2 ± 3.7	13.7 ± 2.1*	11.4 ± 2.8*	15.1 ± 4.8	14.2 ± 3.1*	12.1 ± 3.4*†	16.2 ± 3.8	15.1 ± 3.2*	13.1 ± 3.7*†

Note: BP — blood pressure; SBP — systolic blood pressure; DBP — diastolic blood pressure; NF — nocturnal fall; * — p < 0.05; ** — p < 0.01; † — p < 0.05 compared after 6 months.

fall ($p < 0.05$) was lower bot at baseline and after 3 ($p = 0.002$) and 6 months ($p = 0.025$), respectively (Table 5).

In group III, a strong relationship between the severity of neurological impairment and unfavourable BP parameters was found ($r = 0.56$, $p < 0.05$) and, first of all, of SBP and DBP NF as well as between the incapacity to reach the target average daily BP both at baseline and at 3-months follow-up. In this group at the end of 6 months more patients died ($p = 0.025$) than in the other groups: I — 4 (2.6 %); II — 5 (4.2 %); III — 8 (10.3 %). Listing the data on all patients who died due to the acute cardiovascular events (myocardial infarction and recurrent CS) is reasonable. During 6 months of follow-up, 17 (4.9 %) patients died: 6 patients in the first 3 months and 11 patients in the 4th–6th months. 13 patients with paroxysmal AF died (3.7 %): in group I — 4 (2.6 %); in group II — 3 (2.5 %); in group III — 6 (7.7 %). The average age of the dead patients was 74.3 ± 1.34 years, in all cases AF was diagnosed during the acute CS period and paroxysmal AF was verified (group I — 2 patients, group III — 4 patients). In all patients severe comorbidities were found — diabetes mellitus or chronic kidney disease, all patients passed away in an inpatient facility. The interval between the first CS and recurrent acute cardiovascular event was 37 ± 4.6 days. Retrospective analysis of the DBPM and electrocardiogram readings obtained at baseline was carried out. The analysis of the circadian profile of SBP and DBP NF showed that the patients with the abnormal parameters of SBP (88.2 %) and DBP (82.4 %)

prevailed at baseline; "dippers" constituted 11.8% (SBP) and 17.6% (DBP), respectively. A correlation ($r = 0.56$, $p < 0.05$) between the insufficient SBP and DBP nocturnal fall and the frequency of AF paroxysm was found in patients with AF who died within 6 months after enrollment. Obviously, no direct conclusions can be made because of the small sample size but the obtained data evidence that the disturbances of the BP daily profile in patients with AF and history of stroke are associated with the increased risk of mortality due to repeated acute thrombovascular events in the early rehabilitation period.

Significant changes in the BP daily profile with the predominance of insufficient nocturnal BP fall at baseline and at 3-months follow-up were found in all groups of patients, but especially in group III (patients with a severe neurological impairment, the Barthel index 20.5 ± 4.5 points). It should be noted that in this group marked motor and aphasic disturbances occurred and were determined by the localization and volume of the brain lesion which substantially restricted the scope of rehabilitation measures and decreased the level of therapy compliance.

Discussion

In our study all the patients had diagnosed HTN, and all of them took antihypertensive therapy. Doubtless, pharmacological BP control is an integral part of the management of a patient with AF, since HTN is a factor with a direct influence on the probability of AF development in more than 14% of cases [11]. Obviously, if BP control is insufficient, the structural changes in the myocardium become more and more dramatic, promoting AF and causing thromboembolic complications. Patients with AF already have changes in the myocardial structure due to atrial fibrosis and increased fibroblast number that leads to the impairment of conduction processes with the formation of secondary excitation foci due to the changes in electrophysiological characteristics of cardiomyocytes [12, 13]. Moreover, even in patients with paroxysmal AF without any intravital diagnosis of certain myocardial changes, the atrial biopsy demonstrated inflammatory infiltrates indi cative of myocarditis and fibrosis [14]. It means that patients with the paroxysmal form of the AF, especially in combination with the unfavorable BP profile, have a high risk of thrombosis, first of all CS. Current data evidence that the severity of structural changes and, in particular, atrial fibrosis correlates with the risk of stroke [15].

Our findings show that in general group and in the group of subjects with paroxysmal AF, a significant number of patients had abnormal circadian rhythm, despite antihypertensive therapy. For instance, among the patients with paroxysmal AF, the number of "non-dippers", "over-dippers" and "night-peakers" was significantly higher ($p < 0.05$) than the proportion of patients with normal daily BP profile. This trend was obvious among those patients who died: at baseline (20 days after CS) 88.2 and 82.4% had insufficient nocturnal fall of SBP and DBP, respectively. Moreover, correlation ($r = 0.56$ $p < 0.05$) between the insufficient SBP and DBP nocturnal fall and the frequency of AF paroxysm was found. In group III, the patients with the low level of compliance to the rehabilitation procedures was due to the severity of the neurological impairment with aphasic and cognitive disturbances, the mortality rate was notably higher at the end of 6 months than in the other groups. BP profile, from our point of view, should be carefully investigated, as it would help to answer a number of questions and to define the opportunity to minimize thromboembolic complications in post-stroke patients with AF, and to reduce their mortality rate.

Potential limitations

We admit that our study has a number of limitations, first of all the absence of a comparison group as well as the open design of the study. In addition, taking into account the small sample size, we could not conduct a multivariate analysis. However, we believe that our results are still important, as it is necessary to define the contribution of HTN in evolution of the cardiovascular continuum in patients with AF and the history of stroke. Further studies in a larger cohort might allow to develop the prognostic tools to foresee recurrent cardiovascular accidents applicable in the routine clinical practice, as well as to determine significant relationships between AF and HTN and the risk of recurrent thromboembolic events.

Conclusions

Currently available data evidence that HTN may be an independent risk factor of recurrent

acute thromboembolic events in patients with AF. Further, in the majority of studies, the issues of primary prevention are considered, whereas the risk of mortality and development of a repeated ACVA in patients with AF and the history of CS and HTN is extremely high. At the moment, accumulated data provide insight into the role of the daily BP profile and its variability as an extremely important element of the heart remodeling and AF progression. The information we obtained also gives evidence of the substantial contribution of the unfavorable daily BP profile to the increase in frequency of AF nocturnal episodes and its association with the high mortality rate in patients with a history of cerebral stroke. In our opinion, the study can help to determine the predictors of recurrent stroke and mortality in patients with AF depending on their BP profile.

Financial support

The study was not sponsored. Authors are fully responsible for the publication. All authors took part in the development of study design and paper writing. Final version of the manuscript was approved by all authors.

Conflict of interest

The authors declare no conflict of interest.

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