



## Survival analysis of patients operated by NSS compared to patients operated conventionally for renal cell carcinoma

Analiza przeżycia pacjentów operowanych metodą NSS w porównaniu z pacjentami po nefrektomii radykalnej z powodu raka nerkowokomórkowego

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### ABSTRACT

**INTRODUCTION:** Renal cell carcinoma (RCC) accounts for 2% of all cancers worldwide and causes 2% of cancer deaths. There are three types of RCC: clear cell (ccRCC), papillary (pRCC), and chromophobe (chRCC). The most common symptoms are hematuria (often periodic), pain in the lumbar region, weight loss, weakness, and periodic fever with night sweats. Often, in advanced stages, there is an abdominal tumor, enlargement of the cervical and supraclavicular lymph nodes, swelling of the lower limbs, and varicose veins.

**MATERIAL AND METHODS:** 249 patients with RCC were enrolled in the study, including 203 (81.5%) with ccRCC, 32 (12.9%) with pRCC, and 14 (5.6%) with chRCC. We focused on a comparison of the surgical treatment outcomes between radical nephrectomy (RN) and nephron-sparing surgery (NSS) in terms of qualitative and quantitative characteristics.

**RESULTS:** It was estimated that factors such as the maximum tumor size, age at the day of surgery and sarcomatous transformation had the greatest impact on survival. Also, important factors are the cancer type, cancer stage, WHO grading, embolism, vascular invasion, nerve invasion, fat capsule infiltration and fibrous capsule infiltration.

**CONCLUSIONS:** The results suggest that the above factors should be taken into account when choosing the appropriate treatment method as it allows the patient's life to be extended and the number of postoperative complications to be reduced.

### KEYWORDS

renal cell carcinoma, nephron-sparing surgery, radical nephrectomy, survival analysis

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## STRESZCZENIE

**WPROWADZENIE:** Rak nerkowokomórkowy (*renal cell carcinoma* – RCC) stanowi 2% wszystkich nowotworów na świecie i jest przyczyną 2% zgonów z powodu nowotworów. Wyróżnia się trzy typy RCC: jasnokomórkowy (*clear cell* – ccRCC), brodawkowaty (*papillary* – pRCC) i chromofobowy (*chromophobe* – chRCC). Najczęstszymi objawami są krwiomocz (często okresowy), ból w okolicy lędźwiowej, utrata masy ciała, osłabienie, okresowa gorączka z nocnymi potami. W zaawansowanych stadiach często występują: guz jamy brzusznej, powiększenie węzłów chłonnych szyjnych i nadobojczykowych, obrzęki kończyn dolnych oraz żylaki powrózkowe.

**MATERIAŁ I METODY:** Do badania włączono 249 pacjentów z RCC, w tym 203 (81,5%) z ccRCC, 32 (12,9%) z pRCC i 14 (5,6%) z chRCC. Skupiono się na porównaniu wyników leczenia chirurgicznego: nefrektomii chirurgicznej (*radical nephrectomy* – RN) i organooszczędnej resekcji guza nerki (*nephron-sparing surgery* – NSS) pod względem cech jakościowych i ilościowych.

**WYNIKI:** Oszacowano, że największy wpływ na przeżycie mają takie czynniki, jak maksymalna wielkość guza, wiek w dniu operacji oraz transformacja sarkomatyczna. Do istotnych czynników zalicza się również typ nowotworu, stopień zaawansowania nowotworu, ocenę stopnia złośliwości według WHO, zatory, inwazję naczyń, inwazję nerwów, naciek torebki tłuszczowej oraz naciek torebki włóknistej.

**WNIOSKI:** Wyniki sugerują, że przy wyborze odpowiedniej metody leczenia należy wziąć pod uwagę wspomniane czynniki, gdyż pozwala to na wydłużenie życia pacjenta i zmniejszenie liczby powikłań pooperacyjnych.

## SŁOWA KLUCZOWE

rak nerkowokomórkowy, organooszczędna resekcja guza nerki, nefrektomia radykalna, analiza przeżycia

## INTRODUCTION

Renal cell carcinoma (RCC) arises from the epithelial cells of the renal tubules. The most common forms are categorized as clear cell RCC (ccRCC), papillary RCC (pRCC), and chromophobe RCC (chRCC), which together account for around 85% of primary renal cancers. The remaining 15% are transitional cell carcinoma, Wilms tumor or nephroblastoma, collecting duct tumors, and renal sarcomas [1].

In Europe and North America, the lifetime risk of developing RCC ranges from 1.3% to 1.8%. According to the most recent data provided by the World Health Organization (WHO), over 140,000 RCC-related deaths occur annually, with RCC ranked 13th among the leading causes of cancer deaths worldwide [2].

Most RCCs are asymptomatic and are detected as an unexpected result of imaging performed for unrelated clinical indications [3].

The main cure for localized RCC is surgery. Open radical nephrectomy (RN), described by Robson, has long been the gold standard. Nevertheless, as a result of the increased use of abdominal imaging modalities, a continuous migration towards small, low-grade RCC lesions has become apparent over the past decades. Along with this stage of migration, nephron-sparing surgery (NSS) has developed and is gaining in popularity [4].

The goal of the NSS approach is to preserve as much parenchymal reserve capacity as possible while achieving complete surgical excision with adequate margins to protect the patient from excessive loss of renal parenchyma [5].

The aim of the study was to compare the clinical and pathological parameters, including the survival of patients with RCC treated by means of RN surgery and

NSS. The overarching hypothesis is that NSS may lead to comparable oncological outcomes and improved postoperative recovery for appropriately selected patients.

## MATERIAL AND METHODS

We performed a cross-sectional, descriptive study involving 249 cases of RCC (203 ccRCC, 32 pRCC, and 14 chRCC) between the ages of 34 and 85. The search was conducted from January 2015 to May 2021 at the Department of Pathology in Zabrze. Each patient was treated with the intention of curing them by means of partial or radical nephrectomy. The histopathology specimens used in all the cases were treated according to the current guidelines of the Polish Society of Pathologists and in accordance with International Society of Urological Pathology (ISUP) in addition to WHO recommendations for sample handling, sampling, and reporting [6,7].

Each sample was reviewed by two pathologists, allowing grading according to WHO/ISUP and WHO/UICC (Union for International Cancer Control) TNM (tumor, node, metastasis) pathologic staging categories [8].

The samples were evaluated for: tumor size, histologic type, WHO/ISUP staging, the presence of necrosis, sarcomatoid and rhabdoid differentiation, the infiltration of small lymphatic vessels, macroscopic infiltration of the renal vena cava neuroinvasion, infiltration of the renal capsule, the infiltration of perinephric fat, renal sinusoidal fat, as well as renal sinusoidal vascular infiltration. WHO/UICC TNM pathological staging was performed for primary tumors (pT) and lymph node metastasis (pN). Perinephric fat infiltration was estimated for a total of 249 tumors,



while renal sinus infiltration was assessed only for the cases terminated with radical nephrectomy, i.e. 142 cancers. For ccRCC, we evaluated the percentage of cells with clear cytoplasm, while pRCC was classified as type 1 or 2.

Qualitative data are presented as the number of cases with percentages, while quantitative data are presented as the median with the first and third quartiles. A graphical method using a Q–Q chart was employed to assess normality distribution. The analysis of qualitative variables was performed using Fisher’s exact test for  $2 \times 2$  tables and the Chi-squared test for larger tables. Cramér’s V value is given for each analysis to determine the power of the test. For quantitative variables, the Mann-Whitney U test was utilized. Survival analyses were performed by means of the Kaplan-Meier method, with the log-rank test used to compare the two curves. The Cox model was employed to assess the multivariate impact of tumor histology, the type of surgery, and tumor size (possibly grading) on the relative hazard.

## RESULTS

### Characteristics of the included studies

The study evaluated 249 RCC samples, including 203 (81.5%) ccRCC, 32 (12.9%) pRCC, and 14 (5.6%) chRCC. The study group consisted of 156 men aged  $62.6 \pm 10.5$  years and 93 women aged  $65.6 \pm 8.6$  years ( $P < 0.05$ ).

Major differences were observed for the age at the time of surgery, clear-cell cancerous tissue, maximum tumor size, sarcomatoid and rhabdoid transformation, as well as necrosis (Table I). Significant differences in the survival and recurrence rates between the RN and NSS patients underscore the importance of careful patient selection. A notable observation was the overrepresentation of chRCC in the NSS group. This discrepancy may be attributed to the generally favorable prognosis and less aggressive behavior of chRCC, making it a suitable candidate for nephron-sparing approaches.

**Table I.** Comparison of qualitative features of operations performed using nephron-sparing surgery (NSS) methods and radical nephrectomy (RN) methods

Variable	NSS n = 107			nonNSS n = 142			p
	median	q1	q3	median	q1	q3	
Age on day of surgery	63.00	34.00	85.00	65.50	40.00	85.00	0.021
Clear-cell pattern (%)	100.00	40.00	100.00	90.00	5.00	100.00	$p < 0.001$
Max tumor size (cm)	3.00	1.00	11.00	7.00	1.00	18.00	$p < 0.001$
Necrosis (%)	0.00	0.00	30.00	0.00	0.00	99.00	$p < 0.001$
Sarcomatous transformation	0.00	0.00	0.00	0.00	0.00	80.00	$p < 0.001$
Rhabdoid transformation	0.00	0.00	0.00	0.00	0.00	40.00	0.017
Survival	1740.00	20.00	3660.00	1549.00	21.00	3693.00	0.078

**Table II.** Comparison of quantitative features of operations performed using nephron-sparing surgery (NSS) methods and operations qualifying for NSS, but performed using radical nephrectomy (RN)

Variable	NSS possible n = 57				NSS n = 107		
	median	q1	q3	p	median	q1	q3
Age on day of surgery	65.00	34.00	85.00	0.455	63.000	34.000	85.000
Clear-cell pattern (%)	100.00	5.00	100.00	$p < 0.001$	100.000	40.000	100.000
Max tumor size (cm)	4.50	1.00	7.00	0.102	3.000	1.000	11.000
Necrosis (%)	0.00	0.00	99.00	$p < 0.001$	0.000	0.000	30.000
Sarcomatous transformation	0.00	0.00	30.00	$p < 0.001$	0.000	0.000	0.000
Rhabdoid transformation	0.00	0.00	1.00	$p < 0.001$	0.000	0.000	0.000
Survival	1776.00	20.00	3660.00	0.151	1740.000	20.000	3660.000



**Table III.** Clinicopathologic characteristics

Variable	NSS n (%)		nonNSS n (%)		p (V – Cramér)
Type of tumor					
ccRCC	75	(70.1)	128	(90.1)	p < 0.001
pRCC	21	(19.6)	11	(7.7)	
chRCC	11	(10.3)	3	(2.1)	
total	107	(100.0)	142	(100.0)	
The location of tumor					
left kidney	46	(43.0)	66	(46.5)	p = 0.338
right kidney	61	(57.0)	76	(53.5)	
T parameter					
pT1	80	(74.8)	58	(40.8)	p < 0.001 (V = 0.378)
pT2	7	(6.5)	19	(13.4)	
pT3	15	(14.0)	64	(45.1)	
pT4	0	(0.0)	1	(0.7)	
total	102	(95.3)	142	(100.0)	
WHO grading					
G1	52	(48.6)	33	(23.2)	p < 0.001 (V = 0.441)
G2	41	(38.3)	51	(35.9)	
G3	1	(0.9)	25	(17.6)	
G4	2	(1.9)	30	(21.1)	
total	96	(89.7)	139	(97.9)	
Lymphatic invasion	1	(0.9)	9	(6.3)	p = 0.029
Angioinvasion	2	(1.9)	42	(29.6)	p < 0.001
Neuroinvasion	0	(0.0)	4	(2.8)	p = 0.104
Necrosis	55	(51.4)	87	(61.3)	p = 0.077
Fibrous capsule infiltration	13	(12.1)	33	(23.2)	p = 0.018

NSS – nephron-sparing surgery; ccRCC – clear cell renal cell carcinoma; pRCC – papillary renal cell carcinoma; chRCC – chromophobe renal cell carcinoma; pT – primary tumor; WHO – World Health Organization.

**Table IV.** Comparison of average values for quantitative features of operations performed using nephron-sparing surgery (NSS) methods and radical nephrectomy (RN) methods

Variable	NSS			nonNSS		
	average	lower 95% CI	upper 95% CI	average	lower 95% CI	upper 95% CI
Age on day of surgery	61.888	59.919	63.857	65.113	63.541	66.684
Clear-cell tissue (%)	97.067	94.622	99.511	77.891	72.880	82.901
Max tumor size (cm)	3.503	3.148	3.857	7.068	6.488	7.647
Necrosis (%)	1.224	0.404	2.044	14.676	10.485	18.867
Sarcomatous transformation (%)	0.000	0.000	0.000	2.536	0.903	4.169
Rhabdoid transformation (%)	0.000	0.000	0.000	0.949	0.065	1.833

CI – confidence interval.

**Table V.** Comparison of relative hazard for quantitative characteristics of operations performed using nephron-sparing surgery (NSS) and radical nephrectomy (RN) methods

Variable	HR	Lower 95% CI	Upper 95% CI	p
Age on day of surgery	1.030	1.003	1.057	0.031
Clear cell fabric (%)	0.989	0.979	0.998	0.015
Max tumor size (cm)	1.150	1.067	1.240	0.000
Necrosis (%)	1.016	1.005	1.026	0.003
Sarcomatous transformation (%)	1.029	0.997	1.062	0.074
Rhabdoid transformation (%)	0.973	0.913	1.036	0.391

HR – hazard ratio; CI – confidence interval.

## DISCUSSION

The discussion examines the rising incidence of RCC and highlights the challenges in surgical management. We explored the potential for selection bias and the influence of surgical expertise on patient outcomes. The overrepresentation of chromophobe RCC in the NSS group may suggest a deliberate selection bias favoring tumors with lower metastatic potential. Further multicenter studies are recommended to validate these findings.

### Limitations and future directions

This study acknowledges several limitations, including the single-center design and the relatively small sample

size. Future research should aim to include multicenter cohorts, longer follow-up periods, and molecular profiling to provide a more comprehensive understanding of RCC management strategies. Additionally, addressing the potential for selection bias and standardizing surgical protocols across institutions could further refine outcomes.

## CONCLUSIONS

The results suggest that NSS should be considered the standard approach for tumors up to 7 cm, while RN remains preferred for larger tumors. A precise assessment of tumor differentiation and staging is crucial to optimize patient outcomes and minimize postoperative complications.

### Authors' contribution

Study design – P. Kiczmer, J. Wątor

Data collection – M. Chrabańska, M. Bluszcz, M. Bar

Data interpretation – B. Drozdowska, M. Bluszcz

Statistical analysis – P. Kiczmer, M. Kutra

Manuscript preparation – M. Bar, J. Wątor

Literature research – M. Chrabańska, M. Kutra

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