Complications and Outcomes Associated With Surgical Management of Renal Cell Carcinoma: Review

¹Faisal Mansour Alsenani, ²Meshal Saleh Ali Alsadeq, ³Omar Mohammed Omar, ⁴Nawwaf Jamaan Althobaiti, ⁵Mohammed Ghazi Alsaedi, ⁶Khalid Faisal Alharbi, ⁷Dhaifallah Barrak Alziadi

Abstract: Renal cell carcinoma (RCC) represent 90% to 95% of malignant neoplasms developing from the kidney. Current advances in surgical and systemic treatments have actually significantly altered the management of RCC. Therefore, This review aimed to discuss and evaluate the most common complications and outcomes Associated with Surgical Management of Renal Cell Carcinoma, through different trails from all around the world, which are based evidence ones. We performed a comprehensive review of the literature based on free-text search in the National Library of Medicine Database MEDLINE using the following keywords: partial-nephrectomy, nephronsparing surgery, cytoreductive-nephrectomy and metastatic renal cell carcinoma. Filtered for human trails, articles published in English to November 2016 were included in this article. Surgical resection represents the requirement of take care of handling patients with kidney masses. Radical nephrectomy is the gold requirement for bigger kidney masses, whereas nephron-sparing PN is the preferred treatment modality for T1a growths. NSS, when possible, might be a feasible option for surgical debulking in metastatic RCC. For patients with primary growths open to NSS, developed prognostic factors can be utilized for patient choice.

Keywords: Renal cell carcinoma (RCC), systemic treatments, Surgical Management, bigger kidney masses.

1. INTRODUCTION

Renal cell carcinoma (RCC) represent 90% to 95% of malignant neoplasms developing from the kidney. Current advances in surgical and systemic treatments have actually significantly altered the management of RCC ⁽¹⁾. Regardless of the earlier detection of smaller sized kidney tumors, the rate of RCC-related mortality has actually increased ^(2,3), recommending that recurrence and advanced disease are responsible for mortality. RCC consists of a heterogeneous group of growths with distinct genetic and metabolic defects, in addition to histopathologic and scientific functions (**Table1**) ⁽⁴⁾. Medullary carcinomas are unusual however aggressive, and are specifically associated with sickle cell trait. Targeted treatments against the vascular endothelial development factor (VEGF) pathway have extended the lives of the patients with innovative disease significantly, with average total survival currently surpassing 2 years ⁽¹⁾.

With an estimated incidence of 61,560 cases and 13,040 deaths in 2015, renal cell cancer (RCC) stays a crucial and common reason for cancer death in the United States ⁽⁵⁾. Around 25%-30% of patients have metastatic disease at the time of diagnosis ^(6,7,8,9,10), which is connected with a mean survival of 1-2 years (11,12,13). Up until recently, immunotherapy, such as interleukin-2 and interferon-alpha, was the only readily available systemic treatment choices for metastatic RCC ^(14,15,16,17,18); nevertheless, over the past years, treatment choices have actually increased significantly with the approval of numerous targeted treatment agents ⁽¹⁸⁾. I Few studies exist examining the utility and efficiency of more aggressive surgical intervention for in your area advanced or metastatic RCC including the liver. Furthermore, concurrent surgical resection of the liver at the time of radical nephrectomy is connected with substantial morbidity, which might exceed the benefits of surgically debulking RCC ^(19,20,21,22).

Vol. 4, Issue 2, pp: (628-633), Month: October 2016 - March 2017, Available at: www.researchpublish.com

Even after surgical resection for clinically localized disease, 20 to 40% of patients will regression and have a poor prognosis with respect to long-lasting survival (23,24). Even with the brand-new targeted systemic therapies being developed and authorized in the last years, rarely do they supply long-term or complete reactions. The only possibility of long-lasting treatment and survival of RCC involve surgical interventions consisting of radical nephrectomy, partial nephrectomy (PN), ablative techniques, and, in chosen cases, metastasectomy in mix with multimodal treatment techniques (25).

Histology	Frequency	Cell of Origin
Clear cell	60%-70%	Proximal tubule
Papillary	5%-15%	Proximal tubule
Chromophobic	5%-10%	Cortical collecting duct
Oncocytic	5%-10%	Cortical collecting duct
Collecting duct	<1%	Medullary collecting duct

Table 1: Classification of Renal Cell Carcinoma

This Review aimed to discuss and evaluate the most common complications and outcomes Associated with Surgical Management of Renal Cell Carcinoma, through different trails from all around the world, which are based evidence ones.

2. METHODOLOGY

We performed a comprehensive review of the literature based on free-text search in the National Library of Medicine Database MEDLINE using the following keywords: partial-nephrectomy, nephron-sparing surgery, cytoreductive-nephrectomy and metastatic renal cell carcinoma. Filtered for human trails, articles published in English to November 2016 were included in this article. Based on the relevance of the content, our review consisted of several articles. Of note, the reviewed literature had a low level of evidence, constituted by case reports, small case series and reviews.

3. RESULTS AND DISCUSSION

Less Prognosis of All RCC:

Patients with Small RCC appear to have the worst diagnosis of all RCC. Couple of patients show extended survival; those who do generally present with early-stage disease (phase I and stage II) (26). Most of series report an average survival time of just 4-9 months after medical diagnosis (27,28,29,30,31). Compared to other patients with top-quality RCCs, those with sRCCs still have a worse diagnosis. Numerous series have validated the presence of sarcomatoid features to be an independent predictor of bad survival (27,32,33). The existence of sarcomatoid components might be one of the most prominent prognostic variables for patient result (28). Numerous studies have looked at the impact of the percentage of sarcomatoid transformation on prognosis and demonstrated that greater amounts were associated with a worse result (26,27,28)

Roles of surgical management methods and their complications or RCC:

For most RCC patients who provide at a sophisticated phase with a big, large tumor, surgical treatment can be really difficult, and generally radical nephrectomy is required. Regularly, these growths are connected with an intense desmoplastic reaction and resection of surrounding organs might be needed. In a series of patients undergoing cytoreductive nephrectomy, > 25% of them had T4 disease and 33% had favorable lymph nodes (28). As such, significant morbidity may be inevitable in innovative cases.

Lymph node dissection in the lack of medical disease has actually been omitted due to the fact that of level I evidence ⁽³⁴⁾, Blute and associates at the Mayo Clinic advised extended lymph node dissection if sarcomatoid functions are identified at the time of surgery ⁽³⁵⁾.

Vol. 4, Issue 2, pp: (628-633), Month: October 2016 - March 2017, Available at: www.researchpublish.com

- A) Cytoreductive nephrectomy (CN) is utilized in patients with RCC who initially present in a metastatic RCC (mRCC) setting. 2 prospective randomized trials showed remarkable progression-free survival and OS in patients going through CN followed by immunotherapy compared with immunotherapy alone (36,37). In a combined analysis, patients treated with CN and immunotherapy had a survival benefit of 13.6 versus 7.8 months in patients going through immunotherapy alone (40). This is the factor that CN for patients with mRCC has actually been extensively embraced, although only patients with excellent overall performance status were included and some poor prognostic metastatic sites (brain) were excluded, presenting a selection predisposition. CN is substantially more complex than basic RN, with in-hospital death rates of 5%, suggesting the need for cautious patient selection (41). In the setting of metastatic RCC, level I evidence supports the benefits of cytoreductive nephrectomy prior to prepared immunotherapy (36,37). Although the new era of targeted therapy has demonstrated responses in the primary tumor, cytoreductive nephrectomy typically remains an integral part of therapy (38,39). Whereas cytoreductive surgery still has a major function in the treatment of metastatic RCC, for patients with sRCC, numerous question the survival benefit of cytoreductive surgical treatment (28,29). The aggressive nature of this disease might lead to quick disease progression with postponed initiation of systemic therapy to enable postoperative convalescence (39). Previous experience with these patients has indicated that ~ 60% cannot proceed to systemic therapy after surgery (28).
- B) Radical Nephrectomy (RN); radical nephrectomy has actually been the gold standard of dealing with deadly kidney masses with a curative intent for years ⁽⁴²⁾. In contrast to previously described pericapsular nephrectomy, radical nephrectomy consisted of the en bloc resection of the entire kidney in addition to the surrounding perinephric fat, the ipsilateral adrenal gland, and the local lymph nodes ⁽⁴²⁾. This improved overall survival (OS) significantly at that time to around 65% for localized RCC ⁽⁴²⁾. In the 1990s, minimally intrusive techniques to radical nephrectomy were established, and consequently laparoscopic radical nephrectomy (LRN) has actually ended up being an extensively adopted treatment ⁽⁴³⁾. LRN be carried out by transperitoneal, retroperitoneal, and hand-assisted methods. Due to equivalent oncologic control with lower morbidity, enhanced complication profile, and faster convalescence than ORN, LRN is now considered requirement in a patient population not amenable to NSS and with growth stages approximately T1-3, N0, M0 ^(44,45,46,47). Numerous studies demonstrated improved perioperative and postoperative results such as decreased blood loss, reduced personnel time, shorter hospital stay, less need for analgesia, and faster healing to normal exercise ^(48,49).
- C) Partial nephrectomy or nephron-sparing surgery (NSS); is considered the treatment of option for localized small kidney masses with oncological outcome in cases of renal cell cancer (RCC) comparable to radical nephrectomy (50). Using NSS has the advantage of preserving kidney function with lower cardiovascular death and morbidity (51,52,53,54). NSS is considered the treatment of choice for localized little renal masses, (50) with oncological result comparable to Registered Nurse, and benefits of maintaining renal function and lowering cardiovascular death and morbidity (51,52,53,54). Due to the fact that chronic kidney disease (CKD, glomerular filtering rate <60 mL/min/1.73 m2) is more widespread in a RCC patient, (52,54) the benefit of NSS can be appreciated in this study from Memorial-Sloan Kettering that found the incidence of new-onset CKD in patients with normal serum creatinine and two operating kidneys, who had actually gone through NSS and RN for little renal masses, to be 17% and 69%, respectively (53). There is installing evidence in the literature that tumor characteristics instead of surgical method figured out CSS and OS (55,56). This evidence led to the expansion of the utility of NSS in tumors larger than 4 cm and in your area advanced RCC. In a research study by Margulis et al., the oncological efficacy of NSS versus Registered Nurse in patients with in your area advanced RCC was compared. In the comparison of 34 patients going through NSS and 567 patients undergoing RN, the CSS curves demonstrated comparable result (57).

4. CONCLUSION

Surgical resection represents the requirement of take care of handling patients with kidney masses. Radical nephrectomy is the gold requirement for bigger kidney masses, whereas nephron-sparing PN is the preferred treatment modality for T1a growths. NSS, when possible, might be a feasible option for surgical debulking in metastatic RCC. For patients with primary growths open to NSS, developed prognostic factors can be utilized for patient choice. Patients more than likely to take advantage of a nephron-sparing method are those for whom Registered Nurse is not feasible due to preexisting kidney impairment and patients with restricted metastatic disease anticipated to enjoy extended survival with a mix surgical intervention and systemic treatment. The very same benefit as resection of a systemic metastasis is suggested to be real for isolated local recurrence of RCC. Also, complete and aggressive surgical resection can supply long lasting local growth control, and a multimodal technique with th combination of systemic treatment should be considered in these patients

Vol. 4, Issue 2, pp: (628-633), Month: October 2016 - March 2017, Available at: www.researchpublish.com

REFERENCES

- [1] Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. *J Clin Oncol*. 2009;27(22):3584-3590.
- [2] Rini BI, Campbell SC, Escudier B. Renal cell carcinoma. Lancet. 2009;373(9669):1119-1132.
- [3] Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. J Natl Cancer Inst. 2006;98(18):1331-1334.
- [4] Linehan WM, Srinivasan R, Schmidt LS. The genetic basis of kidney cancer: a metabolic disease. *Nat Rev Urol*. 2010;7(5):277-285.
- [5] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65:5-29. 2.
- [6] Lam JS, Leppert JT, Belldegrun AS, Figlin RA. Novel approaches in the therapy of metastatic renal cell carcinoma. World J Urol. 2005;23:202-212. 3.
- [7] Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. N Engl J Med. 1996;335:865-875.
- [8] Hainsworth JD, Sosman JA, Spigel DR, Edwards DL, Baughman C, Greco A. Treatment of metastatic renal cell carcinoma with a combination of bevacizumab and erlotinib. J Clin Oncol. 2005;23:7889-7896.
- [9] Mickisch GH. Multimodality treatment of metastatic renal cell carcinoma. Expert Rev Anticancer Ther. 2002;2:681-685.
- [10] Staehler M, Rohrmann K, Haseke N, Stief CG, Siebels M. Targeted agents for the treatment of advanced renal cell carcinoma. Curr Drug Targets. 2005;6:835-846.
- [11] Heng DY, Xie W, Regan MM, et al. External validation and comparison with other models of the International Metastatic RenalCell Carcinoma Database Consortium prognostic model: a populationbased study. Lancet Oncol. 2013;14:141-148.
- [12] Wahlgren T, Harmenberg U, Sandstrom P, et al. Treatment and overall survival in renal cell carcinoma: a Swedish population-based study (2000-2008). Br J Cancer. 2013;108:1541-1549.
- [13] Ko JJ, Xie W, Kroeger N, et al. The International Metastatic Renal Cell Carcinoma Database Consortium model as a prognostic tool in patients with metastatic renal cell carcinoma previously treated with first-line targeted therapy: a population-based study. Lancet Oncol. 2015;16:293-300.
- [14] Motzer RJ, Russo P. Systemic therapy for renal cell carcinoma. J Urol. 2000;163:408-417. 11.
- [15] Eton DT, Cella D, Bacik J, Motzer RJ. A brief symptom index for advanced renal cell carcinoma. Health Qual Life Outcomes. 2006;4:68.
- [16] Bukowski RM. Natural history and therapy of metastatic renal cell carcinoma: the role of interleukin-2. Cancer. 1997;80:1198-1220.
- [17] Yang JC, Topalian SL, Parkinson D, et al. Randomized comparison of high-dose and low-dose intravenous interleukin-2 for the therapy of metastatic renal cell carcinoma: an interim report. J Clin Oncol. 1994;12:1572-1576.
- [18] Yang JC, Sherry RM, Steinberg SM, et al. Randomized study of highdose and low-dose interleukin-2 in patients with metastatic renal cancer. J Clin Oncol. 2003;21:3127-3132. 15.
- [19] Lombardi G, Zustovich F, Donach M, Dalla Palma M, Nicoletto O, Pastorelli D. An update on targeted therapy in metastatic renal cell carcinoma. Urol Oncol. 2012;30:240-246.
- [20] Yezhelyev M, Master V, Egnatashvili V, Kooby DA. Combined nephrectomy and major hepatectomy: indications, outcomes, and recommendations. J Am Coll Surg. 2009;208:410-418.
- [21] Staehler MD, Kruse J, Haseke N, et al. Liver resection for metastatic disease prolongs survival in renal cell carcinoma: 12-year results from a retrospective comparative analysis. World J Urol. 2010;28:543-547.
- [22] Dabestani S, Marconi L, Hofmann F, et al. Local treatments for metastases of renal cell carcinoma: a systematic review. Lancet Oncol. 2014;15:e549-e561.

- Vol. 4, Issue 2, pp: (628-633), Month: October 2016 March 2017, Available at: www.researchpublish.com
- [23] Gupta K, Miller J D, Li J Z, Russell M W, Charbonneau C. Epidemiologic and socioeconomic burden of metastatic renal cell carcinoma (mRCC): a literature review. Cancer Treat Rev. 2008;34(3):193–205.
- [24] Lam J S, Shvarts O, Leppert J T, Figlin R A, Belldegrun A S. Renal cell carcinoma 2005: new frontiers in staging, prognostication and targeted molecular therapy. J Urol. 2005;173(6):1853–1862.
- [25] Escudier B. Emerging immunotherapies for renal cell carcinoma. Ann Oncol. 2012;23 08:viii35-40.
- [26] de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: A study of 101 cases. Am J Surg Pathol. 2001;25:275–284.
- [27] Cheville JC, Lohse CM, Zincke H, et al. Sarcomatoid renal cell carcinoma: An examination of underlying histologic subtype and an analysis of associations with patient outcome. Am J Surg Pathol.2004;28:435–441.
- [28] Shuch B, Said J, La Rochelle JC, et al. Cytoreductive nephrectomy for kidney cancer with sarcomatoid histology—is up-front resection indicated and, if not, is it avoidable? J Urol. 2009;182:2164–2171.
- [29] Mian BM, Bhadkamkar N, Slaton JW, et al. Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. J Urol. 2002;167:65–70.
- [30] Tomera KM, Farrow GM, Lieber MM. Sarcomatoid renal carcinoma. J Urol. 1983;130:657-659.
- [31] Sella A, Logothetis CJ, Ro JY, et al. Sarcomatoid renal cell carcinoma. A treatable entity. Cancer.1987;60:1313–1318.
- [32] Shuch B, La Rochelle JC, Wu J, et al. Performance status and cytoreductive nephrectomy: Redefining management in patients with poor performance. Cancer. 2008;113:1324–1331.
- [33] Moch H, Gasser T, Amin MB, et al. Prognostic utility of the recently recommended histologic classification and revised TNM staging system of renal cell carcinoma: A Swiss experience with 588 tumors. Cancer. 2000;89:604–614.
- [34] Blom JH, van Poppel H, Marechal JM, et al. Radical nephrectomy with and without lymph node dissection: Preliminary results of the EORTC randomized phase III protocol 30881. EORTC Genitourinary Group. Eur Urol. 1999;36:570–575.
- [35] Blute ML, Leibovich BC, Cheville JC, et al. A protocol for performing extended lymph node dissection using primary tumor pathological features for patients treated with radical nephrectomy for clear cell renal cell carcinoma. J Urol. 2004;172:465–469.
- [36] Mickisch GH, Garin A, van Poppel H, et al. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: A randomised trial. Lancet. 2001;358:966–970.
- [37] Flanigan RC, Salmon SE, Blumenstein BA, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. N Engl J Med. 2001;345:1655–1659.
- [38] Pantuck AJ, Belldegrun AS, Figlin RA. Cytoreductive nephrectomy for metastatic renal cell carcinoma: Is it still imperative in the era of targeted therapy? Clin Cancer Res. 2007;13:693s–696s.
- [39] Kutikov A, Uzzo RG, Caraway A, et al. Use of systemic therapy and factors affecting survival for patients undergoing cytoreductive nephrectomy. BJU Int. 2010;106:218–223.
- [40] Flanigan R C, Mickisch G, Sylvester R, Tangen C, Van Poppel H, Crawford E D. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol. 2004;171(3):1071–1076.
- [41] Trinh Q D Bianchi M Hansen J et al. In-hospital mortality and failure to rescue after cytoreductive nephrectomy Eur Urol 2012(Sep):7
- [42] Robson C J, Churchill B M, Anderson W. The results of radical nephrectomy for renal cell carcinoma. J Urol. 1969;101(3):297–301.
- [43] Kerbl K, Clayman R V, McDougall E M, Kavoussi L R. Laparoscopic nephrectomy. BMJ. 1993;307(6917):1488–1489.

Vol. 4, Issue 2, pp: (628-633), Month: October 2016 - March 2017, Available at: www.researchpublish.com

- [44] Gill I S, Meraney A M, Schweizer D K. et al. Laparoscopic radical nephrectomy in 100 patients: a single center experience from the United States. Cancer. 2001;92(7):1843–1855.
- [45] Chan D Y Cadeddu J A Jarrett T W Marshall F F Kavoussi L R Laparoscopic radical nephrectomy: cancer control for renal cell carcinoma J Urol 200116662095–2099.2099, discussion 2099–2100
- [46] Wille A H Roigas J Deger S Tüllmann M Türk I Loening S A Laparoscopic radical nephrectomy: techniques, results and oncological outcome in 125 consecutive cases Eur Urol 2004454483–488.488, discussion 488–489
- [47] Hemal A K, Kumar A, Gupta N P, Kumar R. Oncologic outcome of 132 cases of laparoscopic radical nephrectomy with intact specimen removal for T1-2N0M0 renal cell carcinoma. World J Urol. 2007;25(6):619–626.
- [48] Dunn M D, Portis A J, Shalhav A L. et al. Laparoscopic versus open radical nephrectomy: a 9-year experience. J Urol. 2000;164(4):1153–1159.
- [49] McDougall E, Clayman R V, Elashry O M. Laparoscopic radical nephrectomy for renal tumor: the Washington University experience. J Urol. 1996;155(4):1180–1185.
- [50] Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, et al. A Prospective randomized EORTC Intergroup Phase 3 study comparing the complications of elective nephron sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2007;51:1606–15.
- [51] Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc. 2000;75:1236–42.
- [52] McKiernan J, Simmons R, Katz J, Russo P. Natural history of chronic renal insufficiency after partial and radical nephrectomy. Urology. 2002;59:816–20.
- [53] Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial nephrectomy versus radical nephrectomy in patients with small renal tumors-is there a difference in mortality and cardiovascular outcomes? J Urol. 2009;181:55–61.
- [54] Kates M, Badalato GM, Pitman M, McKiernan JM. Increased risk of overall and cardiovascular mortality after radical nephrectomy for renal cell carcinoma 2 cm or less. J Urol. 2011;186:1247–53.
- [55] Patard JJ, Shvarts O, Lam JS, Pantuck AJ, Kim HL, Ficarra V, et al. Safety and efficacy of partial nephrectomy for all T1 tumors based on an international multicenter experience. J Urol. 2004;171:2181–5.
- [56] Becker F, Siemer S, Hack M, Humke U, Ziegler M, Stockle M. Excellent longterm cancer control with elective nephron-sparing surgery for selected renal cell carcinomas measuring more than 4 cm. Eur Urol. 2006;49:1058–63.
- [57] Margulis V, Tamboli P, Jacobsohn KM, Swanson DA, Wood CG. Oncological efficacy and safety of nephron-sparing surgery for selected patients with locally advanced renal cell carcinoma. BJU Int. 2007;100:1235–9.