https://doi.org/10.17816/uroved42529

HYPERTENSIVE NEPHROPATHY AS AN OUTCOME OF UNILATERAL NEPHRECTOMY IN KIDNEY CANCER

© *I.I. Tityaev [1], S.S. Andreev [1, 2], S.V. Andreeva [1], K.V. Udalov [1, 2], D.S. Kasyanov [1]*

[1] City Clinical Hospital No. 1, Novosibirsk, Russia;
[2] Novosibirsk State Medical University of the Ministry of Healthcare of the Russian Federation, Novosibirsk, Russia

For citation: Tityaev II, Andreev SS, Andreeva SV, et al. Hypertensive nephropathy as an outcome of unilateral nephrectomy in kidney cancer. *Urology reports (St. Petersburg)*. 2020;10(3):229-234. https://doi.org/10.17816/uroved42529

Received: 19.08.2020 Revised: 26.08.2020 Accepted: 23.09.2020

Aim. To study the adaptive mechanisms of structural and functional changes in a single kidney after nephrectomy for kidney cancer.

Materials and Methods. A total of 179 operations of two types were performed: nephrectomy and kidney resection in patients with cancerous lesions. Postoperative ultrasound was performed – size control and dopplerography of the vessels of the contralateral single kidney, monitoring-control of blood pressure.

Results. In case of kidney resection, the adaptive mechanisms controlling the volume of functioning tissue are preserved. The load on the organ remains minimal and physiological, and is not redistributed, blood pressure remains close to baseline. Nephrectomy does not lead to functional changes in a single kidney, but to adaptive and pathophysiological structural damage as a result of increased plasma pressure, organ "reboot", its vicarious hypertrophy, which is accompanied by venous edema of interstitium as a pressure factor on the tissue, increased tone of arterioles, the development of secondary organ ischemia, circulatory hypoxia and increased blood pressure. All this fits into the clinical picture of hypertensive nephropathy.

Conclusions. The potential risk of hypertension and hypertensive nephropathy in patients undergoing nephrectomy, compared with patients after organ-saving surgery, is significantly higher. One of the most important manifestations of hypertension in the elderly is a violation of the structure and function of "target organs", which include: the brain, heart, blood vessels, kidney. Nephrectomy forms a pathological vicious circle, contributing to the development and further progression of renal and cardiovascular failure.

Keywords: hypertensive nephropathy; kidney cancer; nephrectomy; kidney resection; vicar hypertrophy; arterial hypertension.

ГИПЕРТЕНЗИВНАЯ НЕФРОПАТИЯ КАК ИСХОД ОДНОСТОРОННЕЙ НЕФРЭКТОМИИ ПРИ РАКЕ ПОЧКИ

© *И.И. Титяев [1], С.С. Андреев [1, 2], С.В. Андреева [1], К.В. Удалов [1, 2], Д.С. Касьянов [1]*

[1] Государственное бюджетное учреждение здравоохранения Новосибирской области «Городская клиническая больница № 1», Новосибирск;
[2] Федеральное государственное бюджетное образовательное учреждения высшего образования «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Новосибирск

Для цитирования: Титяев И.И., Андреев С.С., Андреева С.В., и др. Гипертензивная нефропатия как исход односторонней нефрэктомии при раке почки // Урологические ведомости. – 2020. – Т. 10. – № 3. – С. 229–234. https://doi.org/10.17816/uroved42529

Поступила: 19.08.2020 Одобрена: 26.08.2020 Принята к печати: 23.09.2020

Цель. Изучить адаптационные механизмы структурно-функциональных изменений в единственной почке после нефрэктомии по поводу рака почки.

Материалы и методы. Больным раком почки выполнены 179 оперативных вмешательств двух видов: нефрэктомия и резекция почки. В послеоперационном периоде выполняли ультразвуковое исследование с оценкой

размеров и доплерографию сосудов контралатеральной единственной почки, проводили мониторинг артериального давления (АД) оперированных больных.

Результаты и обсуждение. В случае резекции почки адаптационные механизмы, контролирующие объем функционирующей ткани, сохранены. Нагрузка на орган остается минимальной и физиологической, и не перераспределяется. АД не изменяется. Нефрэктомия ведет не к функциональным изменениям единственной почки, а к адаптационно-патофизиологическим структурным повреждениям в результате повышения плазменного давления, «перезагрузки» органа, его викарной гипертрофии, что сопровождается венозным отеком интерстиция в качестве фактора давления на ткань, повышением тонуса артериол, развитием вторичной ишемии органа, циркуляторной гипоксией и повышением АД. Все это укладывается в картину гипертензивной нефропатии.

Заключение. Потенциальный риск развития артериальной гипертензии и гипертензивной нефропатии у пациентов, перенесших нефрэктомию, по сравнению с пациентами после органосохраняющей операции, существенно выше. Одним из важнейших проявлений артериальной гипертензии у пожилых людей является нарушение структуры и функции «органов-мишеней», к которым относятся: головной мозг, сердце, сосуды, почки. Нефрэктомия формирует патологический замкнутый круг, способствующий развитию и дальнейшему прогрессированию почечной и сердечно-сосудистой недостаточности.

Ключевые слова: гипертензивная нефропатия; рак почки; нефрэктомия; резекция почки; викарная гипертрофия; артериальная гипертензия.

INTRODUCTION

Kidney cancer is one of the most common neoplasms of the urinary system [1]. Worldwide, the number of new cases of renal cell carcinoma (RCC) registered annually is on average approximately 209 thousand, which amounts to 2%–3% in the range of malignant neoplasms in adults, and up to 102 thousand patients die annually. RCC ranks tenth in terms of morbidity among all malignant neoplasms and first in terms of growth rates, as this indicator was 41.35% over the past 5 years [2–4].

In Russia, of all malignant neoplasms, RCC constitutes 4.3% in men and 2.9% in women, and it is more often diagnosed in the decades 6 and 7 of life; the median age of patients at the time of diagnosis is 61 years. The prevalence of RCC is 96.9 per 100 thousand populations, and mortality is 5% [1].

The foremost method of treatment remains surgery. A distinctive feature of modern surgery development is organ-sparing treatment.

The development of hardware in diagnostics have enabled the implementation of mass screening of the population, which in turn have increased the detection rate of early stage RCC and made organ-sparing surgeries possible, with their share reaching 32% [3]. Resection of the kidney is accompanied by the occlusion of the organ vessels. At the same time, great importance is associated with the time of ischemia both in the development of acute kidney damage and the transition of the disease into a chronic form [5, 6]. A decrease in the number of functioning nephrons and/or hypoxic damage to the remaining ones form or cause the progression of chronic kidney disease (CKD), which is an independent factor in the occurrence of cardiovascular complications [7–10].

Nevertheless, the treatment of choice in most cases of kidney cancer remains radical nephrectomy. Studying the compensatory mechanisms of the remaining kidney and the body as a whole after nephrectomy is a pressing task in current medicine. Further, when performing these surgeries, the elderly age of patients and the associated co-morbidity should be taken into account.

Nowadays, fewer cancer patients die from kidney cancer and more from cardiovascular diseases and CKD. As a factor in the natural adaptation of the organ in response to increased load after nephrectomy for cancer, compensatory hypertrophy of the kidney is considered quite acceptable. Vicarious hypertrophy can provide a high stability of homeostatic parameters for a prolonged period. Additionally, in clinical nephrology, many cases that indicate the progression of nephropathy in dyscirculatory or metabolic disorders of the kidney functional apparatus in elderly patients have been described, which lead to a disorder of plasma and platelet hemostasis (toward hypercoagulation). This is accompanied by renal tissue fibrosis [11, 12]. Disorders in the hemostatic system toward hypercoagulation constitute a risk factor in patients with malignant neoplasms.

All this requires active therapeutic and prognostic medical measures [13].

Renal pathology manifests itself with arterial hypertension syndrome; moreover, the causes of its occurrence are associated with the affected kidney. However, the question arises that, is an increase in blood pressure possible after nephrectomy due to the compensatory enhancement of the organ function due to overload?

The description of the mechanisms leading to CKD progression is also relevant. Nephrectomy has been proven to be a reliable aspect in CKD development, which increases the probability of metabolic complications, vascular diseases, and lethal outcome [11, 12]. It is logical to assume that the risk of CKD is prevented or reduced by preserving functioning tissue during kidney resection. Nevertheless, an important factor of kidney damage is systemic hypertension, the long-term effect of which results in the remodeling of the organ tissue accompanied by structural and functional rearrangements and the formation of nephrosclerosis, namely, preglomerular arteriolosclerosis and tubulointerstitial fibrosis.

An assessment of the adaptive mechanisms of the structural and functional state of the solitary contralateral kidney (after nephrectomy for cancer) is of considerable interest due to the complexity of unambiguous interpretation.

This study aimed to analyze the structural and functional changes in the solitary kidney as a compensation mechanism after nephrectomy for kidney cancer.

MATERIALS AND METHODS OF RESEARCH

In the urological and oncourological departments, over an 8-year period, 179 patients with a diagnosis of stage 1–3 kidney cancer were followed up after surgical treatment. The exclusion criterion in the study was a history of arterial hypertension. Distribution of patients by gender showed 104 men and 75 women, and the age of the patients was 39–76 years, with mean age of 59.0 ± 10.8 years. The ratio of men and women was 1.1 : 1. The left kidney was most often affected (101 cases, 56.4%). Tumor sizes ranged from 1.0 to 12.0 cm. CKD was diagnosed in all patients, and three of them had decreased renal function to stage III CKD.

The degree of complexity of the planned kidney resection was determined as per the RENAL scale using computed or magnetic resonance imaging data of the retroperitoneal organs and averaged at 7.4 ± 0.8 points. All patients gave voluntary consent to the surgery and for participation in the study.

The patients underwent prevention of thromboembolic complications before the surgery, which comprised elastic compression of the lower extremities, pharmacological thromboprophylaxis, and early activation of patients in the postoperative period. Blood pressure monitoring, ultrasound examination of the size and structure of the kidneys, and Doppler sonography of the kidney vessels were performed as well as blood urea and creatinine parameters were monitored. Hemostasis was controlled over time during kidney resection, and nephrectomy and photobiomicroscopy of the bulbar conjunctiva and capillaroscopy of the subungual bed were performed during the follow-up period.

RESULTS AND DISCUSSION

In total, 36 (20.1%) nephrectomy surgeries and 143 (79.9%) kidney resections were performed in this study. A histological examination of tumors revealed clear cell renal cancer in 79% of cases. A tendency to an increase in blood pressure on days 2–4 after surgery was noted in 84% of patients who underwent nephrectomy, and in 14% of patients who underwent resection. In 56% of patients after nephrectomy, the levels of urea and creatinine in the blood increased already on day 2 after surgery, which returned gradually to normal on day 10–15 during the course of appropriate therapy.

Ultrasound examination on days 4–5 after surgery showed an increase in size of the solitary remaining kidney on average up to 4% of the initial value. After resection, there were no significant signs of vicarious hypertrophy. Doppler sonography of the vessels of the solitary kidney showed a tendency to increase renal blood flow rate up to 1.15 cm/s in 83.7% of cases. An increase in the resistance index was revealed, the value of which defines the state of the microvasculature and tone of the walls of the arterioles and capillaries. The resistance index of the main trunk of the renal artery was 0.72 ± 0.02 (with a norm of 0.62) whereas that of segmental arteries was 0.69 ± 0.01 (with a norm of 0.61) and that of interlobar arteries was 0.66 ± 0.04 (at a rate of 0.6).

Photobiomicroscopy of the bulbar conjunctiva and capillaroscopy of the subungual bed indicated a slowdown in the capillary blood flow and stasis of blood corpuscles in the microcirculation system. The hemodynamic parameters remained unchanged after the kidney resection in the contralateral organ.

Attention is drawn to initially pronounced fibrinogenemia and an increase in the level of soluble fibrin-monomer complex (SFMC). An increase in the SFMC level was registered when comparing the dynamics of thrombinemia in the early postoperative period. There is a more pronounced decrease in SFMC due to low molecular weight heparins used in the postoperative period, which is nevertheless higher than the control value for up to 10 days.

During the dispensary follow-up period from 2012 to the present, no cases of recurrence or progression of the tumor in kidney resection were recorded. Overall, 22 (61%) patients after nephrectomy and 59 (46%) patients after kidney resection were followed up. The median follow-up was 54.6 ± 21.4 months, and no significant differences between the groups were seen. In the solitary kidney after radical nephrectomy, rapid progression of CKD was noted in six patients, and in two patients compared with kidney resection. One patient from the radical nephrectomy group died during follow-up.

Functional and physiological restructuring of the solitary kidney after nephrectomy and restarting microhemocirculation and transcapillary metabolism are the major aspects of the pathological process, and these require targeted action within pathogenetic therapy. In the case of kidney resection, the adaptive mechanisms that control the volume of functioning tissue are preserved. The load on the organ remains minimal and physiological and is not redistributed; blood pressure remains at the initial level.

Nephrectomy does not lead to functional changes in the solitary kidney, but it does cause adaptive and pathophysiological structural damage due to increased plasma pressure, restarting of the organ, vicarious hypertrophy, tissue ischemia, and circulatory hypoxia accompanied by the increase in blood pressure. This forms a vicious circle, wherein the organ increases in volume, causing venous edema of the interstitium due to the pressure on the tissue, increase in the tone of arterioles, development of secondary tissue ischemia, circulatory hypoxia as an irritant to the cells of the juxtaglomerular apparatus, and increase in blood pressure. All this presents as a pattern of hypertensive nephropathy.

Patients with kidney cancer are initially at high risk of thromboembolic complications; further surgical intervention increases the level of the abovementioned markers of the hemostatic system, which then increases the risk of thrombogenesis in the microcirculation system and development of hemic hypoxia. This can also promote the development of chronic pyelonephritis, nephrosclerosis, and CKD.

Adaptive mechanisms compensate for organ functioning after kidney resection, the total load on the renal tissue remains within the physiological limits, and systemic BP does not change.

CONCLUSION

Compared with patients who undergo organ-sparing surgery, the potential risk of arterial hypertension and hypertensive nephropathy in patients with a history of nephrectomy is significantly higher. One of the most significant manifestations of arterial hypertension in elderly patients is impaired of structure and function of target organs including the brain, heart, blood vessels, kidneys. Simultaneously, the small vessels that make up the microcirculation system are affected, and due to age-related atherosclerosis, dystrophic, necrotic, and sclerotic changes, thereby aggravating the organism aging.

Nephrectomy leads to the formation of pathological vicious cycle that contributes to the development and further progression of renal and cardiovascular failure.

Nephrectomy, a method of forced radical intervention in the treatment of RCC, requires not only pathogenetically substantiated complex medical but also social and economic rehabilitation of patients with a solitary kidney, which cannot be considered complete as its functional load increased twofold.

REFERENCES

1. Лоран О.Б. Онкоурология сегодня: проблемы и достижения // Медицинский вестник. – 2007. – № 13. – С. 7–8. [Loran OB. Onkourologiya segodnya: problemy i dostizheniya. *Meditsinskiy vestnik*. 2007;(13):7-8. (In Russ.)]

2. Давыдов М.И., Аксель Е.М. Заболеваемость злокачественными новообразованиями населения России и стран СНГ в 2008 г. // Вестник РОНЦ им. Н.Н. Блохина РАМН. – 2010. – Т. 21. – № 2S1. – С. 52–86. [Davydov MI, Aksel' EM. Zabolevaemost' zlokachestvennymi novoobrazovaniyami naseleniya Rossii i stran SNG v 2008 g. *Herald of N.N. Blokhin Cancer Research Center RAMS*. 2010;21(2 S1):52-86. (In Russ.)]
3. Алексеев Б.Я., Анжиганова Ю.В., Лыков А.В., и др. Особенности диагностики и лечения рака почки в России: предварительные результаты многоцентрового кооперированного исследования // Онкоурология. – 2012. – № 3. – С. 24–31. [Alekseev BYa, Anzhiganova YuV, Lykov AV, et. al. Some specific features of the diagnosis and treatment of kidney cancer in Russia: preliminary results of a multicenter cooperative study. *Cancer Urology*. 2012;8(3):24-30. (In Russ.)]. https://doi.org/10.17650/1726-9776-2012-8-3-24-30.
4. Keane T, Gillatt D, Evans CP, et al. Current and future trends in the treatment of renal cancer. *European Urology Supplements*. 2007;6(3):374-384. https://doi.org/10.1016/j.eursup.2006.12.006.
5. Sun M, Bianchi M, Trinh QD, et al. Comparison of partial vs radical nephrectomy with regard to other cause mortality in T1 renal cell carcinoma among patients aged ≥75 years with multiple comorbidities. *BJU Int*. 2013;111(1):67-73. https://doi.org/10.1111/j.1464-410X.2012.11254.x.
6. Van Biesen W, Vanhotder R, Lameire N. Determination of acute renal failure: Small and beyond. *Clin J Am Soc Nephrol*. 2006;1:1314-1319.
7. Смирнов А.В., Добронравов В.А., Бодур-Ооржак А.Ш., и др. Эпидемиология и факторы риска хронических болезней почек: региональный уровень общей проблемы // Терапевтический архив. – 2005. – Т. 77. – № 6. – С. 20–27. [Smirnov AV, Dobronravov VA, Bodur-Oorzhak AS, et al. Epidemiology and risk factors of chronic renal diseases: a regional level of the problem. *Ter Arkh*. 2005;77(6):20-27. (In Russ.)]
8. Смирнов А.В., Добронравов В.А., Каюков И.Г. Кардио-ренальный континуум: патогенетические основы превентивной нефрологии // Нефрология. – 2005. – Т. 9. – № 3. – С. 7–15. [Smirnov AV, Dobronravov VA, Kayukov IG. Cardiorenal continuum, pathogenetic grounds of preventive nephrology. *Nephrology (Saint Petersburg)*. 2005;9(3):7-15. (In Russ.)] https://doi.org/10.24884/1561-6274-2005-9-3-7-15.
9. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296-1305. https://doi.org/10.1056/NEJMoa041031.
10. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for management of the clinical T1 renal mass. *J Urol*. 2009;182(4):1271-1279. https://doi.org/10.1016/j.juro.2009.07.004.
11. Дементьева И.И., Чарная М.А., Морозов Ю.А. Патология системы гемостаза: руководство. – М.: ГЭОТАР-Медиа, 2011. – 288 с. [Dement'eva II, Charnaya MA, Morozov YuA. Patologiya sistemy gemostaza: rukovodstvo. Moscow: GEOTAR-Media; 2011. 288 p. (In Russ.)]
12. Есаян А.М., Аль-Шукри С.Х., Мосоян М.С. Почечно-клеточный рак и хроническая болезнь почек: внимание к отдаленным неонкологическим исходам // Нефрология. – 2012. – Т. 16. – № 4. – С. 94–99. [Yesayan AM, Al-Shukri SKh, Mosoyan MS. Renal cell carcinoma and chronic kidney disease: attention to remote non-cancer outcomes. *Nephrology (Saint Petersburg)*. 2012;16(4):94-99 (In Russ.)] https://doi.org/10.24884/1561-6274-2012-16-4-94-99.
13. Балуда В.П., Балуда М.В., Тлепшуков И.К., Цыб А.Ф. Рак и тромбозы. – Москва – Обнинск, 2001. – 153 с. [Baluda VP, Baluda MV, Tlepshukov IK, Tsyb AF. Rak i trombozy. Moscow – Obninsk, 2001. 153 p. (In Russ.)]

Information about the authors:

Igor I. Titjaev – Doctor of Medical Science, Professor, Urologist of Urology Department. City Clinical Hospital No. 1, Novosibirsk, Russia. E-mail: den-sk@ya.ru.

Sergey S. Andreev – Head of Urology Department, City Clinical Hospital No. 1, Novosibirsk, Russia; Assistant of Department of Urology, Novosibirsk State Medical University of the Ministry of Healthcare of the Russian Federation, Novosibirsk, Russia. E-mail: andreev723@yandex.ru.

Svetlana V. Andreeva – Head of the Department of Ultrasound Diagnostics. City Clinical Hospital No. 1, Novosibirsk, Russia. E-mail: andreev723@yandex.ru.

Сведения об авторах:

Игорь Иванович Титяев — д-р мед. наук, профессор, врач-уролог отделения урологии. ГБУЗ НСО «ГКБ № 1», Новосибирск. E-mail: den-sk@ya.ru.

Сергей Сергеевич Андреев — заведующий урологическим отделением, ГБУЗ НСО «ГКБ № 1», Новосибирск; ассистент кафедры урологии, ФГБОУ ВО НГМУ Минздрава России, Новосибирск. E-mail: andreev723@yandex.ru.

Светлана Васильевна Андреева — заведующая отделением ультразвуковой диагностики. ГБУЗ НСО «ГКБ № 1», Новосибирск. E-mail: andreev723@ya.ru.

Information about the authors:

Konstantin V. Udalov – Head of Oncourology Department, City Clinical Hospital No. 1, Novosibirsk, Russia; Assistant of Department of Urology, Novosibirsk State Medical University of the Ministry of Healthcare of the Russian Federation, Novosibirsk, Russia. E-mail: k.udalov@mail.ru.

Denis S Kas'janov – Urologist, Oncologist of the Outpatient Care Center. City Clinical Hospital No. 1, Novosibirsk, Russia. E-mail: kasyanovds@mail.ru.

Сведения об авторах:

Константин Викторович Удалов — заведующий онкоурологическим отделением, ГБУЗ НСО «ГКБ № 1», Новосибирск; ассистент кафедры урологии, ФГБОУ ВО НГМУ Минздрава России, Новосибирск. E-mail: k.udalov@mail.ru.

Денис Сергеевич Касьянов — врач-уролог, врач-онколог Центра амбулаторной поликлинической помощи. ГБУЗ НСО «ГКБ № 1», Новосибирск. E-mail: kasyanovds@mail.ru.