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Long-term Management of Bilateral, Multifocal, Recurrent Renal Carcinoma

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Abstract

Patients with bilateral multifocal renal cell carcinoma (RCC) are at increased risk for development of locally recurrent or *de novo* tumors after nephron sparing procedures. When dealing with recurrent renal masses the options are limited to observation, total nephrectomy, ablation, or repeat surgical intervention. We review the literature for association of bilaterality and multifocality, and multifocality as a main factor for development of locally recurrent renal tumors. The importance of maximal renal preservation and morbidity of renal replacement therapy is discussed. The outcome data of repeat renal interventions are presented and demonstrates reasonable functional and oncologic outcomes despite higher perioperative complications. Our results support use of reoperative renal surgery over total nephrectomy and renal replacement therapy.

Renal cell carcinoma (RCC) is the third most common genitourinary malignancy and a major healthcare concern worldwide. In 2009, kidney cancer will be diagnosed in more than 57,000 patients and will claim the lives of almost 13,000 in the United States.¹ RCC incidence appears to be steadily rising by 3% per year in the US.^{2, 3} The increase in cross-sectional imaging and detection of renal masses can only partially explain the rising incidence of RCC. As many as a third of all RCC patients will present with metastatic disease and as many as 50% of surgically treated patients for localized disease will fail either locally, or more commonly, distally.^{4–7} Identifying high risk patients has been one of the main focuses of clinical and basic research.

Traditionally, patients with bilateral multifocal renal tumors are considered to be in the high risk category, mostly due to the propensity to form locally recurrent tumors. Indeed, long-term follow up of patients with von Hippel-Lindau, characterized by the development of tumors in multiple organs including bilateral multifocal clear renal cell carcinomas, has demonstrated that a vast majority of these patients will develop locally recurrent tumors at 10 years.⁸ Similarly, Blute and colleagues observed a significantly higher rate of local recurrence in patients with bilateral nonhereditary renal masses compared to those treated for unilateral RCC.⁹ Not surprisingly, patients presenting with bilateral, multifocal bilateral, or multifocal ipsilateral renal tumors, end up losing at least one of their renal units after undergoing radical nephrectomy.^{10–12}

While studies of patients with bilateral multifocal disease have enabled identification of a number of kidney cancer genes, the genetic basis of bilateral, multifocal kidney cancer in most patients remains to be determined.^{13–15} Although many investigators have reported excellent oncologic outcomes of patients with multifocal RCC treated by radical

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nephrectomy, the optimal form of management for these patients continues to be an important question.^{16–22} The main unanswered issues address the following three questions:

1. Are patients with bilateral multifocal renal masses at high risk group for distant failures and development of metastatic disease?
2. Does the presence of bilateral multifocal renal masses warrant bilateral nephrectomy or maximal renal preservation?
3. If the path of renal preservation is chosen, is repeat renal surgery better than total nephrectomy?

This review will address the long-term management of a challenging cohort of patients with bilateral multifocal renal masses. In order to answer the questions above, the following topics will need to be considered:

1. Frequency of bilaterality and multifocality of renal masses.
2. Definition of local recurrence.
3. Importance of maximal renal preservation
4. Outcomes of renal replacement therapy.
5. Outcomes of surgical management of recurrent RCC.

Frequency of bilaterality and multifocality of renal masses

Among a growing number of patients with kidney cancer, as many as 5% present with bilateral renal tumors with or without known hereditary renal cancer syndromes.^{11, 23–25} Of those patients with bilateral tumors, a large proportion will be found to have multifocal renal masses.^{9, 10} A recent multi-institutional study of synchronous bilateral RCC reported that multifocality was found in 54% of patients.¹¹ Conversely, in autopsy study by Wunderlich et al, the incidence of bilaterality was almost 90% once multifocal RCC was present.²⁶ Most importantly, however, is the recognition of the close association of bilateral renal masses and multifocality.

The importance of multifocality in RCC has been studied extensively in regards to incidence, risks for development of multifocal lesions, and outcomes of those undergoing surgical treatment. While multifocality appears to be present at a greater frequency in patients with bilateral renal masses (more commonly in those with synchronous than metachronous)^{10, 11, 27} than in those without bilateral involvement, its prevalence in the general population undergoing nephrectomy is not negligible. A review of studies that evaluate multifocality in RCC over the past 2 decades reveals considerable variability among institutions in frequency of multifocality identified in radical nephrectomy specimens.^{17–19, 22, 26, 28–39} Multifocality has been observed in between 4.3 and 25% of patients undergoing nephrectomy (Table 1). It is not clear if such variability is due to the heterogeneity of patients studied or differences in pathological evaluation. Studies utilizing microscopic thin step sectioning rather than gross examination or capsular stripping of the removed kidney, were more likely to identify multifocal renal lesions.^{28, 39} Notably, not only was papillary type 1 RCC multifocal, but clear cell RCC as well as other histologic types were also found to be associated with multifocality.^{17, 19, 22, 28, 30, 33} Additionally, preoperative assessment frequently underestimated the presence of multifocality.^{22, 38}

Meanwhile, the importance of multifocality in kidney cancer and its impact on patients and treating physicians is largely underappreciated. Even the most recent guidelines do not specifically address multifocality as a factor in the follow up algorithm and management.^{4–7, 40} It is possible that lack of specific recommendations for follow up is not

only secondary to the relatively small number of patients with bilateral multifocal RCC, but may also be due to the fact that a large number of patients with multifocal RCC end up losing at least one renal unit.^{10–12} In a study by Krambeck and colleagues, 51% of cases scheduled for nephron-sparing surgery (NSS) were converted to radical nephrectomy in the setting of multifocal tumors (although a large proportion of those treated by radical nephrectomy had RCC tumors greater than 5 cm).¹² Of concern, however, is the possibility that many physicians managing patients with multifocal RCC may perform an unnecessary nephrectomy.

Once the radical nephrectomy is performed, patients with bilateral multifocal renal masses do not seem to be in a higher risk group for the development of metastatic disease. Series comparing outcomes of radical nephrectomy for multifocal versus unifocal RCC found equivalent oncologic outcomes and no additional risks for distant failure secondary to presence of multifocality.^{17, 22} While some clinicians may choose to perform radical nephrectomy due to patients' preference or lack of experience in technical execution of NSS for multiple tumors, the most common rationale for total kidney removal is likely due to concern for effective local control and tumor recurrence. In order to address these issues, it is beneficial to examine the concept of local recurrence in the setting of multifocal RCC.

Definition of local recurrence

Evaluating oncologic outcomes in patients with hereditary or multifocal RCC can be challenging. For those managing patients with multifocal tumors, the oncologic success is measured by metastasis-free survival and the need for subsequent intervention. The local recurrence in this population is difficult to assess. Unless specific studies, designed to assess for clonal origin, are performed on each of the “locally recurrent tumors”, it is difficult to differentiate between local recurrence due to inadequately resected tumors previously, interval development of new tumor(s), or detection of tumors that were present at the time of surgery but were too small to appreciate with pre- and intraoperative imaging modalities. Only if the new tumor is detected in a location remote from the original resection site and clonality studies confirm that the newly detected tumor is not an intrarenal metastasis or a remnant of a previously resected tumor, can one comfortably conclude that the so-called “recurrence” is a representation of multifocality, rather than a “true recurrence”. In fact, in patients with bilateral multifocal RCC that undergo nephron sparing procedures, “local recurrence” is most likely a reflection of the multifocal nature of the disease rather than a failure of a surgical therapy.

The support for the argument that “local recurrences” are due to multifocality come from the studies of renal tumors and normal parenchyma resected from patients with hereditary renal cancer syndromes. Walther and colleagues estimated that a removed kidney from a patient with von Hippel-Lindau may contain as many as 600 solid clear cell carcinoma tumors and 1,100 cysts.⁴¹ A study of the kidneys from patients with Hereditary Papillary Renal Carcinoma, characterized by the development of bilateral multifocal papillary type 1 carcinomas, has predicted that the affected renal unit may contain as many as 3,400 tumors.⁴² Similarly, patients with Birt-Hogg-Dube syndrome, characterized by development of cutaneous fibrofolliculomas, pulmonary cysts, and variety of renal tumors, often are found to have dozens of lesions in an affected kidney.⁴³

Only after appreciating the number of tumors observed microscopically in those with bilateral multifocal RCC, can one quantitate oncologic outcomes in more practical terms, such as metastasis-free survival or subsequent intervention-free survival. Overall survival is an appropriate outcome measure as well; however, it needs to be evaluated carefully in light

of emerging evidence of renal function and its effect on cardiovascular morbidity and survival.

Importance of maximal renal preservation

As diagnosis and imaging of genitourinary malignancies has evolved, notable progress has been made in the management of patients with kidney cancer. One of the most important advances has been the recognition of the adverse effects on longevity of renal insufficiency and the acceptance of the importance of maximal renal preservation. Although randomized prospective studies comparing the nephron sparing approach to a nephrectomy have not been performed, increasing evidence from retrospective analysis reveals the critical role of preservation of functional renal parenchyma. After analyzing over 1,000,000 patients, Go and colleagues found that an incremental decrease in renal function is associated with incremental increase in all-cause hospitalization, cardiovascular morbidity, and all-cause mortality.⁴⁴ Additionally, several authors have demonstrated a close association between renal insufficiency and cardiovascular disease, while others have suggested that patients treated with radical nephrectomy had shorter overall survival when compared to those treated with a partial nephrectomy.^{45–49}

Additionally, the historic rationale that removal of the entire kidney was inconsequential (since most renal donors do well long-term with a solitary renal unit) is no longer supported by the data. The recent findings by Koenig and colleagues demonstrate that those with RCC are more likely to have an underlying renal insufficiency than the healthy donor population.⁵⁰ While it is not clear if patients with multifocal tumors are as likely to have underlying renal insufficiency similar to those with sporadic unifocal RCC, the concept of maximal renal preservation still applies. In the hereditary RCC population, for example, multifocal renal tumors present at a younger age.^{14, 15} Although likely healthier on presentation, these patients still have risks for lifelong co-morbidities with potential renal damage. Additionally, there is a potential need for renal replacement therapy due to bilateral renal involvement and propensity for recurrent or *de novo* tumor formation.

Outcomes of renal replacement therapy

Hemodialysis

Despite significant advances, renal replacement therapy remains a significant source of morbidity and mortality. Patients receiving long-term hemodialysis have a mortality rate due to cardiovascular disease 10 to 30 times higher than the general population.⁵¹ When considering the fatality rate from myocardial infarctions alone, the overall survival of dialysis patients was considerably worse than those without kidney failure, even compared to subjects with comorbid conditions such as diabetes without end-stage renal disease.⁵² According to the US Renal Data System (USRDS) the mortality rates on dialysis is 22% during the first 2 years, and 15% during the next 3 years. Rocco et al reported that during 12 months follow up of patients receiving long-term hemodialysis, excluding inpatients requiring hemodialysis secondary to a medical event, more than 50% of patients required hospitalization, and 20% died.⁵³ The mortality numbers obtained from USRDS may not be representative for the cohort of patients with bilateral multifocal disease, since most patients on dialysis may have had a long-standing history of other serious comorbidities, while those with multifocal renal masses may be healthier. Nevertheless, it is important to recognize the morbidity and risks associated with hemodialysis. Additionally, although beyond the scope of this review, the costs of hemodialysis are not insignificant, and approach \$70,000 per person yearly.⁵⁴

Renal transplantation

Significant progress has been made in the past 2 decades in both management of bilateral multifocal RCC as well as renal transplantation. Earlier management strategies involving bilateral nephrectomy followed by renal transplantation are less frequently recommended, having given way to an approach involving aggressive renal preservation.^{55–62} Several factors have relegated bilateral nephrectomy to a last resort in the management of patients with bilateral, multifocal RCC. First, the risks of dialysis have become more widely appreciated.^{63–65} Second, the guidelines for renal transplantation suggest a 2-year tumor-free interval from RCC, before consideration of kidney transplantation.⁶⁶ This subjects patients to at least a 2-year period of dialysis. Third, the shortage of renal allograft for transplantation may place the patient in a period of prolonged dialysis.⁶⁵ Fourth, despite the advances in renal transplantation, as many as 20 to 33% of renal allografts will fail at 5 years post-transplant.^{51, 67} Fifth, once the patient receives the transplant, only 75 % are alive at 5 years.^{53, 67} Therefore, before bilateral nephrectomy is contemplated, it may be reasonable to identify potential renal donors. In case of directed renal donor, the renal transplantation may become a more viable and reasonable option that may avoid a prolonged period of waiting for an allograft. In fact, some transplant surgeons perform directed renal transplantation as early as 6 weeks after the nephrectomy, allowing only a short interval of time to be bridged by dialysis.

While the data for dialysis and renal transplantation are derived from the patients with other co-morbidities such as coronary artery disease, diabetes and hypertension, and may not necessarily reflect the outcomes for the potentially healthier patients with bilateral multifocal recurrent renal lesions, the long-term complications of renal replacement therapy are significant. In many instances, this justifies an aggressive surgical approach to preserve native renal function.

Outcomes of surgical management of recurrent RCC

Management options

Considering the rate of multifocality discussed earlier, it is not surprising that new kidney tumors are identified in patients treated with prior surgical resection. Whether these tumors represent a true recurrence from incomplete resection of the initial tumor or development/detection of the new tumor in the kidney is not always answerable. The management issue, however, remains the same: the need for repeat intervention on a previously operated kidney.

Management options for recurrent tumors include completion nephrectomy, ablation, or repeat partial nephrectomy. Potential oncologic efficacy of completion nephrectomy must be balanced by the deleterious effect on renal function. In cases of bilateral involvement or “recurrences”, performing bilateral nephrectomy subjects patients to considerable risks of renal replacement therapy. While early and intermediate outcomes for ablative therapies appear to be encouraging in some studies, long-term results are not available. Additionally, the experience with ablative therapy in patients with hereditary kidney cancer or multifocal renal lesions is quite limited.^{68, 69} In certain scenarios, however, ablative technologies may be ineffective or inadvisable for patients with multifocal RCC. Larger tumors, tumors located in close proximity to renal vessels, collecting system or the ureter, as well as new lesions on a previously ablated or operated kidney may not be safe to ablate due to the presence of scarring or adhesions to surrounding viscera.⁷⁰ Figure 1 demonstrates preoperative image of a patient recently treated at the NCI who had prior ablation of 2 left renal masses. The location of the new lesion was not felt to be safe for ablation. This patient required open post-RFA left partial nephrectomy with resection of 9 tumors. This case

illustrates that in patients with bilateral multifocal recurrent tumors, NSS often remains the only and the most reasonable option short of dialysis.

Reoperative renal surgery

Repeat partial nephrectomies may be challenging due to fibrosis, scarring, and obliteration of normal anatomic planes. The complication rates in our series were greater than our previously reported series of *de novo* partial nephrectomies. In our recent report of repeat renal surgeries on 51 renal units, the intraoperative complication rate was 35.3%.⁷¹ Major postoperative complications occurred in 11.8% of cases and included pulmonary embolism, pancreatic leak, hemodialysis, and one mortality due to perioperative myocardial infarction. The complication rates of our series were higher than those reported for surgically naïve patients and repeat surgeries reported by a Mayo Clinic group.^{72–76} Such differences may potentially be explained by a higher percent of hereditary RCC in our cohort and likely a larger number of tumors resected in our series during the repeat intervention. Additionally, it is possible that our primary surgeries were also performed with resection of larger numbers of tumors, resulting in more severe scarring, setting the stage for more difficult repeat procedures.⁷⁷

The management of patients with recurrent or *de novo* renal lesions becomes even more difficult when there is a need for another intervention after one or two prior renal surgeries. In a recent review of salvage partial nephrectomies (defined as three or more surgeries on the same renal unit) the major complication rate was 46%.⁷⁸ One half of all major complications were loss of the renal unit. Nevertheless, three-fourths of the operated kidneys in this series were preserved. Although the median follow up of this cohort was only 25 months, some of the patients remained free from metastatic disease and dialysis as long as 7 years after the surgery. Despite a high complication rate, rationale for salvage NSS comes from the high survival rate (100%) of this cohort.

Additional challenges with reoperative renal surgery are seen in patients who have undergone failed renal ablation, in patients in whom new tumor formation are in locations not amenable to ablation, in patients with post-ablation scarring, or in those who have developed adhesions to adjacent organs. In these patients, surgical resection may be the only remaining option. In a recent study from the Cleveland Clinic partial nephrectomy was performed in only 2 out of 10 patients who underwent attempted extirpation of post-ablative recurrence. One successful NSS surgery was done in the post-RFA group and one was successfully completed in post-cryoablation group.⁷⁹ At our institution we were able to complete all 16 attempted partial nephrectomies after previous RFA without loss of a renal unit. These surgeries, however, were complicated by a higher rate of urine leaks and the need for reoperation, when compared to primary or repeat partial nephrectomies. Twelve of 16 (75%) cases involved very difficult dissection around the previously ablated tumor and five cases (31%) were complicated by intraoperative pleural injury.⁷⁰ Table 2 describes perioperative outcomes of primary, repeat, salvage, and post RFA partial nephrectomies performed at NCI for multifocal renal masses in a similar patient population.^{70, 71, 77, 78}

Similar to any oncologic intervention, the outcomes of renal surgery should be assessed by not only perioperative, but functional and oncologic outcomes. Table 3 demonstrates that while there is an increased incidence of loss of renal units (**atrophy of the renal remnant or nephrectomy**) with each subsequent intervention. In those patients with a remaining kidney, there was only a modest elevation of creatinine and decrease in creatinine clearance, calculated from estimated GFR or 24 hour urine collections at least 3 months after surgery. The oncologic rationale for continued aggressive surgical intervention is depicted in Table 4, demonstrating excellent metastasis-free and overall survival of our cohort in excess of 90% at intermediate follow up.

In addition to the goals of effective oncologic control and maximal renal preservation, management of patients with bilateral recurrent multifocal renal masses is focused on minimizing number of interventions and perioperative morbidity. Over the course of a number of years treating patients with bilateral multifocal disease at the NCI, several management nuances have been developed.

First, as demonstrated in Figure 2 we utilize percutaneous biopsy to guide the next step in the management of patients presenting with bilateral renal masses. Certainly, if the patient presents with bilateral renal masses and known hereditary syndrome the percutaneous biopsy may be avoided as specific hereditary syndromes are associated with certain types of tumors. While the discussion of accuracy, pros and cons of percutaneous renal biopsy is beyond the scope of this review, we find that pathology-specific approach in patients with unknown diagnosis may provide the treating urologist with the best direction for further work up, genetic testing, necessity of intervention, and type of resection. In most cases, percutaneous biopsy allows the urologic surgeon to look more carefully for associated syndromes and plan the type of resection (enucleation versus resection with wider margins). Except for tumors suspicious for papillary type 2 RCC or HLRCC-associated tumors, most patients with familial forms of bilateral clear cell RCC, papillary type 1 RCC, chromophobe RCC, or hybrid oncocyctic neoplasms are observed until the largest mass reaches 3 cm.^{80, 81} This management approach was developed from earlier studies in which we have not detected metastatic disease in VHL, HPRC, or BHD patients managed in this fashion^{62, 80, 81} This approach has been applied to management of familial papillary type 1 RCC, chromophobe RCC, or hybrid oncocyctic neoplasms, without evidence of metastatic disease up to date.^{71, 77, 78, 80} This management strategy allows for an increased interval between procedures, thus preserving native renal function and avoiding the morbidity of premature intervention. Contrary, variants of RCC suspicious for papillary type 2 are not observed and patients are advised to undergo surgical resection early. Finally, many patients with bilateral multifocal clear RCC and bilateral multifocal papillary type 1 RCC without evidence of a known hereditary cancer syndrome or detectable germline mutation are also managed with the above 3 cm rule. This management strategy is utilized after the partial nephrectomy was performed on at least one side and the final pathologic examination does not reveal aggressive histologic pattern, indicative of papillary type 2 RCC or high grade tumors.

Second, to decrease the intraoperative morbidity of subsequent surgeries, we have developed certain technical aspects. We attempt to perform surgeries via retroperitoneal approach (to minimize future adhesions of abdominal viscera to the raw surface of the kidney). Another advantage of maintaining the surgery in the retroperitoneum is maintenance of a small confined space in case of postoperative bleeding. We also attempt to minimize intraoperative dissection of the hilum, and if clamping is needed, we frequently clamp artery and vein en-block to preserve the adventitial layers encasing main renal vessels. We routinely use intraoperative ultrasound and find that it facilitates identification of completely intraparenchymal lesions and allows maximal “debulking” of the operated kidney.^{82, 83} We believe that a more thorough resection allows for a longer interval between subsequent interventions. As we proceed with aggressive resections that not infrequently require resection of dozens of lesions from the same renal unit in a same setting, we attempt to minimize the potential ischemia time by performing the tumor resections off clamp, starting with easier and more superficial tumors, and proceeding to more endophytic and hilar lesions. Additionally, since kidneys with multifocal lesions have a propensity for tumor development and have a “true field defect”, we choose to perform most of the surgeries by enuclear resection with precise repair of the bleeding vessels or hemostasis with thrombin-soaked gel foam and minimizing the resection of unaffected renal parenchyma. Frozen section is rarely needed as most of the surgical planning is performed preoperatively.

Finally, at the end of the case, the Gerota's fascia is approximated over the kidney, if possible. This facilitates easier dissection during subsequent operations and may help with hemostasis.

Conclusions

Using an estimated 5% prevalence of bilateral multifocal RCC, there is a large number of patients that will face complex medical and surgical decisions. These patients are more likely to develop a locally recurrent disease and require repeat interventions to preserve their native renal function. Renal surgery for multifocal bilateral recurrent renal masses is technically demanding and associated with higher rates of intraoperative and postoperative complications. Although these surgeries are associated with higher blood loss and perioperative morbidity most renal units may be saved during repeated interventions. Prior to embarking on repeat renal surgery the patients need to be appropriately counseled regarding risks and benefits of reoperative renal surgery. As of today, facing limited alternatives for this patient cohort, our data argue that despite higher morbidity, repeat nephron-sparing interventions is a better alternative than nephrectomy and renal replacement therapy.

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Key points

- Patients with bilateral multifocal RCC are likely to have a locally recurrent disease and require repeat surgical interventions
- Renal surgery for multifocal bilateral recurrent renal masses is technically demanding and associated with higher rates of perioperative complications
- Repeat renal intervention results in reasonable functional and oncologic outcomes
- Renal replacement therapy results in high morbidity and mortality
- Facing limited alternatives for this patient cohort, we argue that repeat nephron-sparing interventions is a better alternative than nephrectomy and renal replacement therapy

Review Criteria

Pubmed was searched for articles published in the English language in the past 30 years for the following terms: “Multifocal Renal Cell Carcinoma”, “Bilateral Renal Cell Carcinoma”, “Recurrent Renal Cell Carcinoma”, “Ablation of Renal Masses”, “Management of RCC Recurrences”, and “Hereditary Renal Cell Carcinoma”. The full text articles were assessed and reviewed for pertinent information, and the reference lists were searched to identify additional sources of information. Occasionally, the most pertinent abstracts and databases were used to extract the required information.

Figure 1.

Computer tomography of left kidney that was previously treated with radiofrequency ablation. Thick arrow points to the new tumor found to be in locations not amenable for safe ablation because of its close proximity to the spleen and splenic hilum. The thin arrow points to the calcified scar of a previously ablated lesion.

Figure 2.

NCI algorithm for management of patients presenting with bilateral renal masses. VHL (von Hippel-Lindau), HPRC (Hereditary Papillary Renal Carcinoma), BHD (Birt-Hogg-Dube), HLRCC (hereditary Leiomyomata Renal Cell Carcinoma), SDHB or SDHC (Succinate Dehydrogenase Deficiency subunit B or C), TS (Tuberous Sclerosis).

Table 1

Frequency of multifocality in RCC: results from the literature review of the past 2 decades.

First author	Year	# Multifocal	Total	% Multifocal
Dimarco	2004	101	2373	4.3
Richstone	2004	57	1071	5.3
Crispen	2008	60	1113	5.4
Oya	1995	7	108	6.5
Cheng	1991	7	100	7.0
Saiki	1995	3	43	7.0
Nissenkorn	1995	3	27	11.1
Wunderlich	1999	36	260	13.9
Lang	2004	37	255	14.5
Gohji	1997	10	64	15.6
Kletscher	1995	16	100	16.0
Junker	2002	61	372	16.4
Schlichter	2000	48	281	17.1
Karayiannis	2002	10	56	17.8
Mukamel	1988	13	66	19.7
Baltaci	2000	22	103	21.4
Whang	1995	11	44	25.0

Table 2

Perioperative outcomes of partial nephrectomies (Partial Nx) in patients treated at NCI

Procedure	Primary Partial Nx	Repeat Partial Nx	Salvage Partial Nx	Post-RFA Partial Nx
Total patients	50	47	11	13
No. Partial Nx	65	51	13	16
Median tumors removed	15 (1–51)	7 (1–55)	5 (1–27)	7 (2–40)
Median EBL, mL (range)	2,885 (150 – 23,000)	1,800 (50 – 21,500)	2,100 (200 – 12,000)	1,500 (500 – 3,500)
Visceral or vascular injury (%)	5 (8)	2 (4)	6 (46)	0
Ureteral Injury (%)	0	1 (6)	0	1 (6)
Pleural Injury (%)	3 (5)	NA	NA	5 (31)
Urine Leak (%)	3 (5)	8 (15)	2 (15)	3 (19)
Hemodialysis (%)	0	3 (6)	2 (15)	0
Rhabdomyolysis (%)	0	0	1 (8)	1 (6)
Reoperation (%)	2 (3)	2 (4)	4 (36)	2 (13)
CV Events (%)	1 (1)	1 (2)	0	2 (13)

Functional outcomes of initial, repeat, and salvage partial nephrectomy for multifocal RCC performed at the NCI.

Table 3

Procedure	Author	Year	Units lost (%)	Δ in Cr (mg/dl)	Δ in Cr Clear (ml/min)
Initial partial nephrectomy (N=62)	Herring, et al	2001	5%	+0.01	NA
Repeat partial nephrectomy (N=51)	Johnson, et al	2008	6%	+0.19	-10
Repeat partial on a solitary kidney (N=25)	Liu, et al	2009 (in press)	12%	+0.20	-8
Salvage partial nephrectomy (N=13)	Bratslavsky, et al	2008	23%	+0.20	-16

Table 4

Oncologic outcomes of initial, repeat, and salvage partial nephrectomy for multifocal RCC performed at NCI.

Procedure	Median F/U (months)	Metastasis-Free Survival (%)	Overall Survival (%)
Initial partial nephrectomy (N=62)	30	100%	100%
Repeat partial nephrectomy (N=51)	56	94%	98%
Repeat partial on a solitary unit (N=25)	60	95%	92%
Salvage partial nephrectomy (N=13)	25	100%	100%