Radical or simple nephrectomy in localized renal cell carcinoma: what is a choice?

Alexander Shulyak[1], Oleg Banyra[2]

[1]Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
[2]2nd Lviv Municipal Polyclinic, Lviv, Ukraine

KEY WORDS

nephrectomy ◗ localized renal cell carcinoma ◗ overall survival ◗ cancer-specific survival

ABSTRACT

Introduction. Renal cell carcinoma (RCC) accounts for approximately 3% of all adult malignancies. Surgery remains the only effective method of renal tumors treatment. In fact, for advanced RCC, radical nephrectomy (RN) should remain a standard treatment. However, in localized RCC (LRCC) a real increase of survival rates realized by RN compared with simple nephrectomy (SN) or organ-sparing surgery is discussable. The aim of our study was to assess the impact of nephrectomy type on the prognosis of LRCC treatment.
Material and methods. We analyzed the long-term outcomes of RN (n = 248 pts.) and SN (n = 170 pts.) in 418 pts. with LRCC. There were no significant statistical differences in tumor stages, age stratification or gender between these two groups. To compare the efficacy of RN and SN we determined overall survival (OS) and cancer-specific survival (CSS) rates in both divided groups. The 3-year OS in RN group was 93.1% *vs.* 91.8% in SN group.
Results. CSS rates after the same period were 96.8% *vs.* 94.7% respectively. The 5-year OS in RN group was 91.5% *vs.* 88.8% in SN group. After 5 years of follow-up, CSS in RN group was 94.4% *vs.* 92.4% in SN group. Type of nephrectomy does not influence on LRCC outcomes. The 3- and 5-year overall survival rates and cancer-specific survival rates in RN and SN group were almost identical.
Conclusion. Hence, if radical nephrectomy does not ensure better survival than simple nephrectomy, the expediency of vast surgery in localized RCC is doubtful.

INTRODUCTION AND OBJECTIVE

Renal cell carcinoma (RCC) is one of the common oncourological pathologies. On a global scale it accounts for about three percent of all adult tumors and increases at a rate of 2.5% a year [1, 2]. During last 25 years RCC incidence in Ukraine has increased from 4.6 cases per 100 000 population in 1985 till 10.6 cases per 100,000 population in 2009. It has been proved the influence of low-doses ionizing radiation due to Chernobyl disaster on tendency to increase of RCC morbidity [3, 4]. The frequency of RCC is expected to grow slightly in consequence of early neoplasm detection by widespread use of ultrasound investigation and computerized tomography. Early RCC diagnostics significantly improve survival because of high efficacy of operative treatment in T1-2N0M0 stages. Despite the advent of targeted therapy and numerous novel pharmaceutical antitumor drugs, surgery remains the only effective method of renal tumor treatment. Simple nephrectomy (SN) was a standard treatment for RCC until it was replaced by a more vast surgical intervention, radical nephrectomy (RN), which has become the method of choice in RCC surgery [5]. RN started to be use widely after publications had demonstrated a clinical benefit of this method in comparison to SN. In fact, in stages T3-4NxMx, radical nephrectomy should remain a standard treatment. However, in localized RCC (LRCC), a real increase of survival rates realized by RN compared with SN is discussable so far as it has not been confirmed by large investigations.

The aim of our study was to assess the impact of nephrectomy type on the prognosis of localized RCC forms treatment, and to analyze the expediency of lymphadenectomy in patients with LRCC.

MATERIALS AND METHODS

Our study enrolled 418 patients with localized RCC stages (T1-2N0M0) who were treated between 2000 and 2005 at our clinic. For determination of localized RCC stages (T1-2N0M0) we used the American Joint Committee on Cancer (AJCC) staging system proposed by Greene F.L. et al. in 2002 [6]:

T1 – tumor 7 cm or less in greatest dimension, limited to the kidney;

T1a – tumor ≤4 cm, limited to the kidney;

T1b – tumor >4 cm and ≤7 cm, limited to the kidney;

T2 – tumor more than 7 cm in greatest dimension, limited to the kidney;

T3 – tumor extends into major veins or adrenal gland or perinephric tissue, but not beyond Gerota's fascia;

T4 – tumor extends beyond Gerota's fascia.

During calculation of data we used common statistical methods: determination of percentage, Student's distribution, correlation, overall survival, and cancer-specific survival using a standard formula.

Patients (pts.) with LRCC were prospectively allocated to two groups: group 1, n = 248 (110 pts., stage T1N0M0; 138 pts., stage T2N0M0) who were treated with RN; group 2, n = 170 pts. (75 pts., stage T1N0M0; 95 pts., stage T2N0M0) who were treated with SN. No significant statistical differences in tumor stages, age stratification, or gender were registered between these two groups. There were 147 males (59.53%) and 101 females (40.7%) in the RN group with a ratio 1.46 : 1. The mean age of this group was 58.5 years (range 40 to 77 years). In the SN group there were 99 males (58.2%) and 71 females (41.8%) with a ratio 1.39 : 1. The mean age of this group was 62.5 years (range 45 to 80 years). In both groups the prevailing number of patients belonged to the 61-70 years age group (37.5% and 36.4% respectively).

The clinical signs included hematuria (20 pts. (8.0%) in group 1; 13 pts. (7.6%) in group 2), flank pain (29 pts. (11.7%) in group 1; 22 pts. (12.9%) in group 2), weight loss (35 pts. (14.1%) in group 1; 26 pts. (15.3%) in group 2), arterial hypertension (38 pts. (15.3%) in group 1; 23 pts. (13.5%) in group 2), and subfebrile temperature (28 pts. (11.3%) in group 1; 16 pts. (9.4%) in group 2). There were no differences between the two divided

groups to clinical signs, symptoms, and preoperative evaluation. Before the operation all patients were evaluated with chest X-ray, renal sonography, and computerized tomography of the abdomen and retroperitoneum to determine the stage of disease. Primary RCC was diagnosed by ultrasound investigation or computerized tomography. After that we often used excretory urogram for routine detection of the features of urine passage in the tumorous kidney as well as for determination of contralateral kidney condition. Asymptomatic tumors were diagnosed incidentally in 188 pts. (75.8%) from RN group and in 119 pts. (70.0%) from SN group during renal ultrasound evaluation. This data shows that asymptomatic illness is prevailing in the majority of patients with T1-2N0M0 RCC stages. Also this fact advocates a significant role of renal sonography in early RCC detection. In both groups, regional lymphatic nodes involvement and distant metastases were not detected at the time of surgery. None of the patients in SN and RN groups received preoperative medical treatment.

Simple nephrectomy was performed extraperitoneally *via* the lumbar approach and consisted of early ligation of the renal artery and vein and *en bloc* removal of the kidney and perinephric fat within the bounds of Gerota's fascia. Removal of the adrenal gland was performed only if there was an upper pole lesion. In the analyzed group of patients lymphadenectomy was not performed during SN.

Radical nephrectomy usually was performed after chevron of hemi-chevron incision through a subcostal approach. RN was performed by a transperitoneal approach. We performed early ligation of the renal artery and vein and *en bloc* removal of the kidney and perinephric fat within the bounds of Gerota's fascia, and lymph-node dissection. Removal of the adrenal gland was performed only if there was an upper pole lesion.

Principal differences between SN and RN techniques were: operative accesses and performing of lymphadenectomy (only during RN) [7]. Perirenal fat was removed during both operative methods.

After operative treatment all patients with LRCC were under medical observation, which included regular evaluation by chest X-ray, abdominal ultrasound, and computerized tomography if needed. For the tumor histologic grade determination we used the Fuhrman four-grade scale (G1-4) [8].

Major patient characteristics are described in Table 1.

Overall survival (OS) was determined from the date of operation to the date of death or last follow-up. Cancer-specific survival (CSS) was determined from the date of nephrectomy to the date of death in consequence of RCC only or last follow-up.

Table 1. Comparison of patient characteristics between RN and SN groups

Variables	RN group	SN group
Number of patients	248	170
Clinical signs:		
Hematuria	20 (8.0%)	13 (7.6%)
Flank pain	29 (11.7%)	22 (12.9%)
Arterial hypertension	38 (15.3%)	23 (13.5%)
Weight loss	35 (14.1%)	26 (15.3%)
Subfebrile temperature	28 (11.3%)	16 (9.4%)
Asymptomatic tumor	188 (75.8%)	119 (70.0%)
Tumor stage (T1N0M0/ T2N0M0)	110/138	75/95
Mean tumor size, cm.	6.3 ±0.6	6.6 ±0.8
Fuhrman grade:		
G1	40 (16.1%)	26 (15.2%)
G2	122 (49.2%)	88 (51.8%)
G3/4	86 (34.7%)	56 (33.0%)
Histologic subtype:		
Clear-cell	206 (83.0%)	139 (81.8%)
Papillary	25 (10.1%)	19 (11.2%)
Others	17 (6.9%)	12 (7.0%)

RESULTS

We analyzed 3-, and 5-year survival rates in our 418 patients with localized RCC (T1-2N0M0). During the three years after surgery in the RN group, the general mortality rate was 17 pts., in the SN group – 14 pts., during 5 years – 21 pts. and 19 pts. respectively. The 3- and 5-year OS rates in the RN group were 93.1% and 91.5%; and 91.8% and 88.8% in the SN group, respectively. The overall survival rates did not differ significantly between the divided groups (P = 0.463). During three years of observation, cancer-depended mortality in the RN group was 8 pts., in the SN group – 9 pts., during 5 years – 14 pts. in the RN group and 13 pts. in the SN group. The 3- and 5-year CSS rates in the RN group were 96.8% and 94.4%; and 94.7% and 92.4%% respectively in the SN group. Like OS rates, the cancer-specific survival rates were not significantly different between the RN and SN groups (P = 0.647).

In order to make more detailed analysis of survival rates, we stratified the OS and CSS rates depending on tumor stage (T1N0M0 or T2N0M0). Overall survival and cancer-specific survival rates were not significantly different between RN and SN groups for either T1N0M0 (3-year OS: 95.5 % *vs.* 94.7 %; 3-year CSS: 97.3% *vs.* 96.0% and 5-year OS: 93.6% *vs.* 92.0 %; 5-year CSS: 96.4% *vs.* 96%) or T2N0M0 (3-year OS: 91.3% *vs.* 89.5%; 3-year CSS: 96.4% *vs.* 93.7% and 5-year OS: 89.9% *vs.* 86.3%; 5-year CSS: 92.8% *vs.* 89.5%) stages.

Obtained data were systematized in Table 2.

The data presented in this table show that tumor stage is a predictor of LRCC outcomes that were independent on surgery technique.

Table 2. Long-term results of RN and SN in our patients

Variables	Tumor size, cm	Tumor stage	pts.	3-year OS, %	3-year CSS, %	5-year OS, %	5-year CSS, %
RN group	≤7	T1N0M0	110	95.5	97.3	93.6	96.4
	>7	T2N0M0	138	91.3	96.4	89.9	92.8
	TOTAL		**248**	**93.1**	**96.8**	**91.5**	**94.4**
SN group	≤7	T1N0M0	75	94.7	96.0	92.0	96.0
	>7	T2N0M0	95	89.5	93.7	86.3	89.5
	TOTAL		**170**	**91.8**	**94.7**	**88.8**	**92.4**

Table 3. CSS and G-grades in our patients

Variables	RN group, n = 248 pts.				SN group, N = 170 pts.			
	3-year		5-year		3-year		5-year	
	CSS %	LO	CSS %	LO	CSS %	LO	CSS %	LO
G-1 group	**99.6**	1	**99.2**	2	**100.0**	0	**99.4**	1
G-2 group	**99.6**	1	**98.8**	3	**98.8**	2	**98.2**	3
G-3/4 group	**96.8**	7	**96.4**	9	**95.3**	8	**94.7**	9
TOTAL	**96.4**	9	**94.4**	14	**94.1**	10	**92.4**	13

LO – lethal outcomes in the group during observation period; G1-4 – Fuhrman grades

We also have analyzed the CSS rates dependent on G-grades in our patients. Obtained results are presented in Table 3.

Presented results show that in both divided groups the lowest 5-year CSS rates (96.4% in RN group and 94.7% in SN group) were observed in patients with G-3/4 Fuhrman grades, moreover a majority of lethal outcomes in LRCC patients occurs during the first three years after operation. Corresponding survival rates did not differ greatly between both divided groups, as well as the differences between 3- and 5-year survival rates inside the same group were statistically insignificant. This data affirms the equal prognostic value of 3- and 5-year survival rates in patients with localized RCC.

DISCUSSION

Before the wide use of renal sonography and computerized tomography, the majority of patients with RCC at the time of diagnosis presented with large, often symptomatic tumors and many patients had locally advanced disease at the time of surgery. That is why more than 75% patients were managed using RN [9]. During the last decades, due to widespread renal imaging technologies, the detection of organ-confined, incidental tumors has increased. Our data show that, among all T1-2N0M0 renal neoplasms, tumors were diagnosed incidentally by renal imaging in 73.4% of cases. Since organ-confirmed tumors do not require vast surgical intervention, therefore the strategy of localized RCC surgery has aimed at a transition from radical nephrectomy to simple nephrectomy or organ-sparing surgery.

Skinner D.G. et al. in 1971 had analyzed survival rates according to stage in 309 pts. who underwent RN and SN at their hospital. They found that for stages T1-2N0M0 tumors the results of 5- and 10-year survival were a little better in the RN group, but the difference was statistically insignificant. They did not even find a considerable improvement in survival between the RN and SN groups among the patients with stage T3N0M0 [10].

In a review of 109 pts. with RCC treated by RN and SN, Ramon J. et al. in 1991 analyzed 5-year and 10-year OS and CSS rates [7]. Among the patients with stage T1N0M0, RN produced better survival rates at five and 10 years; however, when non-cancer deaths were excluded, the differences in survival rates between RN and SN groups were statistically insignificant. No statistically significant differences in survival rates were noted by investigators when nephrectomies were performed even for T2-3N0M0 stages.

Patel N.R. and Lavengood R.W. did not find improving survival for patients with T1-2N0M0 treated by RN compared with those treated by SN [11].

A dilemma of surgical choice in LRCC stages became controversial during the last years due to numerous publications about equal survival rates in patients who underwent radical, simple or partial laparoscopic nephrectomies [5, 12-14]. Despite the fact that the standard approach for nephrectomy is now a laparoscopic approach [15], during last decade in urologic clinics open surgery was also widely performed. For instance, as noted by Miller D.C. et al., in 2008 open radical nephrectomy remained the most frequent RCC treatment, which occurred in roughly 70–90% of recent US cases. Data presented by authors show that among the 4,872 pts. with RCC who underwent radical nephrectomy, RN were performed laparoscopically in only 515 cases [16]. As well Vander Eekt K. et al., in their review article from 2007, analyzed the efficacy of open surgery in LRCC treatment [2]. Notwithstanding the evidence showing an advantage for either laparoscopic nephrectomy over open RN, open RN remains the most common RCC treatment in many cases because most urologists are unable or reluctant to proceed with any alternative [17].

The necessity for lymphadenectomy, which is the main special feature of the RN technique, at the present time remains questionable in patients with LRCC. It is known that patients with localized RCC have a comparatively low incidence (2-9%) of lymphatic nodal involvement [18, 19]. So in these cases local recurrences are infrequent, even lymphadenectomy is not performed. Local recurrence rates ranged between 2.2-2.8% in patients with LRCC, who underwent nephrectomies and there were no significant statistical differences in local recurrence rates between patients with and without lymphadenectomy performed [20, 21]. In 2009, Blom J.H., van Poppel H. et al. had analyzed oncological outcomes of 772 pts. with LRCC who underwent nephrectomies with (RN) and without (SN) lymph-node dissection. Their study revealed no significant differences in OS and progression-free survival between these two groups of patients. After proper preoperative staging, the incidence of unsuspected lymph-node metastases was low (4.0%) and no survival advantages of a complete lymph-node dissection in conjunction with a radical nephrectomy were demonstrated [22]. Taking into consideration published reports about benefits of enucleation in T1-2N0M0 stages, the expectation of less vast surgery success is logical [23, 24].

Our data also show that radical nephrectomy with lymph-node dissection does not ensure a statistically significant improvement in survival among LRCC patients when compared with simple nephrectomy. The 3-year OS in the RN group was 93.1% *vs.* 91.8% in the SN group. CSS during the same period was 96.8% *vs.* 94.7%, respectively. The 5-year OS in the RN group was 91.5% *vs.* 88.8% in SN group. After 5 years of observation CSS in RN group was 94.4% *vs.* 92.4% in the SN group (Table 2). Cancer-specific survival rates and mortality in localized forms of RCC depend not upon a type of surgery and lymphadenectomy performed, but obviously on tumor characteristics such as size, stage (Table 2), and G-grade (Table 3).

Hence, if radical nephrectomy does not produce better survival than simple nephrectomy, the vast surgeries performed in localized RCC stages are unnecessary. For patients with LRCC, a lymphadenectomy at the time of RN is not likely to lead to a lower risk of local recurrence or improved survival.

We hope that the presented results will supplement numerous studies, while promoting the choice of a less vast surgery in the treatment of LRCC.

CONCLUSIONS

1. Both radical and simple nephrectomies provide high survival rates of patients with localized RCC.

2. Taking into consideration the absence of statistically significant differences in survival rates between the RN and SN groups, the expediency of vast surgery with lymphadenectomy in localized RCC forms is a question for discussion.

REFERENCES

1. Mejean A, Oudard S, Thiounn N: *Prognostic factors of renal cell carcinoma.* J Urol 2004; 169 (3): 821-827.
2. Vander Eeckt K, Joniau S, Van Poppel H: *Open Surgery for Localized RCC.* The Scientific World Journal 2007; 7: 742-752.
3. Richardson DB, Hamra G: *Ionizing radiation and kidney cancer among Japanese atomic bomb survivors.* Radiat Res 2010; 173 (6): 837-842.
4. Vozianov OF, Romanenko AM, Klymenko IO: *Modern Oncourology: Achievements, Problems, and Outlooks.* Oncology 2006; 8 (2): 153-157.
5. Lesage K, Joniau S, Fransis K, Van Poppel H: *Comparison between open partial and radical nephrectomy for renal tumours: perioperative outcome and health-related quality of life.* Eur Urol 2007; 51: 614-620.
6. Greene FL, Page DL, Fleming ID (eds.), et al: *AJCC cancer staging manual, 6th edition.* Springer, New York, 2002.
7. Ramon J, Goldwasser B, Raviv G, et al: *Long-term results for simple and radical nephrectomy for renal cell carcinoma.* Cancer 1991; 67: 2506-2511.
8. Fuhrman SA, Lasky LC, Limas C: *Prognostic significance of morphologic parameters in renal cell carcinoma.* Am J Surg Pathol 1982; 6: 655-663.
9. Robson CJ, Churchill BM, Anderson W: *The results of radical nephrectomy for renal cell carcinoma.* J Urol 1969; 101 (3): 297-301.
10. Skinner DG, Colvin RB, Vermillion CD, et al: *Diagnosis and management of renal cell carcinoma: A clinical and pathological study of 309 cases.* Cancer 1971; 28: 1165-1177.
11. Patel NR, Lavengood RW: *Renal cell carcinoma: Natural history and results of treatment.* J Urol 1978; 119: 722-726.
12. Dash A, Vickers AJ, Schachter LR, et al: *Comparison of outcomes in elective partial vs. radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm.* BJU Int 2006; 97: 939-945.
13. Kim J, Song P, Kim H, et al: *Comparison of Partial and Radical Nephrectomy for pT1b Renal Cell Carcinoma.* Korean J Urol 2010; 51 (9): 596-600.
14. Patard JJ, Shvarts O, Lam JS, et al: *Safety and efficacy of partial nephrectomy for all T1 tumours based on an international multicenter experience.* J Urol 2004; 171: 2181-2185.
15. Ljungberg B, Cowan NC, Hanbury DC, et al: *EAU Guidelines on Renal Cell Carcinoma: The 2010 Update.* Eur Urol 2010; 58 (3): 398-403.
16. Miller DC, Saigal CS, Banerjee M, et al: *Diffusion of surgical innovation among patients with kidney cancer.* Cancer 2008; 112 (8): 1708-1717.
17. Chen DYT, Uzzo RG: *Optimal management of localized renal cell carcinoma: Surgery, Ablation or Active Surveillance.* J Natl Compr Canc Netw 2009; 7 (6): 635-643.
18. Minervini A, Lilas L, Morelli G, et al: *Regional lymph node dissection in the treatment of renal cell carcinoma: is it useful in patients with no suspected adenopathy before or during surgery?* BJU Int 2001; 88: 169-172.
19. Terrone C, Guercio S, De Luca S, et al: *The number of lymph nodes examined and staging accuracy in renal cell carcinoma.* BJU Int 2003; 91: 37-40.
20. Pantuck AJ, Zisman A., Dorey F, et al.: *Renal cell carcinoma with retroperitoneal lymph nodes: role of lymph node dissection.* J Urol 2003; 169: 2076-2083.
21. Rassweiler J, Tsivian A, Kumar AV, et al: *Oncological safety of laparoscopic surgery for urological malignancy: experience with more than 1.000 operations.* J Urol 2003; 169: 2072-2075.
22. Blom JH, van Poppel H, Maréchal JM, et al: *Radical nephrectomy with and without lymph-node dissection: final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881.* Eur Urol 2009; 55 (1): 28.
23. Carini M, Minervini A, Masieri L, et al: *Simple enucleation for the treatment of pT1a renal cell carcinoma: our 20-year experience.* Eur Urol 2006; 50: 1263-1271.
24. Stephens R, Graham SD Jr: *Enucleation of tumor versus partial nephrectomy as conservative treatment of renal cell carcinoma.* Cancer 1990; 65 (12): 2663-2667.

Correspondence

Alexander Shulyak
6, Boguna Street, Apt. 6
Lviv 79013, Ukraine
phone: +38 06 767 08 952
avshulyak@yandex.ua