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Basic Research

Studying the Processes of Myocardial Remodeling in Hypertensive Patients on the Basis of Pathoanatomical Studies

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Abstract

Background: In the study of the arterial hypertension (AH), it is noted that remodeling occurs on both the left and right ventricles of the heart. **Methods and results:** According to the postmortem autopsy of the dead, a retrospective case-control study had being conducted in the Republic of Kazakhstan in Semey city for 11 years, who had suffered from AH during the lifetime. **Conclusions:** It has been revealed that hypertrophy in AH occurs not only of the left, but also of the right ventricle, up to 78.2% in the whole group; a larger part occurs in males (males: up to 81.4%, women: up to 73.7%). The majority of AH patients who died had moderate left ventricular hypertrophy (LVH) (61%), slightly higher among females (65.8%) than males (57.3%). Various degrees of LVH differences by gender in the basic parameters have been identified. It is observed that there is a unidirectional increase in the value of the left and right ventricle depending on the increases of the severity of hypertrophy. Individuals with a strong degree of the right ventricular hypertrophy (44.6%) were predominant among the AH dead patients, greater in males (49.1%) compared with females (38.2%). Differences by gender has been found according to age (P=0.006) and thickness of the wall of the right ventricle (P=0.04). IJBM 2011; 1(2):97-102.

Key words: *pathoanatomical research; hypertension; left ventricular hypertrophy; right ventricular hypertrophy; sex.*

Introduction

Arterial hypertension (AH) is one of the most urgent problems of modern health care, primarily because of its high prevalence [1, 2]. According to the World Health Organization (WHO), in general, approximately 20% of the adult population or about one billion people suffer from AH worldwide [3]. Incidence of AH in the United States among adults aged 20 years and over is 30% or approximately 50 million people [4,5]. It is known that AH significantly increases the risk of cardiovascular complications. Furthermore, it significantly reduces the average life expectancy [3, 6].

The urgency of studying the mechanisms of left ventricles (LVs) remodeling in various diseases of the cardiovascular system is owing to the fact that it is a major factor in triggering the formation of systolic and diastolic dysfunction, basis of emergence, and progression of chronic heart failure [7-13]. If given enough consideration for the study of LV remodeling [12, 14, 15], then the remodeling of the right ventricle (RV) is much smaller. Available evidence indicates a clear correlation between LV and RV [16-21]. In this regard, the features of remodeling and the selection of types with different components has a significant practical value and will encourage the development of optimal approaches for the treatment of patients suffering from AH, and to determine the prognosis as well.

There are age and gender peculiarities in the prevalence of left ventricular hypertrophy (LVH). Numerous studies have demonstrated a direct relationship between age and left ventricular myocardial mass (LVMM) [22-24]. At the same level of blood pressure, LVH is significantly more common among older than younger patients [12]. According to the Framingham study, the prevalence of LVH in 1,000 patients by ECG criteria was 4.0 among patients aged under 40 years; 9.8 for 40–49 years; 12.7 for 50–59 years; 23.6 for 60–69 years; and 40.2 for ≥ 70 years [25]. In the study conducted by Conrady et al. [26], it was shown that age has a significant effect on myocardial mass, with this pattern being more predominant in males. According to Agabiti-Rosei et al. [27], LVH at a

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young age has a lower prevalence among females than males. The frequency of LVH increases progressively with age, and after menopause the prevalence of LVH is higher among females than males. Gender differences have not been practically studied in the remodeling process in AH. It should be noted that gender prevalence of LVH might vary depending on what criteria have been used to diagnose LVMM.

Objective

To continue the studies in remodeling peculiarities of the LV and RV of the heart among dead patients, suffering from AH during their lifetime, depends on the severity of hypertrophy of the LV and RV, gender, and age according to the postmortem autopsy.

Methods

A retrospective case-control study, according to the postmortem autopsy, was conducted by the "Anatomicopathological Bureau" in Semey city, East Kazakhstan, and Semey branch RSCE "Center of Forensic Medicine of the Ministry of Health of the Republic of Kazakhstan" of the dead for 11 years (from 1999 to 2009).

The group included for analysis included the data autopsy of the dead, as a result of acute cerebrovascular accidents, death from acute myocardial infarction during the day, and death in acute surgical pathology of abdominal organs. Criteria not included in the groups analyzed were the presence of respiratory diseases, heart diseases, obesity, and heart failure. Thus, autopsy of the dead was selected, who during their lifetime apart from hypertension had no comorbidities, independently leading to remodeling of RV. Statistical processing was performed using a software package STATISTICA (StatSoft Inc., USA). For all tests, a two-tailed value of $P<0.05$ was required for statistical significance. In total, 372 autopsies were selected (220 (59%) men and 152 (41%) women).

For the analysis of available data in the study group, values that define the parameters of the LV and RV at the moment of autopsy were taken. The following values for a normal LV wall thickness (without papillary muscle) have been taken: 0.7–1.2 cm, RV: 0.2–0.3 cm. Hypertrophy of the walls of LV and RV was divided arbitrarily into two degrees: LVH: I degree: 1.3–2.0 cm, II degree: 2.1 or more; RVH: I degree: 0.4–0.6 cm, II degree: 0.7 cm or more.

Results

Our analysis of the autopsies data of 372 dead suffering from AH has shown that there are a variety of parameters of LV and RV of the heart, depending on their degree of hypertrophy, age, and gender.

When studying the parameters characterizing the state of LV, it has been revealed that the normal LV size are determined in two dead (0.5%); LVH has been noted in 99.5% of cases, I degree of LVH in 61% of cases (226 dead); II degree of LVH in 38.5% of cases (144 dead). Age parameters at different degrees of LV wall thickness are presented in Table 1.

In analyzing the parameters of RV wall thickness at different wall thickness of the LV (normal LV wall thickness, 1 and 2 of LVH), there is a direct correlation between these parameters. Figure 1 shows an amplitude of the RV wall thickness, depending on varying degrees of severity of the LV. A parallel increase in the value of the RV depending on the growth of the severity of LVH has been noted.

When comparing the groups with identified LVH I and II degrees difference calculated by Mann–Whitney *U* test, significant $P<0.05$ have been found by the thickness of the LV as well as RV ($P<0.0001$).

Changing the parameters of the RV in the study group has been defined as: the normal size in 21.8% of cases (81 dead); RVH in 78.2% of cases, whereas I degree determined the degree to 33.6% of cases (125 deaths), II degree in 44.6% (166 dead). Age parameters at different degrees of RV wall thickness are presented in Table 2.

For comparison of three groups of AH patients, rank analysis of variance Kruskal–Wallis has been used. It reveals differences (P=0.003) on indicators of age between one and three groups, and the differences in wall thickness of LV and RV, with varying degrees of severity between the groups ($P<0.001$).

In analyzing the parameters of LV wall thickness at different wall thickness of RV (normal LV wall thickness, I and II degrees of RVH), there is a clear and direct correlation between these parameters. Figure 2 shows the magnitude of LV wall thickness depending on the different degree of RV; it shows a unidirectional increase in the value of the LV, depending on the growth of the severity of RVH. Thus, the autopsy has shown that LVH has been observed in almost all cases, whereas RVH has been observed in 78.2% of the cases (Fig. 3).

From the analysis of 372 autopsies, males were 220 and females 152. Age parameters according to gender are

Table 1
Parameters of age, depending on the varying thickness of left ventricular wall

	Valid N	Mean	Confid. -95%	Confid. +95%	Median	Lower quartile	Upper quartile	Std. Dev.	Std. Error	P
Whole group (1)	372	56.9	55.6	58.1	56.0	49.0	66.5	12.5	0.6	$P_{1-2}= 0.03$
Norm	2	44.5			44.5	35.0	54.0	13.4	9.5	
I degree of LVH (2)	226	56.3	54.6	58.1	55.0	48.0	67.0	13.3	0.9	$P_{1-3}= 0.40$
II degree of LVH (3)	144	57.9	56.0	59.7	57.0	49.5	64.0	11.2	0.9	$P_{2-3}= 0.23$

Table 2
Parameters of age, depending on the varying thickness of right ventricular wall

	Valid N	Mean	Confid. -95%	Confid. +95%	Median	Lower quartile	Upper quartile	Std. Dev.	Std. Error
Whole group (1)	372	56.9	55.6	58.1	56.0	49.0	66.5	12.5	0.6
Norm	81	53.5	50.8	56.2	51.0	46.0	62.0	12.2	1.4
I degree of LVH (2)	125	56.0	54.0	58.0	55.0	49.0	63.0	11.3	1.0
II degree of LVH (3)	166	59.1	57.1	61.2	58.5	49.0	69.0	13.2	1.0

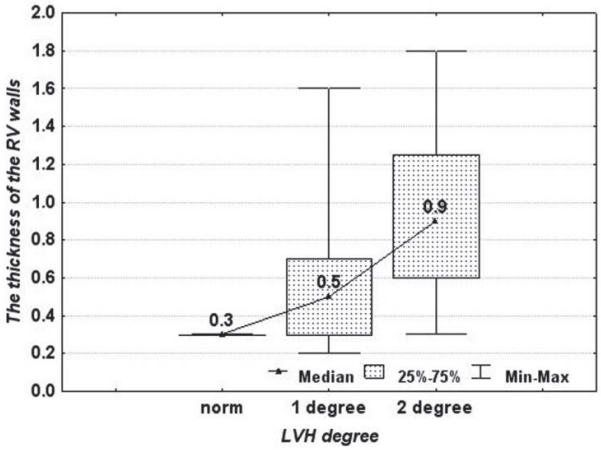

Fig. 1
Diagram of the thickness range of RV walls in different degree of LVH

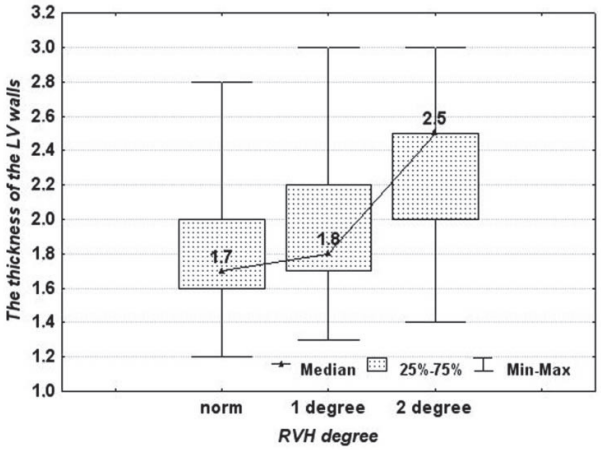

Fig. 2
Diagram of the thickness range of LV walls in different degree of RVH

shown in Table 3.

When studying the parameters characterizing the state of LV, it is observed that there are no gender differences in the thickness of the wall of the LV. Difference by gender on the Mann–Whitney *U* test was *P*=0.093 (marked criteria significant at *P*<0.05). Moreover, there is a difference in the thickness of the wall of RV among females (median, upper, and lower interquartile scale was 0.6, from 0.4 to 1.0) and males (respectively: 0.5, from 0.3 to 0.8), *P*=0.04 difference on the basis of the according to the postmortem study Mann–Whitney *U* test (Fig. 4). For the analysis of these indicators of remodeling in AH to compare two groups, Spearman rank correlation was the method of nonparametric correlation analysis used. So, in the male group (n=220), there is a close correlation between the thickness of the walls of LV and RV (r=0.69), and in the female group (n=152), there is a reasonable relationship between age and wall thickness of RV (r=0.34) and between the wall thickness of LV and RV (r=0.50).

In the male group suffering from AH, according to the autopsy of two dead (0.9%) there is no sign of LVH, in 126 (57.3%) 1 degree of LVH, and in 92 (41.8%) 2 degree of LVH. In the female group suffering from AH, according to the autopsy of 100 dead (65.8%) 1 degree of LV hypertrophy and in 52 (34.2%) 2 degree of LVH.

While studying the changes in LV wall thickness by gender, the following was observed: the male group with AH, according to autopsy of 41 dead (18.6%), no states accompanied by an increase in RV has been detected, in 71 (32.3%) I degree of RVH, and in 108 (49.1%) II degree of RVH. In the female group suffering from AH, according to autopsy of 40 dead (26.3%), there were normal parameters of RV, in 54 (35.5%) I degree of LVH, and in 58 (38.2%) II degree of LVH.

When comparing the groups using the rank analysis of variance by Kruskal–Wallis, the differences between groups in LV wall thickness (P <0.0001) has been revealed.

Table 3.
Parameters of age, depending on gender

	Valid N	Mean	Confid. -95%	Confid. +95%	Median	Lower quartile	Upper quartile	Std. Dev.	Std. Error	P
Whole group (1)	372	56.9	55.6	58.1	56.0	49.0	66.5	12.5	0.6	P_{1-2}=0.10
Norm	220	55.2	53.6	56.8	54.5	48.0	62.5	11.9	0.8	P_{1-3}=0.05
I degree of LVH (2)	152	59.3	57.2	61.4	58.5	49.0	69.5	13.1	1.1	P_{2-3}=0.002
II degree of LVH (3)	372	56.9	55.6	58.1	56.0	49.0	66.5	12.5	0.6	P_{1-2}=0.10

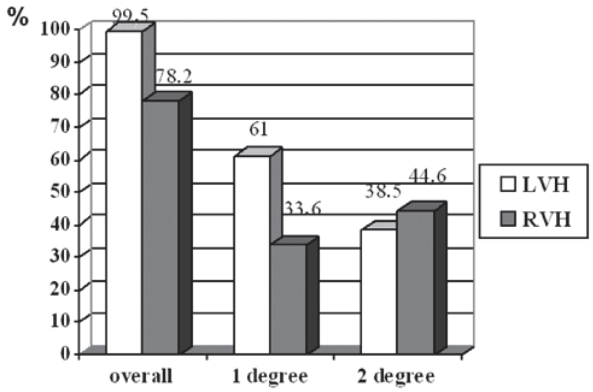

Fig. 3
Frequency of hypertrophy of ventricles of the heart (%)

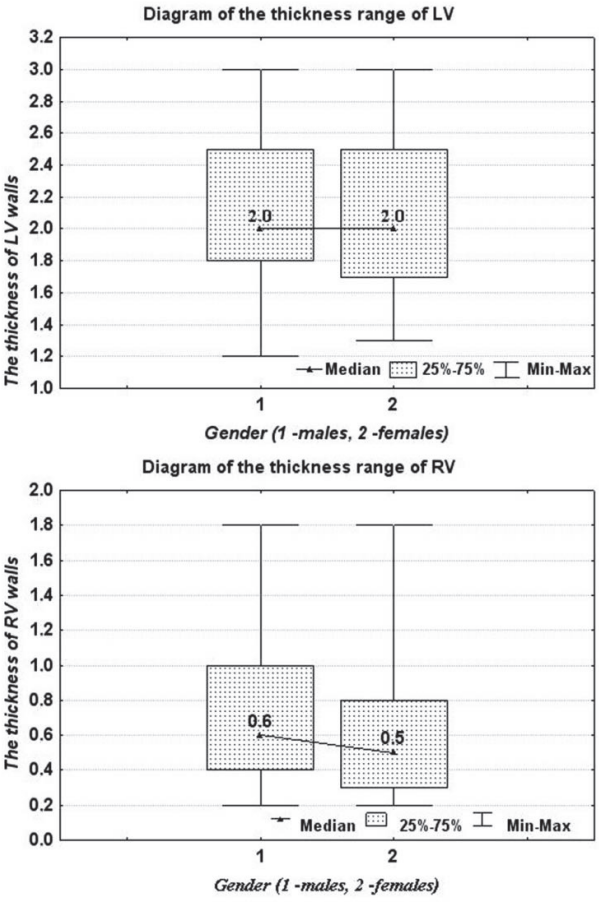

Fig. 4
Diagram of the thickness range of LV and RV

Discussion

In spite of the numerous conducted studies of remodeling in AH in various countries, there is numerous conflicting data.

Results of multicenter large-scale studies completed in recent years have shown the importance of LVH as an independent predictor of risk of death and cardiovascular complications of AH [28-32].

The studies on cardiac remodeling in AH are mainly related to studies of changes in LV. The fact and significance of indicators reflecting the increase in the value of LV myocardium is essential. If it has demonstrated a significant increase in the frequency of LVH in AH by numerous authors, the observation by noninvasive methods, such as ECG and echocardiography, then the study based on autopsy is insignificant. Therefore, during the retrospective postmortem study of 372 dead from acute cerebrovascular accidents, acute myocardial infarction within days, and acute surgical pathology of abdominal organs with AH, LVH was found in almost all cases.

The cases of death of patients with AH are of particular interest from the perspective of clinicians, when the postmortem study does not show LVH. In the group studied with AH in two dead (0.5%), a normal LV geometry was revealed. Among the majority researched, a moderate LVH was revealed: I degree of LVH in 61% of cases. The main known pathological criteria for AH are LVH and target organs lesion. However, if the death of the patient with AH II degree occurred for some acute reasons and there is no reliable anamnestic data of the presence in patients with AH and at postmortem study there is no LVH, it is unlikely that this patient will be determined by anatomopathological diagnosis of AH. Taking into consideration that signs of LVH may be missing among patients with II degree in clinical, then at the formulation of postmortem diagnosis of AH the clinical data should not been underestimated. Available clinical data on the possible presence among patients with AH II and III degree of the normal LV geometry raise the question of the study of other pathological markers of AH, except LVH and blood vessels.

A number of studies [33, 34] have shown that at the early stage of AH, changes are observed in RV, and credible signs of hypertrophy of the right half of the heart are detected early enough among patients with I and II degree of disease. Analysis of long-term clinical experience allowed Myasnikov in 1965 to conclude that some patients with AH signs of right heart failure outpace the development of LV failure, and other patients with AH develop hypertrophy not only of the LV, but also of RV. However, currently there is more attention paid to study changes of RV and AH.

While studying the parameters of the RV, RVH in 78.8% of cases, in which there were no any states accompanied by an increase in RV, was revealed. The revealed changes of RV are confirmed by works, pointing to the possibility of the RV impact on the process of remodeling of the heart muscle in AH [35-37]. The recent studies have shown that the diseases initially damaging LV, RV is involved in the pathological process as well. According to Veber VR et al. [38], there is evidence that LVH is detected in 100% of cases and RVH in 45% of cases, including 21%. According to Avtandilov [39], the usual method of the autopsy RVH in AH is detected in 57.6% cases, with the planimetric weighted in 78.2% and with hystometric method in 93.5% of cases.

Thus, according to the postmortem studies, RVH occurs in almost half of AH patients. Such data should orient us to study in more detail the parameters of changes

of RV with AH during the lifetime. According to the survey, in majority, a more evident degree of hypertrophy of RV was found and was 44.6 against 33.6%. A direct correlation between the increases in the value of LV, depending on the growth of the severity of RVH, was observed.

Therefore, undoubtedly, the study in AH patients not only of the left, but also of the right heart becomes relevant for practical cardiology, because involvement in the pathological process of RV among patients with AH are likely to increase the risk of heart failure. Perhaps, the evolution of AH in these patients is completely different than among patients with isolated LVH.

As seen in the studies of Veber VR et al. [38], there are options for pathological cardiac remodeling in AH:

• isolated LVH

• a combination of LVH and RVH.

There are options when RVH precedes or supersedes over LVH. This issue has not been explored sufficiently. Therefore, it is interesting to study variants of cardiac remodeling in general, both of the left and the right parts among patients with AH, despite certain technical difficulties.

At present, it becomes necessary to study remodeling in general, both of the left and the right parts. We can talk about biventricular hypertrophy in essential hypertension. Important aspects are gender and age of myocardial remodeling in AH patients. This section is poorly understood and controversial. Thus, it has been found that among the examined males (59.1%) and females (40.9%) gender differences in the thickness of the LV wall have not been identified. Statistically, significant gender differences have been found in terms of wall thickness of RV (P=0.04). Closer correlation has been found between the rates of wall thickness of LV and RV of males. Among both groups of males and females, it is marked by more frequent detection of mild LVH (I degree).

According to the thickness of the walls of RV, it has been found that in the female group the normal RV size (26.3 vs. 18.6%) is more frequently revealed. In both groups, there is more evident degree of hypertrophy of RV (II degree: men 49.1% and women 38.2%).

Conclusions

There is LVH among the majority of dead with AH. However, there may be the absence of LVH in AH (two cases). It is observed that the majority of AH patients has moderate ventricular hypertrophy (61%), slightly higher among females (65.8%) than males (57.3%). At various degrees of LVH, the differences by gender in the basic parameters have been identified.

Hypertrophy in AH occurs not only of the LV, but also of the RV up to 78.2% in the whole group (but in large part and more evident among males). Among AH patients who died, there are individuals with a strong degree of RVH, greater among males compared with the females. Differences by gender have been found according to age and the thickness of the wall of RV. There is a substantial correlation in the males between the parameters of the LV and RV myocardial mass compared with females.

The available data substantiate the need for a detailed diagnosis of lifetime changes in the parameters of the LV and RVs in different variants of cardiac remodeling in AH and, the need for further study of the processes of cardiac remodeling in AH.

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