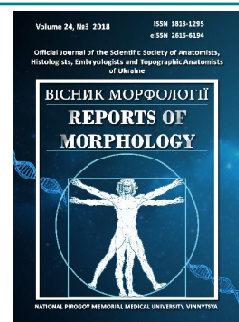




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Changes in the sizes of the kidney after contralateral nephrectomy in the experiment

Monastyrskiy V.M.

National Pirogov Memorial Medical University, Vinnytsya, Ukraine

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CORRESPONDING AUTHOR

e-mail: vova.monastirskiy@gmail.com
Monastyrskiy V.M.

The evaluation of renal measurements such as length, width and thickness, volume is important in the diagnosis and treatment of many renal disorders, since there is a close relationship between the sizes of the kidneys and its function. The purpose of the study was to establish and compare during the postoperative period changes in the mass and sizes of the kidney left after nephrectomy in the sexually mature male rats. An experimental study was carried out on 84 sexually mature white male rats weighing 178-194 grams. Animals were divided into two groups: control (42 rats) and experimental (42 rats). In the control group, the animals under ketamine anesthesia were followed by an abdominal cavity dilation, after which the abdominal wall was applied in a row. All animals of the experimental group performed surgical intervention - nephrectomy of the left kidney. The animals were withdrawn from the trial by intra-pleural administration of thiopental-sodium 50 mg/kg after 7, 14, 21, 30, 90 days after nephrectomy. Macroscopic evaluation and description of the kidneys of animals was performed after their removal. Their weight was determined on the laboratory scale of HLR-200 up to 0.1 mg, and the length, width and thickness of the organ were measured with the help of a caliper to an accuracy of 0.05 mm. Calculated the volume of the kidney. The statistical analysis of the obtained results was carried out using the program STATISTICA 5.5 using parametric methods for evaluating the results. It was established that the mass, length, width, thickness and volume of the kidney of animals in the experimental group, as compared with the control group, were statistically significantly higher in all terms of observation. The fraction of the growth of the width and thickness of the single kidney of animals in the experimental group compared with the control animals in the animals was statistically significantly greater than the proportion of kidney growth during the postoperative period. It was found that the largest increase in the mass and thickness of the kidney, as compared with the control group, was observed after 30 days of the postoperative period, and the greatest increase in the length and width of the kidney, as compared with the control group, was observed after 14 days of the postoperative period.

Keywords: single kidney, nephrectomy, kidney sizes, experiment, sexually grown rats.

Introduction

Despite recent developments in systemic therapy, nephrectomy is still considered the only reliable treatment for kidney cancer, and as a result, the number of performed nephrectomies will increase [25, 28].

The question of the compensation of structure and function in the loss of one of the paired organs is of interest to clinical practice, in this connection, the attention of researchers to the experimental study of the kidneys remaining after the removal of contralateral.

Several studies have found that body weight and body mass index are independent predictors of the development of chronic kidney disease after nephrectomy [23, 29]. The

risk of chronic kidney disease following nephrectomy with regard to kidney cancer has been confirmed in several retrospective studies of populations [5, 24]. The risk of terminal renal dysfunction in renal donor increases with age [17]. It is established that the larger the mass of the kidneys, the greater the predictability of survival after nephrectomy in the elderly [26].

The evaluation of renal measurements, such as length, width and thickness, is important in the diagnosis and treatment of many renal disorders, since there is a close relationship between the size of the kidney and its function [22]. According to researchers after nephrectomy, renal

function of the contralateral kidney decreases in patients regardless of the choice of access (open, laparoscopic) [11] and depends on the volume of loss of renal parenchyma [2]. The volume of kidneys is considered to be the most accurate indicator of the size of the kidneys. Recent studies have shown that kidney volume is an optimal parameter for predicting renal function [8, 12]. Changing the size of the kidneys from one survey to another can be an important indicator of the presence or progression of the disease. The increase in the volume of the kidneys was observed to a greater extent after nephrectomy than after renal resection [19].

We have established the patterns of possible displacements of a single kidney with an increase in its mass after the removal of contralateral using mathematical modeling [13]. The study of the angles of inclination of a single kidney remaining after contralateral nephrectomy, in the frontal, sagittal, and horizontal planes, reveals certain patterns with magnetic resonance imaging depending on somatotypes [21].

According to scientists, the mean values of length, width and thickness of the kidneys should be determined for each population [1, 16]. It is especially important to know the volume of the kidney, the accuracy of which depends on the technique of morphometry, the use of magnetic resonance imaging [15].

Changes in the size of kidney after nephrectomy, direction, size, speed and duration are of value for predicting the change of position, function and possible pathology of the kidney.

The *aim* of the study - to establish and compare changes in organometric parameters of the kidney left after nephrectomy in sexually mature male rats during the postoperative period.

Materials and methods

Experimental study was performed on 84 sexually mature white male rats weighing 178-194 grams, which were kept on the standard diet in vivarium of National Pirogov Memorial Medical University.

Animal retention and manipulation were conducted in accordance with the "General Ethical Principles of Animal Experiments" adopted by the First National Congress on Bioethics (Kyiv, 2001), and were guided by the recommendations of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1985) and the provisions of the "Rules for Preclinical Safety Assessment of Pharmacological Products (GLP)".

All animals were divided into two groups: control (42 rats) and experimental (42 rats). In the control group all animals were performed abdominal section, followed by sewn up of abdominal wall layers under anesthesia by ketamine.

All animals of the experimental group were performed surgical intervention - nephrectomy of the left kidney. Rats

under general intra-muscle anesthesia (aminazine 10 mg/kg and ketamine 20 mg/kg) were treated with left-sided nephrectomy by crossing the renal leg between two ligatures and then removing the organ. The operation was carried out as follows. The animal was inserted and fixed with soft straps for the limbs in the position on the back to the operating table. Pararectal incision was done in the length up to 3-5 cm in layers for opening an abdominal cavity. The small intestine with a gauze napkin was pulled down and medially. Left kidney and its vessels were isolated from the surrounding tissues. The kidney was molded into the wound and isolated from the fatty tissue of the upper third of the ureter. A clamping device was applied to the ureter, under which it was tied with a catgut ligation and then crossed under a clamp. In a droop way, they isolated the renal artery and vein and imposed two clips, between which they were crossed. The kidney was removed, and the stump of the blood vessels were tied together by catgut ligatures. The layer of the wound was tightly sewn.

The animals were withdrawn from the trial by intra-pleural administration of thiopental-sodium 50 mg/kg after 7, 14, 21, 30, 90 days after nephrectomy.

Macroscopic evaluation and description of the kidneys of animals was performed after their removal. Their weight was determined on the laboratory scale of HLR-200 up to 0.1 mg, and the length, width and thickness of the organ were measured with the help of a caliper to an accuracy of 0.05 mm. The volume of the kidney [4] was calculated according to the formula: $V=0.523?a^2b^?c$, where a is length, b is width, c is the thickness of the kidney. It is believed that the method for assessing the volume of the kidney after its hypertrophy using the ellipsoid volume formula is the most accurate and useful for predicting the functional status of the kidney [18].

The kidney mass index was calculated by obtaining a percentage relationship between the weight of the kidney and the weight of the body of the rat being examined. In the investigated animals of the experimental group, the index of hypertrophy of the kidney was calculated. It was calculated by obtaining a percentage correlation between the weight of a single kidney and the weight of the two kidneys of the control group rats at the given time of the study.

Statistical analysis of the obtained results was carried out using the program STATISTICA 5.5 using parametric and non-parametric methods for evaluating the obtained results.

Results

First of all, it is necessary to note changes in the body weight of the animals of the control and experimental groups. At the beginning of the study, no statistically significant change in body mass was detected. After 7 days, the body weight of the experimental group animal was 4.01% lower than the control group animal. Subsequently, the comparison of body mass data showed a lower body weight of experimental group animals in 14 days by 3.67%, in 21 days - by 4.36%, after 30 days - by 5.02%, after 60 days - by 3.18%,

Table 1. Weight of the body and the right kidney of the mature rat of the control and experimental groups.

The term of the postoperative period	Control group (n=42)			Experimental group (n=42)		
	Animal weight (g)	Kidney mass (g)	Kidney Mass Index (%)	Animal weight (g)	Kidney mass (g)	Kidney Mass Index (%)
1 day	184.8±2.9	0.892±0.028	0.483±0.007	185.6±3.2		
7 days	202.4±4.6*	0.975±0.008*	0.493±0.005	194.3±3.2*#	1.027±0.026#	0.532±0.013#
14 days	218.5±3.5*	1.077±0.017*	0.501±0.003	210.5±3.6*#	1.250±0.020*#	0.596±0.011*#
21 days	231.0±4.9*	1.165±0.037*	0.505±0.008	220.9±4.9*#	1.662±0.072*#	0.656±0.031*#
30 days	245.6±4.7*	1.268±0.026*	0.510±0.008	233.3±5.9*#	1.710±0.060#	0.721±0.018*#
60 days	262.4±3.7*	1.352±0.022*	0.510±0.002	254.1±3.8*#	1.757±0.010*#	0.700±0.005#
90 days	274.7±4.7*	1.497±0.023*	0.545±0.002*	265.5±3.7*#	1.858±0.013*#	0.700±0.013#

Note: * - statistically significant differences (p<0.05) according to the Mana-Whitney criterion between the corresponding indicators in comparison with the indicators of the previous term of research; # Are statistically significant differences (p <0.05) according to the Mana-Whitney criterion between the respective indices compared with the control animals.

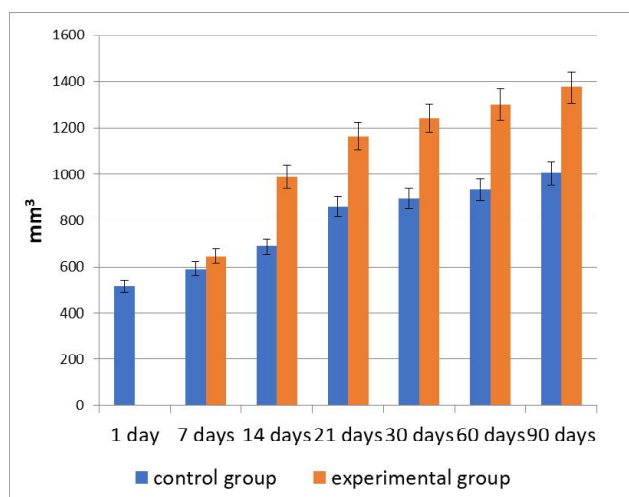


Fig. 1. Volume of the right kidney of the sexually mature rats in different terms after the operation of the control and experimental groups.

after 90 days - by 3.34% compared with similar terms in the control animals. The weight of the kidney increased both in the control and in the experimental groups. However, in the experimental group, the mass of the right kidney was greater compared to the weight of the kidney of the control group in the similar term: after 7 days - 4.85%, 14 days - by 13.6%, in 21 days - by 25.52%, through 30 days - by 25.73%, 60 days - by 24.58%, after 90 days - by 19.35%. Thus, the peak growth rate of the kidney mass in the experimental group relative to the control group data was observed after 30 days (Table 1).

The kidney mass index of the experimental group significantly differed from that of the control group. Thus, in the control group it ranged from 0,49% to 0,54%, and in the experimental group - from 0,53% to 0,72%. The peak in the control group in the 90th day of the experiment, in the experimental group - at 30 days.

The integral index of kidney size - volume, compared with the data at the beginning of the experiment, changed as follows: after 7 days, it increased by 12.43% in the control

group and by 19.87% in the experimental group, after 14 days, it increased by 24.78% and by 47.69%, respectively, in 21 days - by 39.90% and 55.48% respectively, after 30 days - by 42.22% and 58.33% respectively, after 60 days - by 44.54% and 60.23% respectively, after 90 days - by 48.40% and 62.39% respectively (Fig. 1).

The length of the right kidney compared with the same indicator of animals in the control group was greater after 7 days after nephrectomy by 2.87%, after 14 days - by 6.21%, 21 days - by 3.86%, 30 days later - by 2, 65%, after 60 days - by 4.62%, after 90 days - by 5.34%. The width of the right kidney was greater after 7 days after nephrectomy by 3.38%, after 14 days - by 13.99%, after 21 days - by 12.16%, after 30 days - by 13.24%, after 60 days - by 12,88%, after 90 days - by 11,69%. The thickness of the right kidney was greater after 7 days after nephrectomy by 2.51%, after 14 days - by 13.76%, in 21 days - by 12.32%, after 30 days - by 14.57%, after 60 days - by 13,68%, after 90 days - by 12,74% (Fig. 2).

Discussion

Compensatory and adaptive reactions of a single kidney after removal from the body of the contralateral form part of the general system of adaptation of the body in cases of its damage. We have established an increase in the mass of the right kidney of rats after the removal of the left kidney, which reached its peak after 30 days, consistent with the data of other authors [7]. By comparing the mass of a single kidney remaining after contralateral nephrectomy, with the weight of two kidneys of the control group in a given experiment period, we found that the index of hypertrophy of the kidney during the postoperative period ranged from 52.35% to 65.22%. The maximum index of kidney hypertrophy was observed in the period of 30 days. In the future there was a decrease in the index. Several authors note that the maximum hypertrophy of a single kidney, after removal of contralateral, is 77% of the sum of volumes of two kidneys in the control group [10].

The fraction of the growth of the width and thickness of the single kidney of animals in the experimental group

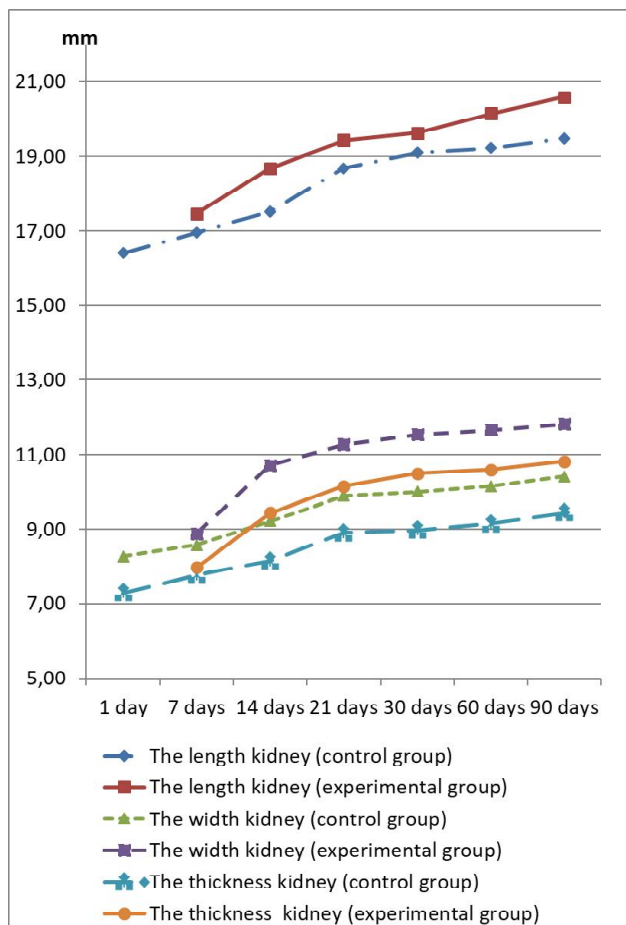


Fig. 2. Length, width and thickness of the right kidney of the control and experimental groups during the experiment.

compared with the control animals in the animals was statistically significantly greater than the proportion of kidney growth during the postoperative period. According to scientific literature, the length of the kidneys directly correlates with the clearance of creatinine [6], and the width of the kidneys better reflects the influence of environmental factors than the length of the kidneys. The results of the research show that the width of the kidney, and not the length, is a predictor of renal insufficiency [27].

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Adjustment-compensatory changes after the performed nephrectomy were manifested in the early stages of the experiment by compensatory hypertrophy of the area of the renal cortex and the reorganization of the vascular bed. In the later stages of the experiment, part of the nephrons develop morpho-functional changes of a destructive nature [14]. We have found that at the 7th and 14th day after nephrectomy in the vascular glomeruli of the renal corpuscles hemocapillaries have blood-filling enlightenment. On the 21st day after the experimental nephrectomy there are significant changes in the vessels and structural components of the nephrons. There is swelling of the stroma, focal infiltration. On the 30th and 60th day organelles are destructively altered and poorly detected against the background of osmophilic hyaloplasm. Membrane folds in the basal region of these cells and microvilli on the apical surface are affected [20].

The significance of damage to podocytes and swelling of the kidneys as a universal mechanism of development of renal failure [3] has been confirmed today. The relevance of the study of the dependence of the renal function on its size is established [9].

Conclusions

1. The weight, length, width, thickness and volume of the kidneys of animals in the experimental group were statistically significantly higher in all terms of observation compared with the control group ($p < 0.05$).
2. The increase in the width and thickness of the single kidney of animals in the experimental group compared with the control animals was statistically significantly greater than the proportion of kidney growth during the postoperative period.
3. The largest increase in the mass and thickness of the kidney, as compared to the control group, was observed after 30 days of the postoperative period.
4. The largest increase in the length and width of the kidney, as compared to the control group, was observed after 14 days of the postoperative period.

In the future, it is planned to compare changes in organometric parameters of the kidney, remaining after nephrectomy, in non-sexually mature and mature animals.

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ЗМІНИ РОЗМІРІВ НИРКИ ПІСЛЯ НЕФРЕКТОМІЇ КОНТРАЛАТЕРАЛЬНОЇ В ЕКСПЕРИМЕНТІ

Монастирський В.М.

Оцінка ниркових вимірювань, таких як довжина, ширина і товщина, об'єм важлива при діагностиці і лікуванні багатьох ниркових розладів, оскільки існує тісний зв'язок між розміром нирок і їх функцією. Мета дослідження - встановити та порівняти протягом післяопераційного періоду зміни маси та розмірів нирки, що залишилась після нефректомії, у статевозрілих щурів-самців. Експериментальне дослідження виконано на 84 статевозрілих білих щурах-самцях масою 178-194 грамів. Тварин розподілили на дві групи: контрольну (42 щури) та дослідну (42 щури). У контрольній групі тваринам під кетаміновим знеболенням проводили розтин черевної порожнини, після чого поширено ушивали черевну стінку. Усім тваринам дослідної групи виконували оперативне втручання - нефректомію лівої нирки. Тварин виводили з досліду шляхом

внутриплеврального введения тiopенталу-натрия 50 мг/кг через 7, 14, 21, 30, 90 дiб пiсля нефрeктомiї. Макроскопiчну оцiнку та описання нирок тварин проводили пiсля їх вилучення. Масу нирок визначали на лабораторних вагах ВЛР-200 з точнiстю до 0,1 мг, довжину, ширину i товщину - за допомогою штангенциркуля з точнiстю до 0,05 мм. Розраховували об'єм нирки. Статистичний аналіз отриманих результатiв проведений iз застосуванням програми "STATISTICA 5.5" з використанням параметричних методiв оцiнки отриманих результатiв. Встановлено, що маса, довжина, ширина, товщина та об'єм нирки тварин дослiдної групи, порiвняно з контрольною групою, були статистично значуще бiльшими у всi термiни спостереження. Частка зростання ширини та товщини єдиної нирки тварин дослiдної групи у порiвнянні з показниками у тварин контрольної групи була статистично значуще бiльше, нiж частка зростання довжини нирки пiд час пiсляоперацiйного перiоду. Встановлено, що найбільша величина приросту маси та товщини нирки, порiвняно iз показниками контрольної групи, спостерiгалася через 30 дiб пiсляоперацiйного перiоду, а найбільша величина приросту довжини та ширини нирки, порiвняно з показниками контрольної групи, спостерiгалася через 14 дiб пiсляоперацiйного перiоду.

Ключові слова: єдина нирка, нефрeктомiя, розміри нирки, експеримент, статевозрiлі щури.

ИЗМЕНЕНИЯ РАЗМЕРОВ ПОЧКИ ПОСЛЕ НЕФРЭКТОМИИ КОНТРАЛАТЕРАЛЬНОЙ В ЭКСПЕРИМЕНТЕ

Монастырский В.Н.

Оценка почечных измерений, таких как длина, ширина и толщина, объем важна при диагностике и лечении многих почечных расстройств, поскольку существует тесная связь между размерами почек и их функций. Цель исследования - установить и сравнить в течение послеоперационного периода изменения массы и размеров почки, оставшейся после нефрeктомии, у половозрелых крыс-самцов. Экспериментальное исследование выполнено на 84 половозрелых белых крысах-самцах массой 178-194 граммов. Животных разделили на две группы: контрольную (42 крысы) и опытную (42 крысы). В контрольной группе животным под кетаминowym обезболиванием проводили вскрытие брюшной полости, после чего послойно ушивали брюшную стенку. Всем животным опытной группы выполняли оперативное вмешательство - нефрeктомия левой почки. Животных выводили из опыта путем внутриплеврального введения тiopентала натрия 50 мг/кг через 7, 14, 21, 30, 90 суток после нефрeктомии. Макроскопическую оценку и описание почек животных проводили после их удаления. Определяли их массу на лабораторных весах ВЛР-200 с точностью до 0,1 мг, измеряли длину, ширину и толщину с помощью штангенциркуля с точностью до 0,05 мм. Рассчитывали объем почки. Статистический анализ полученных результатов проведен с применением программы "STATISTICA 5.5" с использованием параметрических методов оценки полученных результатов. Установлено, что масса, длина, ширина, толщина и объем почки животных опытной группы по сравнению с контрольной группой, были статистически значимо больше на всех сроках наблюдения. Доля роста ширины и толщины единственной почки животных опытной группы по сравнению с показателями у животных контрольной группы была статистически значимо больше, чем доля роста длины почки в течение послеоперационного периода. Установлено, что наибольшая величина прироста массы и толщины почки по сравнению с показателями контрольной группы, наблюдалась через 30 суток послеоперационного периода, а наибольшая величина прироста длины и ширины почки по сравнению с показателями контрольной группы, наблюдалась через 14 дней послеоперационного периода.

Ключевые слова: единственная почка, нефрeктомия, размеры почки, эксперимент, половозрелые крысы.