Structural Remodeling of the Renal Vascular Bed during Experimental Pulmonary Stenosis and after Its Correction

Yu. V. Novikov, S. V. Shormanov, and I. S. Shormanov

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Renal vessels in pups with experimental pulmonary stenosis, animals with corrected defect, and control dogs were examined by histological and morphometric methods. Pulmonary stenosis was followed by remodeling of the renal vascular bed and adaptive and pathological reconstruction of veins, arteries, and glomeruli. Correction of the defect was followed by regression of pathological changes.

Key Words: *pulmonary stenosis; renal vascular bed; reconstruction; reversibility*

Study of morphological reconstruction of the vascular system in vital organs (*e.g.*, kidneys) during circulatory disorders typical of congenital heart diseases is an urgent medical problem [4,6,9,12]. Little is known about reversibility of this reconstruction. However, preoperative patient health and effectiveness of corrective therapy depend on the state of arteries and veins. It is not always possible to examine quantitatively the renal vascular bed in patients.

Here we studied remodeling of the renal vascular bed during experimental pulmonary stenosis and after defect correction.

MATERIALS AND METHODS

Experimental stenosis in 34 pups was produced as described elsewhere [13]. Twelve pups undervent surgical correction. The animals of both groups were examined over 2 years. The control group included 12 age-matched dogs. The animals were narcotized and euthanized by bloodletting. Kidney samples were taken from various areas, fixed with 10% neutral formalin, and embedded in paraffin. Histological sections were stained with hematoxylin and eosin by the methods of van Gieson, Masson, Hart, and Gomori. The arteries, veins, and capillary glomeruli were analyzed quantitatively. The specific area was measured by means of stereometry with point counting [1]. Morphometry was performed using a screw ocular micrometer. We measured the outer and inner diameters of interlobar (ILBA), arcuate (AA), and interlobular arteries (ILLA). The thickness of the vascular wall and area of the cross section were calculated as follows: $m=(D-d)/2$ and $S=\pi m(D-m)$, where D and d are the outer and inner diameters, respectively [1]. Smooth muscle cells were counted in the media of ILLA. The size of these cells was determined by the volume of nuclei [3]. This index was calculated by the formula: $V=0.523cd^2$, where c and d are the major and minor diameters of the nucleus, respectively [1]. We estimated the percentage of arteries that differed in branching and had oblique and longitudinal smooth muscle cells in the intima. The thickness of the wall of renal veins was estimated by dividing the values for the thickest and thinnest segment. The number of glomeruli in the middle zone of the renal cortex was calculated in the field of view

Department of Operative Surgery and Topographic Anatomy, Department of Pathological Anatomy, Yaroslavl State Medical Academy. ***Address for correspondence:*** s_v_shormanov@rambler.ru. S. V. Shormanov

(×80). We measured the diameter of glomeruli and estimated the number of cells in the cross section. The numerical results were analyzed by the method of variational statistics.

RESULTS

Experimental disease was accompanied by widening and 2.3-fold increase in the specific area of renal veins (Fig. 1). We observed hypertrophy of smooth muscle cells and excessive growth of collagen and elastic fibers in the wall of these vessels (Fig. 2, *a*). Their thickness increased from 3.0±0.5 to 5.0±0.5 μ ($p<0.01$).

Renal glomeruli were enlarged (due to plethora) or anemic and collapsed. Signs of sclerosis were often observed (Fig. 2, *b*). The specific area of these structures decreased by 1.1 times (Fig. 1). The number of glomeruli in the standard area remained practically unchanged, while the diameter and count of cells decreased by 1.1 times (Table 1).

Signs of hypertension were revealed in renal arteries (increased rugosity of the intima; Fig. 2, *c*). The specific area decreased by 1.2 times (Fig. 1). Sclerotic changes were found in the wall of several vessels. The area of cross section in ILBA, AA, ILLA, and arterioles increased by 2.8, 1.6, 1.3, and 1.4 times, respectively (Table 2). The volume of smooth muscle cell nuclei in the media of ILLA increased from 68.0±1.8 to 102.0±2.0 μ^3. The count of smooth muscle cells increased from 12.0±0.2 to 17.0±0.4 ($p<0.001$). We revealed an increase in the number of renal arteries with oblique and longitudinal smooth muscle cells in the intima. These changes were found in AA (increase from 2.3 to 4.5%) and ILLA (increase from 2.5 to 34.0%). Such vessels were also identified among arterioles (5.5%). Control samples did not include these vessels.

Defect correction reduced plethora of renal veins. The specific area decreased by 1.8 times (Fig. 1). The thickness of the wall decreased to 3.6± 0.5 μ ($p<0.05$), which was related to atrophy of smooth muscle cells and fibrous structures (Fig. 2, *d*).

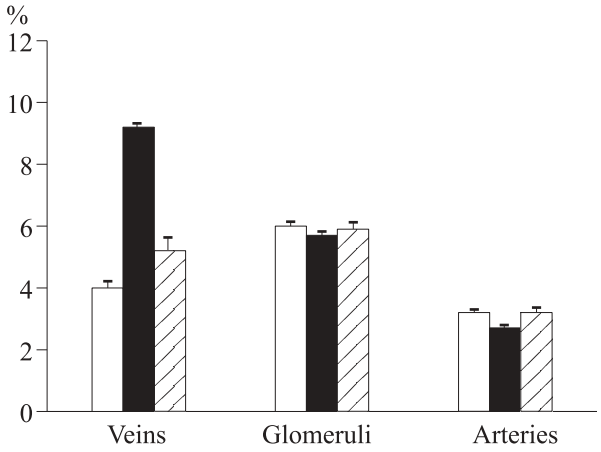

Fig. 1. Specific area of various compartments in the renal vascular bed during experimental pulmonary stenosis and after its correction. Light bars, control; dark bars, stenosis; shaded bars, correction of stenosis.

Blood filling in renal glomeruli partly or completely returned to normal after surgical correction (Fig. 2, *e*). The number of sclerotic glomeruli decreased. The specific area and number of these structures in the standard area little changed (Fig. 1, Table 1). The average size of glomeruli practically did not differ from normal (Table 1).

Correction of pulmonary stenosis was followed by a decrease in the tone and widening of renal arteries (Fig. 2, *f*). The specific area of vessels increased by 1.2 times (Fig. 1). Sclerotic changes in renal arteries became less pronounced. The wall of arteries was thinned. The cross section area in ILBA, AA, ILLA, and arterioles decreased by 1.3, 1.4, 1.2, and 1.3 times, respectively (Table 2). The volume of smooth muscle cell nuclei in the media of ILLA decreased to 78.0±4.7 μ^3 ($p<0.001$). The count of muscle cells decreased to 14.0±0.2 ($p<0.001$). After correction of stenosis we revealed a decrease in the number of arteries that had oblique and longitudinal smooth muscle cells in the intima. The number of these structures among AA, ILLA, and arterioles decreased to 2.8, 6.6, and 2.5%, respectively.

TABLE 1. Renal Glomeruli under Control Conditions, during Experimental Pulmonary Stenosis, and after Stenosis Correction (*M*±*m*)

Experimental conditions	Number of glomeruli	Diameter of glomeruli, μ	Number of glomerular cells
Control	12.2±0.2	103.4±0.6	131.4±0.9
PS	12.3±0.1*	94.4±0.4***	122.2±0.7***
PS+C	12.0±0.2	103.1±0.2$^+$	128.6±0.4**$^+$

Note. Here and in Table 2: PS, pulmonary stenosis; PS+C, correction of PS. *$p<0.05$, **$p<0.01$, and ***$p<0.001$ compared to the control; $^+p<0.01$ compared to PS.

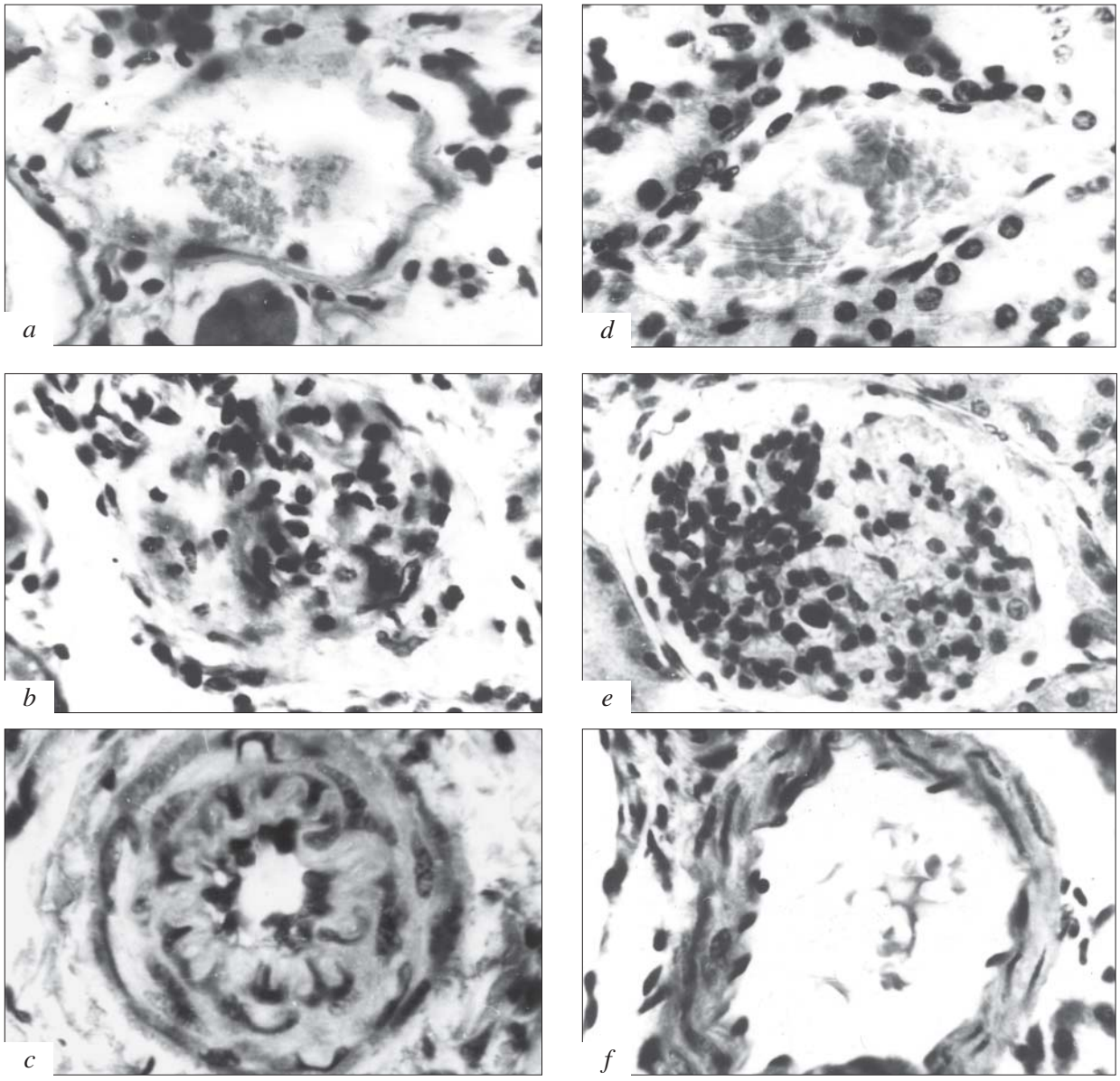

Fig. 2. Compartments of the renal vascular bed during experimental pulmonary stenosis (*a-c*) and after its correction (*d-f*). Thickening of the wall of the interlobular vein due to excess growth of connective tissue and hypertrophy of smooth muscle cells (6 months, *a*); anemia and sclerosis of the renal glomerulus (12 months, *b*); hypertension, narrowing of the lumen, and thickening of the wall of the interlobular artery (10 months, *c*); thinning of the wall of the interlobular vein due to atrophy of smooth muscle cells and fibrous structures (6 months after surgical correction, *d*); recovery of blood filling in several capillary loops of the renal glomerulus (12 months, *e*); decrease in the tone, widening of the lumen, and thinning of the wall of the interlobular artery (12 months, *f*). Hematoxylin and eosin staining, ×400.

Our results suggest that pulmonary stenosis is accompanied by structural reconstruction of the vascular system, which results from functional overload of the right ventricle and abnormal blood outflow from the kidneys [2,14]. The venoarterial reaction [2] suggests that the increase in the tone of arteries is accompanied by an increase in their resistance [10,11]. These changes contribute to reduction of blood pressure in glomerular capillaries, which prevents the development of severe dysfunction [7]. Under conditions of hypertension, the development of circular muscles in renal arteries with different degree of branching corresponds to functional load. The wall of arteries is thickened. However, this compensatory reaction is insufficient to protect the microcirculatory bed in the kidneys. It determines the formation of bands of oblique and longitudinal smooth muscles in the intima of renal arteries. They appear due to migration of smooth muscle cells from the media [5]. Pulmonary stenosis in animals is followed by impairment of renal hemodynamics, which results in activation of se-

TABLE 2. Area of the Cross Section in Renal Arteries under Control Conditions, during Experimental Pulmonary Stenosis, and after Stenosis Correction (μ^2, $M \pm m$)

Experimental conditions	Branching of arterial vessels			
	ILBA	AA	ILLA	arteries
Control	27 150±564	5620±168	2012±58	420±15
PS	77 300±4819***	9040±575***	2635±69***	600±11***
PS+C	58 640±3680***++	6396±850+	2198±34*+++	470±5**+++

Note. *p<0.01, **p<0.002, and ***p<0.001 compared to the control; +p<0.02, ++p<0.01, and +++p<0.001 compared to PS.

veral protective mechanisms and remodeling of various compartments in the renal vascular bed.

Correction of this experimental defect led to recovery of blood outflow from the kidneys [8] and regression of morphological changes in veins, arteries, and glomeruli.

Our results show that surgical correction of pulmonary stenosis prevents adaptive and pathological reconstruction of the renal vascular bed and promotes reparative processes.

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