# Method of Experimental Constriction of Renal Artery for Modeling of Renovascular Hypertension in Rats

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We propose a method of constriction of the renal artery consisting in pulling of a loop of isolated artery into a thin plastic tube with calibrated inner diameter. This method can be used in experiments with constriction of other small blood vessels to diminish the local blood flow.

**Key Words:** *renal artery; renovascular hypertension; arterial pressure; myocardial hypertrophy; rat*

Renovascular hypertension is a widely spread form of symptomatic arterial hypertension in humans [3,4]. For modeling of renovascular hypertension and concomitant left ventricular hypertrophy, the researchers constrict the renal artery according to model of Goldblatt [5,6]. There are several techniques of graduated constriction of the artery for modeling renovascular hypertension in animals [1]. However, these methods have certain limitations in small laboratory animals — specifically, in the rodents: troublesome attachment of the constricting clamp, poor efficiency, operation complexity, laborious production, and high price. Our aim was to develop a simple and easy method of graduated and controlled constriction of the renal artery in rats for modeling chronic renovascular hypertension.

## MATERIALS AND METHODS

For constriction of the renal artery [2], the loop of folded-in-two silk thread 1 tunneled through a plastic tube is inserted by the ends of silk thread 2 preliminary passed under the prepared artery (Fig. 1). Then the ends of thread 1 are pulled thereby towing both ends of thread 2 into the plastic tube. After passing the thread 2 across the tube, its protruding ends are pulled with small effort while supporting the tube cautiously. This maneuver pulls the folded-in-two artery into the tube (Fig. 1). Then the ends of thread 2 are cut, leaving its short piece in the space between arterial bend and the flange of the tube, which prevents slip of the vessel from the tube. To constrict the artery in a graduated and controlled mode, the diameter of plastic tube should be chosen with due account of the fact that it must accommodate folded-in-two artery.

The experiments with modeling renovascular hypertension were carried out under ether anesthesia on male ($n$=30) and female ($n$=50) Wistar rats aging 6-11 months and weighing 170-375 g (239±49 g). The plastic tube to constrict the left renal artery by the above technique was made of insulating sleeve of a wire with the length of 1.5-2.0 mm and internal diameter of 0.5 mm. One month after surgery, blood pressure in the abdominal artery was measured invasively with an EAGLE 1000 diagnostic monitor. Then the weights of the heart and kidneys were determined. The control group included age-matched normotensive male ($n$=15) and female ($n$=13) rats weighing 200-330 g (250±35 g). The data were processed statistically using Student's $t$ test and presented as $M\pm m$.

## RESULTS

Arterial hypertension with systolic pressure surpassing 130 mm Hg developed in 74% experimental rats (38 females and 21 males, Table 1). The mean values of systolic, diastolic, pulse, and mean arterial pressure were 150±16, 93±14, 56±8, and 112±14 mm Hg, re-

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**TABLE 1**. Left Ventricle Hypertrophy in Rats with Different Degree of Arterial Hypertension (*M*±*m*)

| Systolic pressure, mm Hg | Mean arterial pressure, mm Hg | Body weight, g | Weight of left ventricle | |
|---|---|---|---|---|
| | | | absolute, mg | relative, % |
| 105-126, control (13/15) | 87±5 | 250±35 | 640±73 | 0.258±0.026 |
| 130-139 (9/7) | 99±5* | 247±43 | 696±84** | 0.286±0.036* |
| 140-149 (9/6) | 107±5* | 242±57 | 708±148** | 0.295±0.029* |
| 150-159 (7/4) | 112±5* | 238±38 | 745±104* | 0.317±0.049* |
| 160-169 (8/1) | 122±5* | 205±24* | 681±97 | 0.333±0.037* |
| 170-190 (5/3) | 141±9* | 257±54 | 834±86* | 0.330±0.038* |

**Note.** Numbers of females/males are shown in parentheses. *$p<0.01$, **$p<0.05$ compared to the control.

spectively, which significantly differed from the corresponding values in normotensive rats 115±5, 73±6, 43±6, and 87±5 mm Hg. During two weeks after surgery, 11% rats (4 females, 5 males) died for unknown reasons. In 15% rats (5 females, 7 males) arterial hypertension did not develop, which probably resulted from insufficient constriction of the renal artery due to mismatch in the diameters of the plastic tube and renal artery. In these rats, the mean values of systolic, diastolic, pulse, and mean arterial pressure were 118±8, 72±4, 46±8, and 87±4 mm Hg, respectively.

The development of arterial hypertension resulted in hypertrophy of the left ventricle (Table 1), atrophy of the left kidney, and hypertrophy of the right kidney (Table 2). In hypertensive rats, the absolute and relative weight of the left ventricle surpassed the control by 14 and 20% ($p<0.01$, Table 2). The weight of the right ventricle in hypertensive rats did no significantly differ from the corresponding control values. The decrease in the left kidney weight was accompanied by a compensatory increment in the weight of the right kidney, so the intergroup difference in the total weight of both kidneys was insignificant.

During the development of arterial hypertension, hypertrophy of the left ventricle was more pronounced in females. In hypertensive females the relative weight of the left ventricle (0.327±0.036%) was greater than in control females (0.271±0.027%) by 20% ($p<0.01$). Similarly, in hypertensive males, the relative weight of the left ventricle (0.276±0.037%) was greater than in control males (0.247±0.019%) by 12% ($p<0.01$). This difference was caused by greater rise in the mean arterial pressure during the development of arterial hypertension in females (by 35%) compared to males (by 24%, $p<0.01$). The mean arterial pressure in experimental and control females was 113±14 and 84±4 mm Hg, respectively, while the corresponding values in males were 111±15 and 89±7 mm Hg.

Thus, the use of original technique for graduated constriction of the renal artery induced the development of renovascular hypertension in 74% rats, which was accompanied with corresponding morphometric alterations: atrophy of the kidney supplied by operated artery, hypertrophy of the contralateral kidney, and hypertrophy of the left ventricle of the heart. The latter was caused by renovascular hypertension, and was more pronounced in females. The described technique of renal artery constriction is simple, easy, and efficient method to model renovascular hypertension and hypertrophy of left ventricle of the heart in the rats. However, similarly to other methods of renal artery constriction, the efficiency of the described technique depends on close match of arterial diameter (determined by the age, sex, and the weight of the animals) to the diameter of vascular constricting clamp. In addition, this match depends on biological features of experimental animals. The developed method can be used in experiments with constriction of small arteries

**TABLE 2**. Morphometric Changes in the Heart and Kidneys during the Development of Renovascular Hypertension in Rats (*M*±*m*)

| Index | Control rats (*n*=28) | Hypertensive rats (*n*=59) |
|---|---|---|
| Body weight, g | 250±35 | 239±46 |
| Left ventricle | | |
| absolute weight, mg | 640±73 | 728±123* |
| relative weight, % | 0.258±0.026 | 0.309±0.0.43* |
| Right ventricle | | |
| absolute weight, mg | 166±28 | 166±39 |
| relative weight, % | 0.067±0.011 | 0.070±0.013 |
| Left kidney | | |
| absolute weight, mg | 746±114 | 278±140* |
| relative weight, % | 0.327±0.029 | 0.114±0.046* |
| Right kidney | | |
| absolute weight, mg | 790±125 | 1159±247* |
| relative weight, % | 0.346±0,037 | 0.482±0.067* |

**Note.** *$p<0.01$ compared to the control.

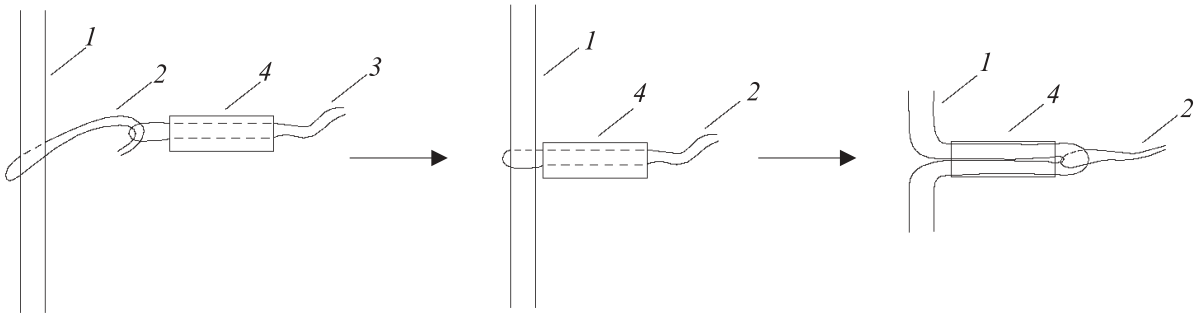


**Fig. 1**. Sequence of procedures to impose the vascular graduated constricting clamp on renal artery in rat. *1*) renal artery; *2*) and *3*) thin silk threads, *4*) plastic tube.

in small laboratory animals to limit the blood supply to the target organ and to produce graduated regional ischemia.

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