Renal Function Outcomes after Nephrectomy for Kidney Cancer in Elderly Patients

Markić, Dean; Valenčić, Maksim; Španjol, Josip; Materljan, Mauro; Fučkar, Dora

Source / Izvornik: **Collegium antropologicum, 2011, 35 - supplement 2, 121 - 124**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:681812

Coll. Antropol. **35** (2011) Suppl. 2: 121–124
Original scientific paper

Renal Function Outcomes after Nephrectomy for Kidney Cancer in Elderly Patients

Dean Markić[1], Maksim Valenčić[1], Josip Španjol[1], Mauro Materljan[1] and Dora Fučkar[2]

[1] Department of Urology, Rijeka University Hospital Center, Rijeka, Croatia
[2] Department of Pathology, School of Medicine, University of Rijeka, Rijeka, Croatia

A B S T R A C T

The kidneys are organs with multiple functions and essential to maintain life. Ablative procedures, such as nephrectomy, diminish nephron mass and can have a potentially negative impact on renal function. We investigated renal function outcome in patients who underwent nephrectomy for renal cell cancer with special emphasize on elderly patients. Data from 104 patients who underwent nephrectomy for kidney cancer in the Department of Urology, University Hospital Rijeka from January 2005 to December 2010 were retrospectively analyzed. All patients had a normal concentration of serum creatinine and a normal contralateral kidney before surgery. Renal function, as estimated by the glomerular filtration rate (eGFR), was determined before and after nephrectomy using the abbreviated Modification of Diet in Renal Disease equation. We compared the eGFR before and after nephrectomy in the patients of different age. The mean preoperative eGFR was 75.2 mL/min, and the mean postoperative eGFR was 52.7 mL/min ($p<0.0001$). In the group of patients ≥65 years old, the mean preoperative GFR was 69.2 mL/min, and the mean postoperative eGFR was 47.4 mL/min ($p<0.0001$). Our data indicate that the eGFR significantly decreased after nephrectomy for kidney cancer. In elderly patients, diminished renal function following nephrectomy was more prominent.

Key words: *nephrectomy, renal cell carcinoma, chronic kidney disease*

Introduction

Renal cell carcinoma (RCC) has affected approximately 50,000 people in 2009, with more than 10,000 deaths in the United States[1]. These deaths are the consequence of metastatic disease. The incidence of RCC has increased during the last decades[2,3]. The reason for the increased incidence is due to the aging population and widespread use of diagnostic imaging modality. Recently, more than 70% of patients have localized disease and can be treated surgically. Radical nephrectomy with removal of the kidney, perinephric fat and ipsilateral adrenal gland was the standard procedure in the past. However, nephrectomy diminishes nephron mass and can potentially have a negative impact on renal function. Chronic kidney disease can be defined as an estimated glomerular filtration rate (eGFR) lower than 60 mL/min per 1.73 m^2 or by the presence of markers of kidney damage (albuminuria or abnormal imaging studies) for three or more months[4]. The major outcomes of chronic kidney disease are: hypertension, anemia, neuropathy, reduced quality of life and increased risk of cardiovascular morbidity and mortality[4,5]. We investigated renal function outcome in patients who underwent nephrectomy for RCC, with special emphasis on elderly patients.

Patients and Methods

We retrospectively analyzed data from our patients who underwent surgery for kidney cancer from January 2005 to December 2010 in the Department of Urology, University Hospital Rijeka. Patients included in the study had the following characteristics: diagnosis of renal cell carcinoma without metastasis, normal preoperative concentrations of serum creatinine (defined as <126 μmol/L) and normal contralateral kidney before surgery. In all patients, a complete nephrectomy was performed.

The patients records were evaluated using information about the patients age, gender, ECOG status, pathohistological findings and eGFR. From pathological findings we determined the histological subtype, Fuhrman

Received for publication May 11, 2011

nuclear grading system and TNM classification. The histological subtype was divided in to clear-cell RCC (RCC-CC) and non clear-cell RCC (RCC-NCC), which included chromophobe and papillary type of carcinomas. We separated the patients according to their age, where »elderly« has been defined as a chronological age of 65 years old or older.

Renal function was determined by calculating the eGFR using the abbreviated Modification of Diet in Renal Disease (MDRD) equation. The serum creatinine concentrations were determined immediately before and after surgery. The creatinine concentrations after nephrectomy were estimated one month to a few months after nephrectomy when kidney function was stabilized. Chronic kidney disease was defined as an eGFR<60 mL/min/1.73 m^2, and severe chronic kidney disease was defined as an eGFR<30 mL/min/1.73 m^2. We separated patients with an eGFR<45 mL/min/1.73 m^2 to establish a group of patients with a greater risk for development of severe chronic kidney disease.

Written informed consent and approval was obtained from all participants. The study was in adherence with the Declaration of Helsinki.

Statistical analysis was conducted using Statistica 8 software (StatSoft, Inc., Tulsa, OK, USA). The distribution of results was normal (Kolmogorov-Smirnov test). Results were presented as mean (X) ± standard error of mean (SEM). The Student t-test was used to compare eGFRs before and after surgery. The χ^2 test was used to compare the renal function of patients after nephrectomy. Differences were considered statistically significant with $p<0.05$.

Results

In all, 104 patients met the inclusion criteria. Table 1 presents the basic demographic and clinicopathological characteristics of patients. The comparison of eGFR values before (75.2±1.5 mL/min/1.73 m^2) and after (52.7±1.3 mL/min/1.73 m^2) surgery showed that renal function is diminished after nephrectomy ($p<0.0001$). This was true for all patients and both age groups ($p<0.0001$) (Table 2). In the patients <65 years old, the eGFR was statistically significantly higher before surgery ($p<0.0004$) and after surgery ($p=0.0001$) than in the patients ³65 years old. Of all of the 104 patients, 16 (15.4%) had a preoperative eGFR <60 mL/min/1.73 m^2 and 74 (71.2%) had a postoperative eGFR <60 mL/min/1.73 m^2 (Table 3). After the nephrectomy, a eGFR <60 mL/min/1.73 m^2 was observed in 38/46 (82.6%) elderly patients compared to 36/58 (62.1%) younger patients (Table 3). The analysis of renal function in 88 patients with a preoperatively normal eGFR showed that after nephrectomy an eGFR <60 mL/min/1.73 m^2 was observed in 28/36 (77.8%) elderly patients compared to 30/52 (57.7%) patients below 65 years old (Table 4).

TABLE 1
CLINICOPATHOLOGICAL CHARACTERISTICS OF THE PATIENTS (N=104)

Characteristic	N (%)
Age:	
<65 years	58 (55.8%)
≥65 years	46 (44.2%)
Gender:	
Male	67 (64.4%)
Female	37 (35.6%)
Histological subtype:	
Clear-cell	81 (77.9%)
Non clear-cell	23 (22.1%)
Staging:	
T1	60 (57.7%)
T2	19 (18.3%)
T3	25 (24%)
T4	0 (0%)

TABLE 2
THE DETERMINATION OF RENAL FUNCTION BY ESTIMATING THE GLOMERULAR FILTRATION RATE BEFORE AND AFTER NEPHRECTOMY

Patients group (N)	eGFR before surgery ($\overline{X}$±SEM)	eGFR after surgery ($\overline{X}$±SEM)	p
All patients (104)	75.2±1.5	52.7±1.3	<0.0001*
<65 years (58)	79.8±2.1	57.2±1.5	<0.0001*
≥65 years (46)	69.2±1.8	47.4±1.8	<0.0001*

eGFR – Estimated glomerular filtration rate (mL/min/1.73 m^2), * – $p<0.05$ (statistically significant difference), $\overline{X}$±SEM – mean±standard error of mean

TABLE 3
RENAL FUNCTION AFTER NEPHRECTOMY (N=104)

eGFR	≥65 years	<65 years	p
≥60	8	22	*0.010
<60	38	36	0.816
<45	22	6	*0.002
<30	3	0	/

eGFR – Estimated glomerular filtration rate (mL/min/1.73 m^2), * – $p<0.05$ (statistically significant difference)

TABLE 4
RENAL FUNCTION IN THE PATIENTS WITH PREOPERATIVELY NORMAL GLOMERULAR FILTRATION RATES AFTER NEPHRECTOMY (N=88)

eGFR	≥65 years	<65 years	p
≥60	8	22	*0.010
59–45	14	26	0.057
44–30	13	4	*0.029
<30	1	0	/

eGFR – Estimated glomerular filtration rate (mL/min/1.73 m^2), * – $p<0.05$ (statistically significant difference)

Discussion

Experimental models showed that reduction of nephron mass can lead to kidney damage[6]. The development of kidney damage after complete nephrectomy in humans has been documented in a few studies. Huang et al. analyzed 662 patients with normal concentrations of serum creatinine who underwent partial or radical nephrectomy for a solitary renal tumor (T1a – 4 cm of below in diameter)[7]. After surgery, the 3-year probability of freedom from new-onset of a GFR lower of 60 mL/min/1.73 m^2 has been 80% after partial nephrectomy and 35% after radical nephrectomy; the probability of a GFR lower than 45 mL/min/1.73 m^2 after partial and radical nephrectomy has been 95% and 64% respectively. In another study, 52% of patients after nephrectomy developed new-onset GFR<60 mL/min/1.73 m^2[,8]. A group from Korea observed the development of chronic kidney disease (GFR<60 mL/min/1.73 m^2) in 66.7% of patients who underwent radical nephrectomy and in 11.5% patients who underwent partial nephrectomy[9]. Our results also support this observation (Tables 2–4). In all studies, multivariable analysis showed that radical nephrectomy is an independent risk factor for the development of chronic kidney disease[7–11].

Diabetes, age, type of operation, preoperative GRF and proteinuria have been risk factors for the development of adverse renal outcomes after nephrectomy for renal cell cancer[7–10]. Hepps et al. found that African-Americans have a greater risk of renal insufficiency after radical nephrectomy for kidney cancer compared to non-African-American group[12].

Chronic kidney disease is present when the eGFR is below 60 mL/min/1.73 m^2, according to the Kidney Disease Outcomes Quality Initiative (KDOQI) staging system from 2002; however, that level has included a large number of patients who may have had no symptoms and are at low risk for progression to end-stage renal disease (ESRD)[13]. Severe chronic kidney disease is defined as an eGFR <30 mL/min/1.73 m^2, and this value has defined renal outcomes that are likely to be clinically relevant for patients. In addition, this level of chronic kidney disease has been related to conditions such as anemia and mineral metabolism disturbances, with possible progression to ESRD[10].

To prevent the development of kidney failure, nephron-sparing procedures have been advocated in patients with localized tumors. More than 60% of newly diagnosed RCCs have been 4 cm or less in diameter, which means that they are amenable for partial nephrectomy based on the size criteria. In addition, because no significant difference was found in cancer-specific survival between patients who underwent partial nephrectomy for RCC <7 cm and those who underwent surgery for RCC <4 cm, the potential number of patients who are eligible for this procedure is even higher[14]. Crépel et al. have shown that nephron-sparing surgery is equally effective as radical nephrectomy for T1 RCC[15]. The oncological outcomes must not be compromised by such a procedure.

Nephron-sparing approaches are associated with a greater number of surgical complications, but with experience, this rate of complications diminishes[16]. Currently, open partial nephrectomy, laparoscopic partial nephrectomy and robotic partial nephrectomy are utilized in the management of T1 renal tumors. Open partial nephrectomy and laparoscopic partial nephrectomy are comparable in the terms of oncological outcomes, positive surgical margin, warm ischemia time and morbidity[16]. The evaluation of robotic partial nephrectomy needs additional studies.

It is necessary for patients to be informed of the future risk of developing adverse renal outcomes after nephrectomy. Although oncologic outcomes are important, renal outcome is also important because patients who develop ESRD have a poor quality of life and an increased risk of death. In addition, patients who have developed chronic kidney disease have increased cardiovascular morbidity and mortality[10]. Lane et al. showed that the survival of patients aged 75 years and older who are treated with nephrectomy for localized RCC (T1) is not increased compared to patients who undergo surveillance[17]. Cancer progression has been responsible for death in only 4% of patients, and the most common cause of death has been cardiovascular (29%). Because nephrectomy diminishes renal function and renal dysfunction is related to cardiovascular mortality, it can be suggested that there is overtreatment of localized renal tumors in patients with limited life expectancy[17].

Experience with kidney transplant patients (living donors) has shown that one normal kidney is sufficient for normal life without an influence on life span, quality of life and susceptibility for significant comorbidities. There have been no reports documenting that donors have an increased rate of kidney failure requiring dialysis or causing death[18]. This fact is essential for increasing the pool of living donors. On the other hand, nephrectomy in patients with RCC can lead to deleterious renal function outcomes[8–10]. An explanation for such diverse renal outcomes can be found in the patients themselves. Donors must be healthy individuals, without significant comorbidities, and they are usually younger. Patients with kidney cancer are usually older, smokers, obese, and have significant illnesses such as diabetes, cardiovascular diseases (hypertension, coronary artery disease), and metabolic syndrome[19]. Bijol et al. documented that in nonneoplastic renal parenchyma of nephrectomy specimens for RCC, unremarkable renal parenchyma is found in only 10% of cases; 28% of cases has had some degree of vascular sclerosis, and in the remaining cases (62%), evidence of pathological abnormalities has been present[20]. Because this conditions is always bilateral, the risk for development of chronic kidney disease is present in these patients.

In our study, the mean eGFR before surgery was 75.2 mL/min/1.73 m^2, and after surgery it was 52.7 mL/min/1.73 m^2 ($p<0.0001$). Before the operation, only 15.4% of the patients had an eGFR <60 mL/min/1.73 m^2; and after the operation, the percentage increased to 71.2%. In

three patients (2.9%), severe chronic kidney disease was developed. This observations confirmed that nephrectomy significantly diminishes renal function. It is important to note that in this study were included only patients with normal preoperative serum creatinine concentrations. If other patients had been included, the results of renal outcome would have been much worse.

Normally, the GFR decreased progressively with age in individuals after the age of 40 (approximately 0.4–1.2 mL/min per year). Age, according to our study, was a very important factor influencing renal function. The elderly patients had lower preoperative ($p=0.0004$) and postoperative eGFR ($p=0.0001$) values than people <65 years old. Initially, a preoperative eGFR <60 mL/min/1.73 m^2 was observed in 16 patients, but 75% of them were older than 65 years. After nephrectomy, 82.6% of the elderly patients had a eGFR <60 mL/min/1.73 m^2 compared to 62.1% of the younger patients. All three patients with postoperative eGFR below 30 mL/min/1.73 m^2 were older than 65 years. It was obvious that elderly patients have a greater chance to develop chronic kidney disease after nephrectomy for RCC. To the best of our knowledge, this is the first study that emphasized deleterious renal outcomes after nephrectomy in patients ≥65 years old.

Conclusion

The baseline kidney function of patients with RCC was lower than usually thought, and the assessment of kidney function was necessary before surgery. Nephrectomy was a risk factor for the development of chronic kidney disease, especially in elderly patients. Nephron-sparing procedures should be the treatment of choice in patients with existing renal dysfunction or in patients with recognized risk factors (elderly, proteinuria, diabetes). Oncologic outcome should also be considered.

REFERENCES

1. JEMAL A, SIEGEL R, WARD E, HAO Y, XU J, THUN MJ, CA Cancer J Clin, 59 (2009) 225. — 2. CHOW WH, DONG LM, DEVESA SS, Nat Rev Urol, 7 (2010) 245. — 3. MARKIĆ D, ĆELIĆ T, ŠPANJOL J, GRŠKOVIĆ A, BOBINAC D, FUČKAR Ž, Coll Antropol, 34 (2010) 149. — 4. GO AS, CHERTOW GM, FAN D, McCULLOCH CE, HSU CY, N Engl J Med, 351 (2004) 1296. — 5. GALIĆ G, TOMIĆ M, GALEŠIĆ K, KVESIĆ A, ŠOLJIĆ M, MOZETIČ V, LONČAR Z, MARIČIĆ A, MARTINOVIĆ Z, Coll Antropol, 33 (2010) 59. — 6. SIMONS JL, PROVOOST AP, DE KEIJZER MH, ANDERSON S, RENNKE HG, BRENNER BM, J Am Soc Nephrol, 4 (1993) 1362. — 7. HUANG WC, LEVEY AS, SERIO AM, SNYDER M, VICKERS AJ, RAJ GV, SCARDINO PT, RUSSO P, Lancet Oncol, 7 (2006) 735. — 8. BARLOW LJ, KORETS R, LAUDANO M, BENSON M, MCKIERNAN J, BJU Int, 106 (2010) 489. — 9. JEON HG, JEONG IG, LEE JW, LEE SE, LEE E, Urology, 74 (2009) 1064. — 10. KLARENBACH S, MOORE RB, CHAPMAN DW, DONG J, BRAAM B, Eur Urol, 59 (2011) 333. — 11. LUCAS SM, STERN JM, ADIBI M, ZELTSER IS, CADEDDU JA, RAJ GV, J Urol, 179 (2008) 75. — 12. HEPPS D, CHERNOFF A, Urol Oncol, 24 (2006) 391. — 13. HALLAN SI, ORTH SR, Nephron Clin Pract, 116 (2010) 307. — 14. LEIBOVICH BC, BLUTE ML, CHEVILLE JC, LOHSE CM, WEAVER AL, ZINCKE H, J Urol, 171 (2004) 1066. — 15. CRÉPEL M, JELDRES C, PERROTTE P, CAPITANIO U, ISBARN H, SHARIAT SF, LIBERMAN D, SUN M, LUGHEZZANI G, ARJANE P, WIDMER H, GRAEFEN M, MONTORSI F, PATARD JJ, KARAKIEWICZ PI, Urology, 75 (2010) 271. — 16. VAN POPPEL H, Int J Urol, 17 (2010) 314. — 17. LANE BR, ABOUASSALY R, GAO T, WEIGHT CJ, HERNANDEZ AV, LARSON BT, KAOUK JH, GILL IS, CAMPBELL SC, Cancer, 116 (2010) 3119. — 18. FEHRMAN-EKHOLM I, DUNÉR F, BRINK B, TYDEÉN G, ELINDER CG, Transplantation, 72 (2001) 444. — 19. RUSSO P, Eur Urol 59 (2011) 340. — 20. BIJOL V, MENDEZ GP, HURWITZ S, RENNKE HG, NOSÉ V, Am J Surg Pathol, 30 (2006) 575.

D. Markić

Department of Urology, Rijeka University Hospital Center, Tome Strižića 3, 51 000 Rijeka, Croatia
e-mail: dean.markic@ri.htnet.hr

BUBREŽNA FUNKCIJA U LJUDI STARIJE ŽIVOTNE DOBI NAKON NEFREKTOMIJE ZBOG KARCINOMA BUBREGA

SAŽETAK

Bubrezi su organi s mnogobrojnim funkcijama neophodnim za održavanje života. Ablativne procedure, kao nefrektomija, smanjuju bubrežnu masu i imaju potencijalno negativan učinak na funkciju bubrega. Istraživali smo bubrežnu funkciju nakon nefrektomije zbog karcinoma bubrega, s posebnim naglaskom na ljude starije životne dobi. Retrospektivno smo analizirali 104 pacijenta u kojih je učinjena nefrektomija radi karcinoma bubrega. Pacijenti su bili operirani na Klinici za urologiju, Kliničkog bolničkog centra u Rijeci, a promatrano razdoblje je bilo od siječnja 2005. do prosinca 2010. godine. Svi pacijenti su prije operacije imali normalnu vrijednost kreatinina kao i normalni kontralateralni bubreg. Bubrežnu funkciju smo odredili mjerenjem stupnja glomerularne filtracije (eGFR) prije i nakon nefrektomije koristeći skraćenu Modification of Diet in Renal Disease jednadžbu. Usporedili smo eGFR prije i nakon nefrektomije te u pacijenata različite dobi. Srednja eGFR prije operacije je bila 75,2 mL/min, a nakon operacije 52,7 mL/min ($p<0,0001$). U grupi pacijenata ^{3}65 godina srednja vrijednost eGFR prije operacije je bila 69,2 mL/min, a nakon operacije 47,4 mL/min ($p<0,0001$). Dobiveni podaci pokazuju da je stupanj glomerularne filtracije značajno snižen u pacijenata u kojih je učinjena nefrektomija zbog karcinoma bubrega. U ljudi starije životne dobi smanjenje bubrežne funkcije nakon nefrektomije je još i izraženije.