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Pathomorphological Characteristics of Cardiac Remodeling after Myocardial Infarction

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Dilatational, hypertrophic, aneurysmal, and endocardial variants of remodeling were revealed in the postinfarction heart. The most prevalent dilatational remodeling is characterized by uniform or nonuniform elongation of ventricular cavities and increase in ventricular volume. Characteristic features of the hypertrophic type are hypertrophied interventricular septa and left ventricular wall and reduced or unchanged left ventricular volume. Pronounced changes in the configuration of the left ventricle due to the formation of single or multiple aneurysms were typical of aneurysmal remodeling. Endocardial remodeling was characterized by cicatricial changes and smoothed relief of the parietal endocardium. These variants and forms of remodeling determine disturbances in intracardial hemodynamic and thanatogenesis in the postinfarction period.

Key Words: *postinfarction myocardium*; *types of remodeling*; *ventriculography*; *cardiac morphometry*

According to current concepts, postinfarction myocardial (PM) remodeling is a complex dynamic process involving all chambers and histological structures of the heart [13]. Cardiac remodeling in the postinfarction period is primarily associated with pronounced rearrangements in left ventricular myocardium changes in its shape of the perinecrotic area, as well as shifts in the functional state of the myocardium at the boundary and non-injured areas [11]. So, cardiac remodeling is a constellation of shape, volume and mass rearrangements in ventricles caused by critical shifts in hemodynamics, which are incompatible with the normal function of the heart [1,13].

Our aim was to determine morphological criteria of postinfarction ventricular remodeling, which can be used for postmortem description of the PM and adequate interpretation of relevant clinical data.

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MATERIALS AND METHODS

The hearts of 260 patients (184 men and 76 women, aged 56.4±0.6) dead at various periods after myocardial infarction were studied. The mean postinfarction period in these patients was 8.4±0.2 years. The control group comprised the hearts without cicatricial lesions from 40 accidentally dead humans of comparable age.

Ventricular geometry was studied by the method of postmortem contrast polypositional ventriculography [6,10]. Polypositional radiographic examination was performed before filling of the ventricles with the contrast dye and after polymerization of gelatin.

Scar lesions in the myocardium were measured after cardioventriculography by morphological examination of serial sections according to standards of World Health Organization. The samples containing transmural scars 2 cm or more in diameter were analyzed. Functional characteristics of PM were evaluated using morphometric and histological data, ventricular

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weight and the results of volume-weight and planimetric cardiometry [8].

Samples for light microscopy were fixed in neutral 10% formaldehyde and embedded in paraffin. Paraffin sections were stained with hematoxylin and eosin, Van-Gieson's picrofuchsin or Weigert's resorcin-fuchsin (visualization of elastic fibers). Muscle and connective tissues were identified by a trichromatic staining method [6]. The number of capillaries and muscle fibers per 1 mm^2, and diameters of capillaries and muscle fibers in myocardial sections were evaluated visually using an Avtandilov grid. The results were analyzed using standard statistical methods.

RESULTS

Morphological analysis revealed several types of postinfarction ventricular remodeling: dilatational, hypertrophic, aneurysmal, and endocardial. Left ventricular dilation (n=112, 43%), the most frequent type of remodeling had various forms. In most cases (46%), it manifested in marked elongation of the left ventricle and displacement of the interventricular septum (IVS) towards the right ventricle. This displacement was usually observed in the distal parts of the septum. The second most frequent form of left ventricular dilation after myocardial infarction was the so-called nonuniform dilation (38%). This form was characterized by a slight displacement of IVS combined with considerable enlargement and deformation of the ventricle. In 18% cases, left ventricular dilation was accompanied by a sharp increase in its volume, displacement of thinned IVS towards the right ventricle, and specific sphere-like shape of the remodeled ventricle (Fig. 1, *a*).

Morphometric data indicated an increased ratio of cicatrical-to-myocardial tissue weights for this type of remodeling (Table 1). Other peculiarities were decreased number and diameter of muscle fibers and noticeable capillarization of PM.

The description of dilatational remodeling of the left ventricle includes estimation of IVS displacement (or "pathologic movements"). The displacement of IVS can lead to a volume-capacitance compensation of abnormal hemodynamics in PM and, at the early stages of remodeling, promote relatively stable hemodynamics in the peripheral vessels [3,6,9]. However, pronounced dilation of the left ventricle drastically increases intramyocardial stress both in systole and diastole and decreases stroke volume and cardiac output.

Severe left ventricular dilation with IVS shifting towards the right ventricle leads to the rise of end-diastolic pressure in the remodeled ventricle, which sometimes induces the secondary pulmonary hypertension. This dilation can also cause mitral regurgitation. A combination of these factors acts as a starting mechanism for the development of cardiac failure [1, 4,5,7], which in most cases (n=62) was an immediate cause of death in patients with postinfarction dilated cardiomyopathy.

The hypertrophic type was the second most frequent type of ventricular remodeling (n=62, 24%), which had two forms. In 55% cases, significant postinfarction hypertrophy of IVS and left ventricular walls was observed. Despite various modifications in the shape, the volume of remodeled ventricle changed insignificantly. In other cases (45%), significant septal and left ventricular hypertrophy was accompanied by a large decrease in the left ventricular volume and noticeable changes in its configuration (Fig. 1, *b*). Diminution of the left ventricular cavity occurred predominantly due to hypertrophy of the "boundary" myocardium. Ventricular filling changed dramatically due to both abnormal relaxation and deformation of the ventricular shape [10,11].

Morphometric analysis revealed a reduction of capillary bed in the left ventricle of PM during hypertrophic remodeling (Table), which occurred mainly due to hypertrophy of muscle fibers. However, the number of muscle fibers per 1 mm^2 decreased due to increased ratio of scar-to-muscle tissue weights. As a rule, hypertrophic remodeling produced profound changes in diastolic left ventricular function as a consequence of disturbed isovolumetric myocardial relaxation and impairment of ventricular filling associated with specific postinfarction ventricular geometry [10, 11]. This peculiarity underlies various causes of death, such as chronic heart failure, thrombosis and thromboembolism, and cardiogenic collapse [2,10,14].

The aneurysmal type of remodeling of PM was observed in 44 patients (17%). Singular or multiple aneurysms in the postinfarction cicatricial regions were the characteristic feature of this type of remodeling. Irrespective of the exterior form of the left ventricle its internal cavity was oblong, with aneurysmal masses adjacent to the postinfarction scar. Apex aneurysms dominated (73%). They developed in the apex area if the postinfarction scars were localized in the border zones of the ventricle. Sometimes, several aneurysms were observed in one scar area (9%). Such aneurysms, which appeared in the marginal zones of the scar and occupied the adjacent myocardium, drastically modified the configuration of the left ventricular cavity (Fig 1, *c*). As quantified by morphometry, this type of left ventricular remodeling was accompanied by a significant growth of the scarry tissue mass in PM relative to the muscle tissue mass, a decrease in diameter and number of muscle fibers, and a reduction of the capillary bed (Table 1).

The aneurysmal type of remodeling caused a pronounced deformation of the left ventricle cavity of PM

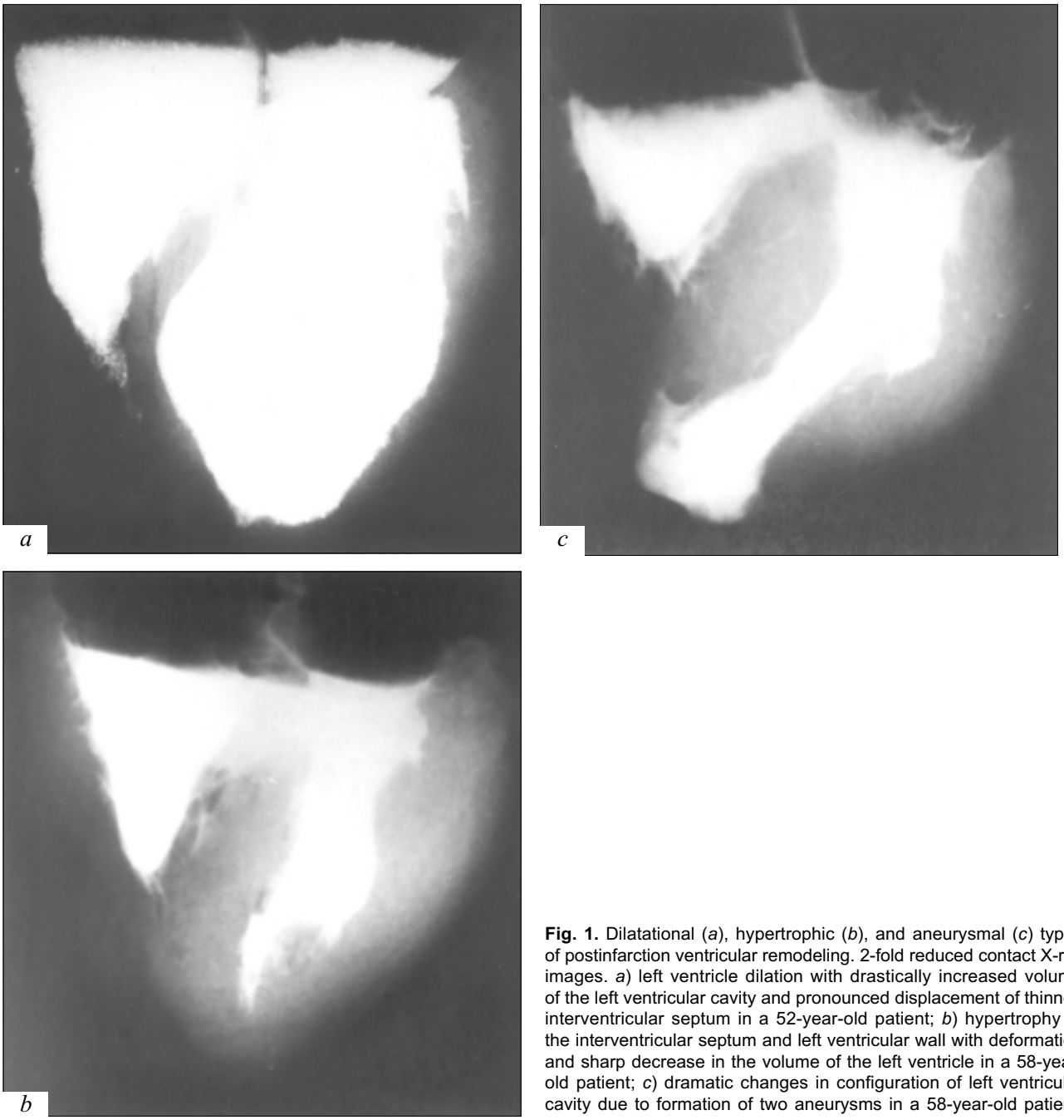

Fig. 1. Dilatational (*a*), hypertrophic (*b*), and aneurysmal (*c*) types of postinfarction ventricular remodeling. 2-fold reduced contact X-ray images. *a*) left ventricle dilation with drastically increased volume of the left ventricular cavity and pronounced displacement of thinned interventricular septum in a 52-year-old patient; *b*) hypertrophy of the interventricular septum and left ventricular wall with deformation and sharp decrease in the volume of the left ventricle in a 58-year-old patient; *c*) dramatic changes in configuration of left ventricular cavity due to formation of two aneurysms in a 58-year-old patient.

resulting in contraction asynchronicity. This biophysical mechanism can underlie low effectiveness of systolic contraction and further progression of cardiac failure in PM [1,2,15]. This can be responsible for the fact that the major causes of death are cardiac failure and, specifically, ventricular fibrillation.

The endocardial type of remodeling of PM was observed in 16% cases. Irrespective of localization of the postinfarction scar, we observed a peculiar cicatricial covering of the parietal endocardium spreading from the scar area. This phenomenon led to smoothening of the endocardial relief and the formation of connective tissue contouring of the left ventricular chamber (Fig. 2). According to morphometric data, this type of remodeling was characterized by a relatively low cicatrical-to-myocardial tissue ratio and decreased number and diameter of muscle fibers compared to the control. In the hearts with endocardial type of remodeling, the number and diameter of capillaries decreased to a lesser extent.

The morpholfunctional changes, which are specific for this type of postinfarction remodeling, induced profound impairment of diastolic function and considerable increase in diastolic pressure resulting in

TABLE 1. Morphometric Parameters of Left Ventricle in Various Types of Remodeling (*M*±*m*)

Index	Control	Variants of remodeling			
		dilatational	hypertrophic	aneurysmal	endocardial
Number of capillary per 1 mm^2	2286±28	2222±12	1922±22*	1804±22*	2112±14*
Number of muscle fibers per 1 mm^2	1826±42	1614±16*	1338±24*	1212±12*	1612±12*
Diameter of capillary, μ	6.4±0.04	6.20±0.04*	5.20±0.06*	5.80±0.04**	6.20±0.02*
Diameter of muscle fibers, μ	16.20±0.18	14.80±0.14*	18.80±0.12*	14.40±0.16*	15.80±0.18
Relatively cicatrical-to-myocardial tissue ratio	16.7±1.4	30.2±1.8*	22.4±1.5**	62.2±1.2*	28.6±1.4*

Note. *p<0.001, **p<0.01 compared to the control.

restriction of the ejection capacity of the left ventricle. These are the basic thanatogenic factors specific for the postinfarction endocardial cardiomyopathy [6,12].

Thus, there are various types of postinfarction remodeling — dilatational, hypertrophic, aneurysmal, and endocardial. The most frequent type is the dilatational remodeling. It has certain forms: uniform, nonuniform, and large-volume dilation of the left ventricle. The characteristic feature of the hypertrophic type is the interventricular septal and left ventricular wall hypertrophy, without changes in the volume of left ventricular chamber or its drastic reduction. Aneurysmal remodeling was accompanied by pronounced changes in the configuration of the left ventricular chamber due to singular or multiple aneurysms appeared near the postinfarction scars.

Specific characteristic of endocardial remodeling was cicatricial endocardium with smoothed relief of the parietal tissue in some areas. Established different types and forms of remodeling specify the character

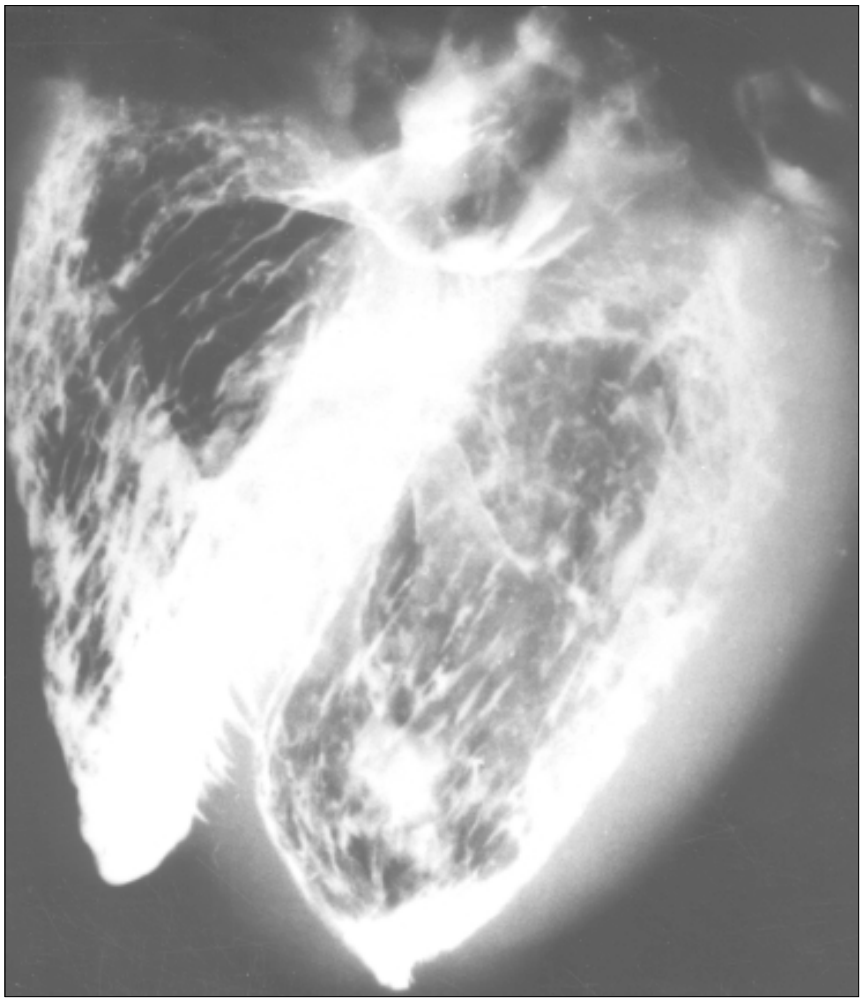

Fig. 2. Endocardial remodeling in the postinfarction heart. Contact X-ray image. Smoothed relief, connective tissue cavity contouring and cicatricial surface of the parietal endocardium of the left ventricle in a 56-year-old patient with the posterior septal localization of the scar.

of intracardial hemodynamics and thanatogenesis in the postinfarction period. Irrespective of localization of the postinfarction scar, we observed a peculiar cicatricial covering of the parietal endocardium determining smoothened endocardial relief and connective tissue contouring of the left-ventricular cavity. These phenomena were typical of endocardial type of postinfarction remodeling. The established morphological types of remodeling of PM combined with the data on the state of intracardiac hemodynamics (compensation or decompensation) constitute the morphofunctional criteria of postinfarction remodeling important for differential diagnostics.

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