Original Article

Clinical laboratory and instrumental peculiarities of atrial fibrillation in obese patients

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Abstract

Considering the conflicting results, which on the one hand revealed an increase in the relapse rates and severity of atrial fibrillation (AF) symptoms in obese patients and on the other hand revealed the reduced mortality risk and cardiovascular events compared to patients with normal body weight and AF, the problem of studying AF peculiarities in obese patients remains relevant. Based on the Federal State Budget Educational Institution of Higher Education "North State Medical University" of the Ministry of Healthcare of the Russian Federation, Arkhangelsk, the research involving 220 patients with AF and AH was carried out. Inclusion criteria were the newly diagnosed AF form and arterial hypertension in past medical history and at the time of inclusion in the study. The aim of the research was to identify AF peculiarities in overweight and obese patients. BMI was calculated, leptin blood concentration was determined, ECHO was made, and AF paroxysms were detected again by means of ECG. The study showed that patients with AF in obese groups had enlarged left ventricular and left atrium and higher incidence of left ventricular hypertrophy than that of the group with normal body weight. The increase in body weight is associated with an increase in the incidence of AF paroxysm relapses. Leptin concentration is significantly higher in the group of patients with paroxysm relapses. Findings: Obesity causes myocardial remodeling progression and an increase in AF paroxysm relapses. Leptin blood concentration is higher in patients with AF paroxysm relapses.

Keywords: Atrial fibrillation, structural cardiovascular system indicators, obesity, paroxysm, leptin

Introduction

Atrial fibrillation (AF) is a heart rhythm disorder with a high prevalence rate and high risk of thromboembolic events [1, 2].

Arterial hypertension (AH) and obesity significantly increase AF risks and its progression [3-5].

Obesity is a major problem in the modern world and its incidence is high among the population [6, 7]. Adipose tissue acts as a secretory organ capable to produce biologically active substances - adipokines influencing cardiac remodeling processes [8].

Few studies have been carried out to show that excess body weight and obesity predispose to repeated paroxysmal events and raise the symptom class [9, 10] but data have been published describing better survival rate and lower cardiovascular event rate in patients with AF having a history of obesity [11, 12].

The study was carried out at the Department of Polyclinic Therapy and Nursing of the Federal State Budget Educational Institution of Higher Education “Northern State Medical University” of the Ministry of Healthcare of the Russian Federation, Arkhangelsk

The aim of the study was to identify the features of AF in patients with overweight and obesity.

Materials and Methods

Patients from 7 Arkhangelsk prevention and treatment facilities were examined in the period between January 2014 and December 2016. 220 patients took part in the study. Inclusion criteria: 1) the first AF event was traced in electrocardiogram not earlier than 1 year before the study entry, 2) 1st - 3rd degree AH in the history and at the moment of inclusion.

Exclusion criteria: 1) the patient was under the age of 18, 2) permanent AF, 3) valvular heart disease (rheumatic disease,

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How to cite this article: Ryabaya I.N. Clinical laboratory and instrumental peculiarities of atrial fibrillation in obese patients. Arch Pharma Pract 2020;11(2):1-6.

as well as hemodynamically significant atherosclerotic valvular disease), hyperthyroidism, and WPW syndrome.

Initial examination of patients was carried out, AF history was studied, BMI was calculated, and blood leptin level was determined at the beginning of the study by means of the ELISA test.

Electrocardiographic examination (ECG) was administered to all patients.

The body weight index was calculated: BMI (kg/m^2) = weight (kg)/height (m^2). Based on BMI, four groups of patients were defined: the 1st group - BMI was up to 25 kg/m^2 (normal body weight) - 42 people (19.09%), the 2nd group – BMI was 25≤ BMI <30 kg/ m^2 (overweight) - 90 people (40.9%), the 3rd group - 30 ≤ BMI <35 kg/ m^2 (first-degree obesity) - 59 people (26.81%), the 4th group - BMI ≥ 35 kg/ m^2 (second or third-degree obesity) - 29 people (13.2%).

Echocardiographic examination (ECHO) was administered in case of the study entry and 1 year later studying the following parameters: left atrial end-diastolic dimension (LA EDD), left ventricle end-systolic dimension (LV ESD), left ventricle end-diastolic dimension (LV EDD), ejection fraction (EF). The left ventricular myocardium mass index (LV MMI) was determined. Normal LV MMI indicator for men is ≤115g/m^2 and ≤95g/m^2 for women [13].

Patients were trained to control the radial artery pulse, and also information on symptoms common to AF was provided. AF paroxysmal events were traced on ECG in case of symptoms common to AF. Asymptomatic diseases were detected controlling the regular pattern for radial artery pulse twice a day (morning, evening), then ECG was made to confirm AF.

The average age of patients included in the study was 67.34±8.4.

When included in the study, patients did not differ in the hypertensive disease (HD) stage. HD stage classification: HD I had 3 (1.3%) persons, HD II−23 (10.5%) persons, HD III−194 (88.2%) persons. 21 persons (9.5%) had isolated systolic arterial hypertension.

To eliminate thyroid pathology, all patients were examined for blood thyroid hormone level (TSH, T3, T4) and had thyroid gland ultrasonic examination.

All patients in the study had AH in history and at the time of the study enrollment. The following treatment patterns were used to treat AH:

1) ACEI /sartan + beta-blocker + amlodipine
2) ACEI /sartan + beta-blocker + diuretic
3) Beta-blocker + sartan/ACEI
4) ACEI /sartan + diuretic
5) ACEI /sartan + amlodipine
6) ACEI /sartan + amlodipine + diuretic
7) ACEI /sartan

Antiarrhythmic therapy applied to patients: 1) Amiodarone, 2) sotalol 3) beta-blocker, 4) beta-blocker + amiodarone combination.

Treatment persistence was about 70%.

The duration of patient monitoring was 1 year.

Clinical Study was registered in the Integrated National Information System For Research, development and technological works created for civil purposes "(INIS RDTW) No. 01201465727.

Statistical data processing was executed by means of the software packages by IBM SPSS for Windows (version 24.0), the developer is IBM, the USA. The sample size was determined using EpiInfo software. To describe variables and carry out a comparative analysis, non-parametric descriptive statistics methods were used, quantitative data distribution was tested for normality using the Shapiro-Wilk test. A median was used to describe abnormally distributed data and a 25%-75% percentile is shown, some data are presented in M±SD format. Quantitative comparisons of these three groups were based on the non-parametric Kruskal-Wallis test.

Quantitative comparisons of the two groups were based on the non-parametric Mann–Whitney test. The conditions required for the application of the above-mentioned methods were tested. The statistical significance level was recorded at the 5% α-error probability. The influence of arterial hypertension treatment regimens on the reduced relapse of AF paroxysmal events was assessed using a multivariate logistic regression method.

Multivariate regression analysis including all potential predictors in the model was carried out when determining predictors of the AF paroxysmal event relapse. The relapse relative risk was assessed using the odds ratio.

Results

The study involved 220 patients: 73 (33.2%) men and 147 (66.8%) women. The average patient monitoring time is 13.2 months.

When included in the study, all 220 patients (100%) had newly diagnosed AF. 220 people (100%) had a history of arterial hypertension, 198 (90%) - chronic heart failure, 115 (52.3%) - CAD, including 23 (10.5%) people with previous myocardial infarction, and 22 (10%) - diabetes mellitus. The groups did not differ in concomitant diseases for different BMI groups.

LV EDD, LV ESD, FB, and LA EDD were compared, left ventricular hypertrophy was diagnosed in groups of patients with normal body weight, patients with excess body weight, first-degree obesity, and second- and third-degree obesity.

The results obtained at the beginning of the study showed that the groups differed in LA EDD indicators.

LA EDD indicator in the study groups was significantly higher in the overweight group - 40.0 (37.0-43.0) mm compared to the group of patients with normal body weight – 38.0 (36.0-41.0) mm, (p = 0.036), in the group with first-degree obesity - 42.0 (38.0-44.0) mm compared to the group of patients with normal body weight (P = 0.001) and in the group with second and third-degree obesity -42.0 (39.0-45.0) mm compared to the group of patients with normal body weight (p = 0.013). When comparing the group with first-degree obesity and the group with second and third-degree obesity, no statistically significant differences were detected.

Structural changes analysis held 1 year later showed that groups diverged from each other in many structural cardiovascular system indicators: LV EDD, LV ESD, and BDR LP (Table 1). The LV EDD indicator in the group with second- and third-degree obesity was higher than in the group of patients with normal body weight (p = 0.002), as well as LV EDD was higher in the group of patients with second and third-degree obesity compared to the group with excess body weight (p = 0.003).

The LV ESD indicator in the group with first-degree obesity was higher than in the group of patients with normal body weight (p = 0.04), as well as LV ESD was higher in the group of patients with second and third-degree obesity compared to the group with normal body weight (p = 0,005) and compared to the group with excess body weight (p = 0.020).

LV EDD indicator in the group with excess body weight was higher than in the group of patients with normal body weight (p =0.035) and LV EDD was higher in the group of patients with first-degree obesity compared to the group with normal body weight (p =0.01), LV EDD was higher in the group with second and third-degree obesity in comparison to the group of patients with normal body weight (p = 0.01).

Table 1. Structural cardiovascular system indicators in different BMI groups after 1 year of patient monitoring

Indicator	BMI groups			
	normal body weight	overweight	first-degree obesity	second and third-degree obesity
LV EDD (mm)	48,5 (45,0–52,0)	49,0 (46,0–54,0)	51,0 (49,0–55,0)	53,0 (51,0–56,0)
LV ESD (mm)	31,0 (29,0–34,0)	32,0 (30,0–35,0)	33,0 (32,0–36,0)	35,0 (33,0–38,0)
EF (%)	63,0 (61,0–68,0)	63,0 (58,0–65,0)	62,0 (58,0–65,0)	61,0 (58,0–63,0)
LA EDD (mm)	38,0 (36,0–41,0)	41,0 (38,0–43,0)	42,0 (39,0–44,0)	43,0 (39,0–44,6)

* Indicators are presented as Me (Q 25%– Q 75%)

Women's LV MMI had the following trend: LV MMI (g/height m^2) in patients with normal body weight − 86.61±1.8 g/m^2, with the excess body weight − 95.45±2.3 g/m2, first-degree obesity − 102.1±3.57 g/m^2, in patients with second and third-degree obesity − 112.03±4.08 g/m^2.

Depending on the BMI group, men's LV MMI was distributed as follows: 109.8±2.41 g/m^2 − in the group of patients with normal body weight, 114.63±2.92 g/m^2 − in the group of patients with excess body weight, 119.86±3.47 g/m^2 − first-degree obesity group, 124.47±5.09 g/m^2 – in patients with second and third-degree obesity.

Women's LV MMI had the following trend after 1 year of monitoring: LV MMI (g/height m^2) in patients with normal body weight −91.83±2.2 g/m2, 100.68±2.9 g/m^2 - with the excess body weight, 105.6±3.63 g/m2 - first-degree obesity group, 116.28±4.62 g/m^2 - in patients with second and third-degree obesity.

Depending on the BMI group, men's LV MMI was distributed as follows: 112.3±2.6 g/m^2− in the group of patients with normal body weight, 118.51±3.73 g/m^2−in the group of patients with excess body weight, 124.49±3.95 g/m^2 - first-degree obesity group, 127.40±5.2 g/m^2 – in patients with second and third-degree obesity.

The incidence of AF paroxysm relapses was compared depending on body weight and obesity rate. When assessing relapses, it was detected: 52 people (23.6%) out of 220 did not show paroxysm relapses. More than half of the patients - 168 (76.4%) - showed AF paroxysm relapses.

AF paroxysm relapses were more frequently diagnosed in patients from the first-degree obesity group - 81% compared to the group with normal body weight - 45% (p = 0.002) and in patients from the second and third-degree obesity group - 90% compared to the group with normal body weight - 45% (p = 0.001).

AF paroxysm relapses were reliably more frequently diagnosed in patients from the first-degree obesity group - 81% compared to the group with excess body weight - 66%, (p = 0.003) and reliably more frequently diagnosed in patients from the second and third-degree obesity group - 90% compared to the group with excess body weight - 66%, (p = 0.001).

To analyze the influence of arterial hypertension treatment regimens on AF paroxysm relapses, a multivariant analysis using the multivariate logistic regression method was carried out. No statistically significant correlations were established.

Leptin level analysis in groups of patients with AF paroxysm relapses and groups of patients without AF paroxysm relapses was performed.

Groups of patients with AF paroxysm relapses during 1 year of monitoring and patients without AF paroxysm relapses differ in leptin level. Leptin concentration was significantly higher in the group of patients with AF paroxysm relapses - 20.1 (12.4 - 32.1) ng/ml, 8.9 (7.3 - 21.6) ng/ml - leptin level in the group of patients without AF paroxysm relapses ($p = 0.001$).

We identified male and female predictors for AF paroxysm relapses. A multivariant analysis was carried out using the multivariate logistic regression method (step-wise selection of independent variables) to achieve this goal. The following predictors were considered to be potential: leptin concentration, BMI, age, LV ESD, LV EDD, EF, LA EDD, LV MMI, SBP, DBP, heart rate, diabetes mellitus, myocardial infarction, CHF, and CHD.

Based on the analysis results, male predictors of the AF paroxysm relapse include: BMI and LV EDD, female predictors - SBP, BMI.

Discussion

LV EDD, LV ESD, EF, and LA EDD indicators were compared; left ventricular hypertrophy was diagnosed in the groups of patients with normal body weight, excess body weight, first-degree obesity, and second and third-degree obesity. The current study showed that the incidence of structural changes after 1 year of monitoring is higher in patients with AF and higher BMI.

The obtained results are consistent with the studies proving that patients with obesity have an enlarged left atrial and left ventricle cavity [14, 15]. Obesity is a risk factor for left ventricular hypertrophy development [15], and a large group of patients included in the study, especially those with obesity, did not have normotension despite the antihypertensive therapy.

Myocardial remodeling in patients with obesity and overweight develops mainly due to two mechanisms: due to adipose tissue synthesis by precursor cells localizing in the myocardium and due to displacement from epicardial adipose tissue. Adipose tissue then partially goes through fibrous degeneration and causes inflammatory reactions in the myocardium involving macrophages and pro-inflammatory cytokines, leading to myocardial remodeling [16, 17].

Incidence of paroxysm relapses was significantly higher in the groups with first-degree obesity and in the groups with second and third-degree obesity than in patients from normal weight and overweight groups.

The results obtained in few studies confirmed the greater incidence of AF paroxysm relapses in obese patients. The data obtained can be probably justified by the fact that obesity contributes to systemic inflammation development and myocardial fibrosis, structural and electrical atrial myocardium remodeling develops, which in turn leads to the formation of ectopic focus points in the pulmonary vein ostia and disruption of normal electrical flow through the atrial [16, 17].

In our study, patients with AF paroxysm relapses and patients without AF paroxysm relapses differed in the leptin level. Leptin concentration is significantly higher in the group of patients with AF paroxysm relapses ($p = 0.001$).

This pattern may be associated with the profibrotic leptin effects, which was experimented on mice by A. Fukui with his colleagues, as well as with the systemic inflammatory adipose tissue influence on the myocardium [18], which causes myocardial remodeling and AF paroxysm relapses. Yermakov and co-authors revealed high leptin levels in women with AF compared to that of the patients without AF, the study involved 4,937 patients, 892 having AF [19].

Based on the results of the multivariant analysis, male predictors for AF paroxysm relapses included: BMI and LV EDD, female predictors - SBP, BMI.

The existing directly proportional correlation between the BMI value and AF is proved by major clinical studies, obesity affects the myocardial remodeling processes, which is a predisposing factor for AF development [10, 20].

The increase in ABP level causes triggered activity in the atrial, structural, and electrical atrial remodeling development. Structural remodeling leads to fibrosis, electrical remodeling causes slowing of atrial conduction, system and local inflammation responses are triggered. Re-entry is developed as a result of these processes [21, 22].

Myocardial remodeling causes ectopic focuses development and disruption of normal electrical conduction, thereby causing arrhythmia [16, 17]. In our study, LV EDD was the male predictor for AF paroxysm relapses.

In their study involving patients with AF relapses, Dedov and co-authors also revealed an increase in LV EDD in patients with AF relapses compared to the control group without AF [23]

Conclusion

The study showed that patients with obesity had enlarged left ventricular and left atrium and a higher incidence of left ventricular hypertrophy than patients with normal body weight.

Excess body weight and obesity cause AF progression: the incidence of paroxysm relapses increases from normal body weight to excess body weight, from excess body weight to first-degree obesity, second and third-degree obesity.

Leptin concentration is higher in the group of patients with AF paroxysm relapses compared to the group without paroxysm relapses.

Male predictors for AF paroxysm relapses were BMI and LV EDD, and female predictors were SBP, BMI.

The prospects for further study of the issue involve more comprehensive myocardial remodeling assessment, including assessment after excess weight and obesity correction. Studying the influence of other adipokines on AF development and searching for new predictors for AF paroxysm relapses seems to be promising as well.

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