RESIDENT'S CORNER

Management of bilateral synchronous renal cell carcinoma in a single versus staged procedure

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Objectives: The presentation of synchronous bilateral renal lesions is rare. We report our experience with the surgical management of these lesions in both a single and staged procedure.
Methods: We retrospectively reviewed the records of all patients with bilateral synchronous renal lesions who underwent surgical management by one surgeon between 2000-2007. We compared characteristics including pre and postoperative renal function, complication rates, and oncological outcomes between the single and staged cohorts. Data were analyzed using descriptive statistics, Student's t-test, and Fisher's exact test.
Results: A total of 26 patients (73% male, mean age 65.5 ± 12.2 years) with bilateral synchronous lesions were identified with a mean follow-up of 25.9 ± 19.7 months. Of these, 18 (69%) were performed as a single procedure, 5 (19%) were done as a staged procedure, and 3 (12%) had only the first part of the staged procedure performed. The single and staged cohorts were comparable in regards to preoperative creatinine (Cr) (1.1 ± 0.4 mg/dl versus 1.1 ± 0.2 mg/dl, p = 0.70), postoperative Cr (1.5 ± 1.0 mg/dl versus 1.4 ± 0.5 mg/dl, p = 0.73), and median hospital length of stay (HLOS) (5 days versus 4 days). The complication rate was 22% and 20% for the single and staged cohorts, respectively. One patient had a local recurrence and one patient developed metastatic disease in the single cohort versus no local recurrence or metastatic disease in the staged cohort.
Conclusion: In the appropriate setting, surgical management of synchronous bilateral renal lesions can be done safely in a single procedure with comparable outcomes to those done in a staged manner.

Key Words: renal cell carcinoma, synchronous bilateral tumor, kidney, nephron sparing surgery

Introduction

Kidney cancer is projected to affect more than 54000 people in 2008, with an expected mortality of greater than 13000 people in the United States.[1] Surgery remains the primary treatment for localized disease.[2] Radical nephrectomy (RN) is not feasible in patients

with a solitary kidney or bilateral lesions without contingent plans for dialysis or transplantation. Thus, nephron sparing surgery (NSS) has become the treatment of choice in these patients.[3] The management of bilateral renal cell carcinoma (RCC) poses a surgical challenge in which the goal is to achieve oncological control while preserving renal function in order to avoid future dialysis.[4]

Sporadic bilateral synchronous RCC is rare, occurring in 1%-4% of patients with RCC.[2,5] With surgical treatment of sporadic bilateral synchronous RCC, the prognosis is similar to that of unilateral RCC of the same histiological subtype.[5] Whether sporadic or hereditary, bilateral RCC tends to be multifocal.[5] Traditionally, bilateral RCC was surgically managed in a staged procedure in which lesions were first removed from one kidney and then, after a full recovery, the lesions on the contralateral kidney were addressed.[4,6] In the appropriate setting, surgical management of bilateral RCC can be approached in a single procedure.[2,5,7] The potential advantages of this approach include decreased anesthesia exposure and decreased convalescence time. We report our experience of 26 patients with synchronous bilateral renal lesions and compare patient characteristics, oncological outcomes, postoperative complication rates, and long term renal function between those done as a single versus a staged procedure.

Material and methods

We retrospectively reviewed the records of all patients with bilateral synchronous renal masses between 2000-2007 who underwent either single or staged procedures by one surgeon at our institution. Information regarding renal function, operative complications, and oncological outcomes were analyzed.

We preferred a transperitoneal approach for open radical and partial nephrectomies. In a single setting procedure a chevron or upper midline incision was used, while a subcostal incision was used for staged procedures. For RN's, the kidney was mobilized outside Gerota's fascia and an ipsilateral adrenalectomy was only performed for large upper pole lesions or lesions that were in close proximity to the adrenal gland. For partial nephrectomies, the kidney was mobilized and Gerota's fascia was dissected away from the capsule to inspect the whole kidney thoroughly. When ischemia time was anticipated to be in excess of 20 minutes, the kidney was packed with ice before clamping the renal vessels. Lesions were enucleated and frozen sections were sent to pathology to ensure negative margins. For laparoscopic radical nephrectomies, we used a hand-assisted technique in which the specimen was removed intact through the hand-port. For laparoscopic partial nephrectomies, we used three ports and enucleate lesions without hilar clamping.

Follow-up included a 2 week postoperative evaluation along with physical exams and CT or MRI (if indicated) of the chest, abdomen, and pelvis at 6 months and yearly thereafter to exclude local recurrence or systemic progression. We checked patients' renal function yearly prior to their CT scans.

Tumors were staged according to the 2002 TMN classification and Fuhrman nuclear grade, and the patient's stage was based on the tumor with the highest stage and nuclear grade.[8] Data were analyzed using descriptive statistics, Student's t-test, and Fisher's exact test. Values were considered statistically significant at $p \leq 0.05$.

Results

Twenty-six patients (73% male, mean age 65.5 ± 12.2 years) presented with synchronous bilateral renal lesions between 2000-2007, with a mean follow-up of 25.9 ± 19.7 months. Of the 26 patients, 18 (69%) underwent a single procedure, 5 (19%) underwent a staged procedure, and 3 (12%) had only the first part of the staged procedure. Seventy percent of patients underwent bilateral partial nephrectomies while 30% underwent a RN and a contralateral partial nephrectomy. In the single procedure cohort, one patient had a history of von Hippel-Lindau (VHL) disease, one patient had Birt-Hogg-Dubé (BHD) syndrome, and the remainder had sporadic lesions. All patients in the staged procedure cohort had sporadic lesions, and one patient who only underwent the first part of the staged procedure had VHL. Twenty-four patients (92%) had open surgery while two cases (8%) were done laparoscopically. Three patients in the staged procedure cohort were converted from a single procedure due to difficulty in removing the tumor (1), length of the operation (1), and poor kidney function (1). The three patients who did not undergo the second part of the staged procedure were due to comorbidities (1), contralateral lesions < 2 cm (1), and multiple partial nephrectomy lesions that were all oncocytoma with a contralateral 2 cm lesion (1); these patients have been followed closely with serial imaging.

We compared the 18 patients who had undergone a single procedure with the five patients who had staged procedures. The patient characteristics of the two cohorts are listed in Table 1. Specifically, the mean preoperative creatinine (Cr) (1.1 ± 0.4 mg/dl versus 1.1 ± 0.2 mg/dl, p = 0.70), estimated blood loss (EBL) (1832 ± 1784 cc versus 1186 ± 861 cc, p = 0.21), postoperative

TABLE 1. **Patient characteristics**

Characteristic	Single procedure n = 18	Staged procedure n = 5	p value
Mean age (yrs)	65.7 ± 10.8	69.4 ± 10.3	0.50
Male/female (n)	13/5	3/2	0.62
Mean preoperative Cr (mg/dl)	1.1 ± 0.4	1.1 ± 0.2	0.70
Mean postoperative Cr (mg/dl)	1.5 ± 1.0	1.4 ± 0.5	0.73
Mean change in Cr (mg/dl)	0.4 ± 0.8	0.3 ± 0.4	0.83
Mean size of lesion (cm)	3.1 ± 2.0	3.5 ± 2.5	0.63
Mean number of lesions per kidney	1.6 ± 1.9	1.3 ± 0.7	0.46
Mean EBL (cc)	1832 ± 1784	1186 ± 861	0.21
Mean follow-up (months)	29.2 ± 19.7	25.6 ± 21.4	0.76

Cr = creatinine; EBL = estimated blood loss

Cr (1.5 ± 1.0 mg/dl versus 1.4 ± 0.5 mg/dl, p = 0.73), and change between preoperative and postoperative Cr (0.4 ± 0.8 mg/dl and 0.3 ± 0.4 mg/dl, p = 0.83) were not significantly different between the single and staged cohorts, respectively. The median hospital length of stay (HLOS) for the single and staged cohorts was 5 and 4 days, respectively.

In the single procedure cohort, there were four complications (22%) including pneumonia (1), intraoperative splenectomy (1), pulmonary embolism (1), and acute renal failure requiring dialysis (1); four patients required blood transfusions. In the staged procedure cohort, one patient had a urine leak requiring a stent (20%) and three patients required blood transfusions. The complication rates between the two cohorts were not significantly different (p = 1.0), Table 2.

The tumor with the highest stage and grade was counted. Among the 20 patients with cancerous lesions, the distribution of tumor stage was pT1a (65%), pT1b (15%), pT2 (10%), and pT3 (10%); the histological subtypes of RCC were clear cell (50%), papillary (40%), chromophobe (10%); four percent of patients had oncocytoma and 9% had benign cysts, Table 3. In both the single and staged cohorts, 80% of the tumors were either pT1a or pT1b. There was not a significant difference in mean size of the lesions (3.1 ± 2.0 cm versus 3.5 ± 2.5 cm, p = 0.63) in the single and staged groups, respectively.

The mean follow-up was 29.2 ± 19.7 months versus 25.6 ± 21.4 months (p = 0.76) for the single and staged cohorts, respectively. The average time between operations in the staged cohort was 5.3 ± 2.3 months. In the single procedure cohort, one patient was lost to follow-up, and two patients had not had follow-up imaging yet. Of the remainder, one patient (8%) had a local recurrence and one patient (8%) with VHL progressed to metastatic disease. In the staged procedure cohort, all patients had follow-up imaging and none had local recurrence or metastatic disease.

TABLE 2. **Patient complications**

Complication n (%)	Single procedure n = 18	Staged procedure n = 5
Pneumonia	1	0
Splenectomy	1	0
Dialysis	1	0
Pulmonary embolism	1	0
Urine leak	0	1
Any	4 (22%)	1 (20%) p = 1.0

No patients had a deep vein thrombosis, myocardial infarction, wound infection or sepsis.

TABLE 3. **Clinical and pathological features**

Characteristic	Single procedure n = 18	Staged procedure n = 5
Stage*	n (%)	
T1a	9 (50)	4 (80)
T1b	3 (17)	0 (0)
T2	2 (11)	0 (0)
T3	1 (6)	1 (20)
Benign	3 (17)	0 (0)
Histology		
Clear cell	5 (28)	5 (100)
Papillary	8 (44)	0 (0)
Chromophobe	2 (11)	0 (0)
Oncocytoma	1 (6)	0 (0)
Benign cysts	2 (11)	0 (0)
Fuhrman grade†		
I	2 (14)	0 (0)
II	3 (21)	2 (40)
III	9 (64)	3 (60)

*TMN stage based on the AJCC Cancer Staging Manual. Patient's pathological features were based on the tumor with the highest stage and nuclear grade.
†One patient's Fuhrman grade was unknown.

Discussion

In patients with synchronous bilateral renal lesions, surgical removal in a single procedure is feasible in the appropriate setting with comparable renal function, complication rates, and oncological outcomes to those done in a staged manner. Historically, RN has been the gold standard for the management of renal cancer that is confined within Gerota's fascia with a normal contralateral kidney.[9] However, in patients with bilateral renal tumors, tumors in a solitary kidney, a unilateral renal tumor and compromised renal function, or renal insufficiency due to irreversible benign disease, there is an absolute indication for NSS.[3,10] Several studies have shown that NSS is an effective treatment for low stage and low grade RCC.[3,10-13] In contrast to elective NSS, however, many patients with bilateral renal lesions undergoing NSS have tumors of unfavorable size and location, thereby increasing the challenge of completely excising the renal tumors for adequate cancer control while preserving enough renal parenchyma in order for patients to avoid dialysis or transplantation.[2,4,10]

Several studies have reviewed the surgical management of synchronous bilateral renal lesions.[2,4-7] Pahernik et al identified 57 patients with sporadic bilateral RCC; all patients except one underwent staged procedures.[4] In their study, NSS was the treatment of choice for bilateral synchronous sporadic RCC whenever possible.[4] NSS provided adequate tumor control and cancer-specific survival; and preserved renal function more efficiently than unilateral NSS and contralateral RN.[4] Klatte et al retrospectively studied 153 patients with synchronous bilateral renal lesions from 12 urologic centers.[7] Fifty-four patients had a single procedure and 63 had staged surgery, although comparisons were not made between these two groups.[7] They found that patients with non-metastatic synchronous bilateral RCC and non-metastatic unilateral RCC had a similar prognosis.[7] In two separate studies, Blute et al looked at synchronous bilateral renal lesions and showed that patients can be treated with a single procedure with comparable complication rates and renal function with an excellent prognosis.[2,5]

Preoperative characteristics that influenced the decision to approach bilateral lesions in a single or staged fashion included the patient's comorbidities and size and number of lesions. Nephron sparing surgery was performed whenever possible, however, RN was considered for larger, central tumors especially if the contralateral kidney had small lesion(s) and appeared to have good renal function. Although removing bilateral synchronous lesions in a single operation was preferable, this was not always possible due to intraoperative factors such as blood loss, degree of hemostasis, urine output, operating time, how well the patient tolerated the first part of the surgery, and the level of abuse to the initial kidney. Due to these factors, a single procedure was aborted in favor of a staged procedure in three cases. The overall complication rates between the single and staged cohorts were not significantly different (p = 1.0).

In our series, the more life threatening lesion was always addressed first. In this scenario, if a case were aborted after the lesion(s) on one kidney was removed, the lesion(s) on the contralateral kidney would be less likely to metastasize and ultimately cause mortality in the time period between the first and second stage of the operation. Blute et al reported their series of 44 patients of which 37 patients underwent bilateral surgery in a single operation and, as in our study, approached the more involved kidney first; if there was a question of kidney viability, the lesion(s) on the contralateral kidney was addressed during a staged procedure.[5] This approach was in contrast to Pahernik et al in which the more favorable tumor was addressed first.[4] In this study, however, the surgery for all patients except one was done in a staged manner. The second

stage of the operation was performed approximately 6 weeks after the first stage when renal function recovered and thus, by removing the more favorable tumor first, perhaps renal function recovered faster and the second operation could be performed sooner than if the more complex lesion were addressed first.[4]

Long term renal function is a major concern in patients with bilateral RCC.[4] When comparing patients with a single versus a staged procedure in our study, the preoperative Cr (p = 0.70), postoperative Cr (p = 0.73), and difference between the pre and postoperative Cr (p = 0.83) were not significantly different between the two cohorts. One patient in the single procedure cohort required dialysis.

In looking at oncological outcomes, one patient (8%) in the single procedure cohort had a local recurrence and one patient (8%) had metastatic disease. No local recurrences or systemic progression occurred in the staged cohort. Pahernik et al had a 16% local recurrence rate with mean time of recurrence at 3.4 years and Blute et al had a 5% local recurrence rate and a 21% metastatic rate with a mean follow-up of 5.9 years.[2,4] We recognize that our lower local recurrence and metastatic disease rates are largely due to our shorter mean follow-up time of 2.2 years, and we continue to follow these patients closely.

Our study has some limitations. This is a single surgeon retrospective study involving a limited number of patients. It is difficult to compare patients undergoing a single procedure with those undergoing a staged procedure when so few have undergone the staged procedure; the findings in this study would be strengthened by a greater number of patients. Moreover, our average follow-up time of 25.9 ± 19.7 months is short, making it difficult to accurately predict our overall local recurrence and metastatic disease rates; in addition longer follow-up is needed in order to predict survival rates.

In our series of patients with synchronous bilateral renal lesions, patients who underwent a single procedure had comparable renal function, complication rates, and thus far oncological outcomes to those who underwent a staged procedure. These findings are in agreement with Blute et al, who also looked at their experience with performing removal of bilateral renal lesions in a single procedure.[5]

Conclusion

Synchronous bilateral renal lesions present a challenging problem in which the surgeon must achieve oncological control while preserving enough renal function so that patients avoid dialysis or transplantation. In the right setting, bilateral renal lesions can be addressed in a single procedure with results equivalent to those done in a staged procedure, while only having to be exposed to the risks of anesthesia and postoperative morbidity once. Future prospective studies recruiting large numbers of patients with synchronous bilateral renal lesions are needed to further evaluate the utility in managing these patients with a single operation. ☐

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