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Laparoscopic Radical Nephrectomy for Renal Masses 7 Centimeters or Larger

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ABSTRACT

Objective: To report our operative experience and oncologic outcomes for the laparoscopic management of large renal tumors.

Methods: All laparoscopic and hand-assisted laparoscopic radical nephrectomies performed at our institution were reviewed. Thirty patients with tumors ≥7cm and a pathologic diagnosis of renal cell carcinoma were included.

Results: Mean operative time was 175.7±24.5 minutes, and mean estimated blood loss was 275.5±165.8 mL. No case required conversion to open radical nephrectomy. The mean hospital stay was 2.4±1.6 days. Four patients (13%) had minor complications. Of the 30 tumors, 18 were pathologic stage T2, 9 were stage T3a, 2 were stage T3b, and one was stage T4. At a mean follow-up of 30 months (range, 10 to 70), 22 patients (73%) were alive without evidence of recurrence, and 5 patients (17%) were alive with disease. One patient (3%) died of complications related to renal cell carcinoma, and 2 patients (7%) died from other causes. Overall survival was 90%, cancer-specific survival was 97%, and recurrence-free survival was 80%.

Conclusion: Laparoscopic radical nephrectomy for large tumors is a technically challenging operation. However, in experienced hands, it is a reasonable therapeutic option for the management of larger RCC neoplasms.

Key Words: Renal cell carcinoma (RCC), Kidney neoplasm, Large tumors, Minimally invasive surgery.

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INTRODUCTION

Following the first laparoscopic nephrectomy in 1990, this procedure rapidly became an accepted alternative for the surgical management of T1 renal tumors. At present, laparoscopic radical nephrectomy (LRN) is considered the standard of care for management of T1 renal cell carcinoma (RCC) not amenable to nephron-sparing surgery. Over time, minimally invasive approaches have been extended towards treatment of larger lesions with several groups reporting equivalent oncologic outcomes for stage T2[1–5] and even T3 lesions.[6,7]

The standard advantages of laparoscopy over open surgical approaches are well known. Intraoperative blood loss, length of hospital stay, analgesic requirements, and time of convalescence have all been shown to be lower for laparoscopic surgery, without sacrificing oncologic efficacy.[8] For these reasons, LRN has become the standard of care for renal masses <7 cm in size. In this series, we further demonstrate that, in the hands of experienced laparoscopic surgeons, these benefits can be extended to the management of larger, locally advanced tumors (T2 and greater). Furthermore, we discuss our operative technique and highlight modifications necessary to accommodate these larger tumors.

METHODS

A retrospective chart review of all laparoscopic and hand-assisted laparoscopic radical nephrectomies was performed. All of the procedures were done at our institution by 2 surgeons (JJD and RES). All tumors ≥7 cm in greatest dimension with a pathologic diagnosis of RCC were included in our study. The review produced 30 patients, 23 who underwent a laparoscopic radical nephrectomy (LRN) and 7 who underwent hand-assisted laparoscopic nephrectomy (HALRN). Seventeen nephrectomies were performed on the left side and 13 on the right. The average tumor size was 8.8±2.3 cm. The mean age of the patients was 60.4±10.7 years with a mean ASA score of 2.3±0.9 and a mean BMI of 28.8±3.5 kg/m^2 **(Table 1)**.

Table 1.
Patient Demographics (N=30)

No. Male/Female	18/12
No. Left/Right	17/13
Mean±SD Age (years)	60.4 ± 10.7
Mean±SD ASA score	2.3 ± 0.9
Mean±SD BMI (kg/m^2)	28.8 ± 3.5
Mean±SD Tumor Size (cm)	8.8 ± 2.3
Mean±SD OR Time (min)	175.7 ± 24.5
Mean±SD Estimated Blood Loss (mL)	275.5 ± 165.8
No. Open Conversions (%)	0 (0)
Mean±SD Hospital Stay (days)	2.4 ± 1.6
No. Complications (%)	4 (13)
No. Clavien Grade 1 Complications (%): ileus	2 (7)
No. Clavien Grade 2 Complications (%): wound infection, delayed bleeding	2 (7)
Mean±SD Change in Serum Creatinine (mg/dL)	0.5 ± 0.2
Stage	
T2 (%)	18 (60)
T3a (%)	9 (30)
T3b (%)	2 (7)
T4 (%)	1 (3)
Histology	
Clear cell (%)	22 (73)
Papillary (%)	4 (13)
Chromophobe (%)	4 (13)
Positive Margin (%)	1 (3)

Laparoscopic Radical Nephrectomy and Hand Assisted Laparoscopic Radical Nephrectomy Technique

Patients underwent a bowel preparation with a clear liquid diet and a bottle of magnesium citrate. Perioperative antibiotics were infused in the operating room, and general anesthesia with endotracheal intubation was used in all cases. An oral gastric tube was used to decompress the stomach, and pneumatic compression boots were used to prevent lower extremity stasis.

The patient was placed in the flank position with adequate padding for the brachial plexus and the dependent hip, knees, and ankles. The lower leg was flexed while the upper leg was gently extended and a pillow placed between them. Then, the operating table was gently flexed to optimize exposure.

For right-sided LRN, 4 ports were utilized: a 12-mm trocar just lateral to the midline, 2 cm above the umbilicus (working instrument), a 5-mm trocar at McBurney's point (working instrument), a 5-mm trocar at the midline 5 cm above the umbilicus (camera), and a second 5-mm trocar just under the costal margin for the liver retractor. For the cases that required a hand-assist device, a 7-cm right lower quadrant incision was utilized in lieu of the trocar at McBurney's point **(Figure 1)**.

Left-sided LRN utilized a 12-mm trocar at the midclavicular line 2 cm inferior to the umbilicus (working instrument), a 5-mm trocar adjacent to the umbilicus (working instrument), a 5-mm trocar at the midline 2 finger breadths below the xiphoid process (camera), and a 7-cm vertical lower midline incision for the hand device when needed in lieu of the 5-mm umbilical trocar **(Figure 2)**. Of note, these port placements are shifted medially and inferiorly compared with the traditional transperitoneal laparoscopic approach to afford more space in working with larger lesions.

For the left nephrectomy, the colon was mobilized medially from the level of the iliac vessels to the splenic flexure. The lateral splenic attachments were incised to

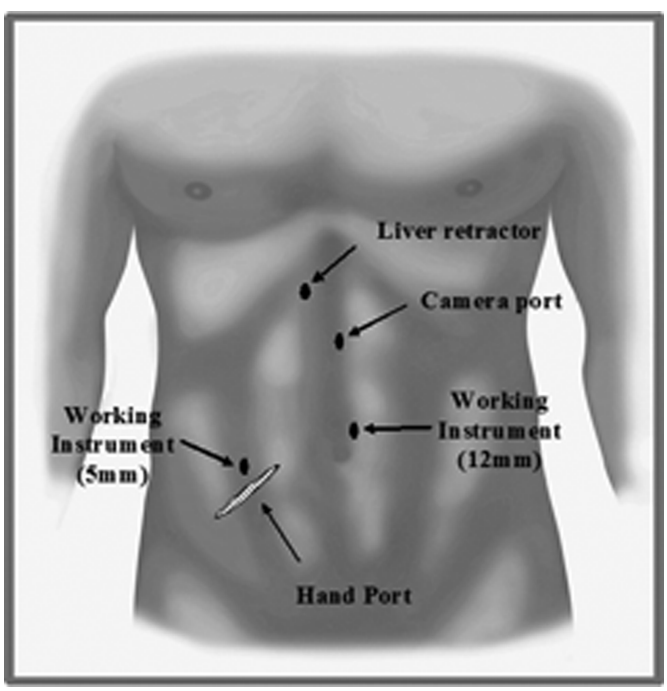

Figure 1

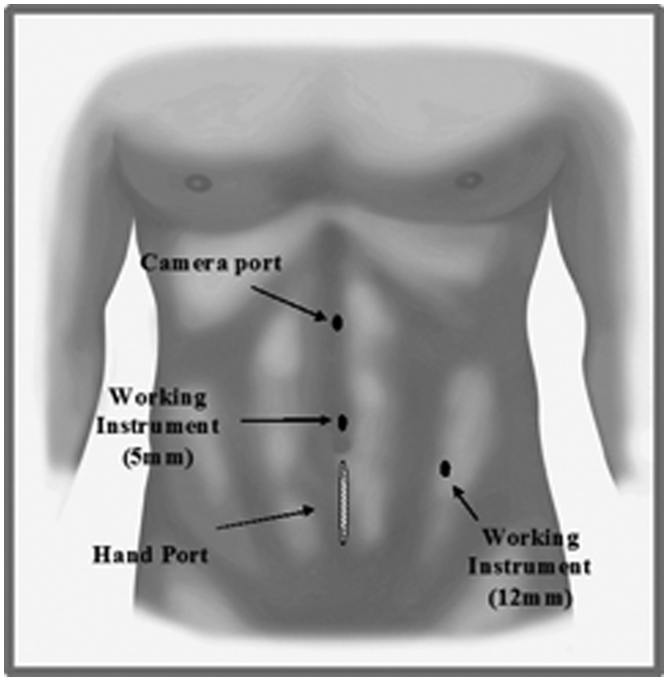

Figure 2

expose the gastric fundus. The colon, spleen, and pancreas were mobilized en bloc resulting in exposure of the anterior aspect of Gerota's fascia. Then, the attachments cephalad and medial to the adrenal were identified and divided with the Harmonic scalpel. The investing tissues over the renal hilum were lifted and incised to expose the renal vein. A Maryland dissector was used to dissect the tissues off the renal vein and to expose the adrenal and gonadal veins. The adrenal vein was dissected free of surrounding tissues, clipped, and divided. In a similar manner, the gonadal vein was dissected, controlled, and divided. The ureter was then identified, clipped, and divided. Then, the kidney was retracted in a lateral and posterior direction to expose the renal artery. The renal artery was divided using the Endo-GIA vascular stapler. Next, the renal vein was dissected free of surrounding tissues and divided, again using a vascular stapling device. The kidney and adrenal gland along with Gerota's fascia were delivered intact inside a laparoscopic specimen bag via the hand-device incision or through a low abdominal 5-cm Pfannenstiel incision.

For the right nephrectomy, a similar procedure was performed. Again, the ports were placed medially and inferiorly to allow for more working room. The right colon and hepatic flexure were medially mobilized, and the right lobe of the liver was released from the body wall. The coronary ligament was incised to expose the upper pole of the kidney, the upper border of the adrenal gland, and the inferior vena cava. The inferior phrenic vessels were divided with a Harmonic scalpel, and the adrenal vein was controlled with clips and divided. The duodenum was mobilized medially with the Kocher maneuver for exposure of the renal hilum. The renal hilum was then adequately dissected for identification of the renal artery and vein. The renal artery and then the renal vein were divided using the Endo-GIA vascular stapler, leaving the gonadal vein intact. The remaining attachments of the kidney and adrenal were then dissected from surrounding tissues with the Harmonic scalpel. Gerota's fascia and the adrenal gland were removed intact with the specimen.

Indications for the use of the hand port were preoperative planning and intraoperative conversion due to failure to progress. None of the cases were converted to HALRN due to intraoperative bleeding.

RESULTS

The mean operative time was 175.7±24.5 minutes, and the mean estimated blood loss (EBL) 275.5±165.8 mL. Four complications (13% of cases) occurred that were classified according to the modified Clavien system.[9] Complications included 2 cases of ileus that resolved after conservative management (grade 1), 1 superficial surgical site infection requiring intravenous antibiotics (grade 2), and 1 episode of delayed bleeding that required a blood transfusion but no other intervention (grade 2). HALRN was utilized in 7 cases; 4 were based on preoperative decision, and 3 were converted intraoperatively. No case required conversion to open radical nephrectomy. The mean hospital stay was 2.4±1.6 days. At time of follow-up, the mean increase in serum creatinine was 0.5±0 mg/dL **(Table 1)**.

Pathology

Of the 30 tumors, 18 were pathologic stage T2, 9 were stage T3a, 2 were stage T3b, and one was stage T4. Histological analysis of the 30 specimens revealed 22 clear cell tumors, 4 papillary tumors, and 4 tumors of the chromophobe subtype. One pathologic specimen (pT4 tumor) had margins positive for renal cell carcinoma **(Table 1)**.

Follow-up

At a mean follow-up of 30 months (range, 10 to 70), 22 patients (73%) showed no evidence of disease recurrence, and 5 patients (17%) were alive with disease. One patient

(3%) died of progression of disease, and 2 patients (7%) died from other causes. At 30 months, the overall survival was 90%, the cancer-specific survival was 97%, and the recurrence-free survival was 80%. Of the 18 patients with pathologic T2 lesions, no lesion had recurred by the time of follow-up. Five of the 11 patients with pathologic T3 lesions experienced a recurrence, and the one patient with a T4 lesion died of complications of his disease **(Table 2)**.

DISCUSSION

Since the first LRN was described in 1991 by Clayman et al,[10] the indications for this procedure have expanded considerably. Numerous studies have demonstrated the benefit of laparoscopy over open nephrectomy for T1 RCC with respect to convalescence and morbidity. Now regarded as the standard of care for T1 lesions not amenable to partial nephrectomy, we suggest that the laparoscopic approach is a reasonable option for management of larger renal tumors.

Steinberg et al[11] compared surgical outcomes for radical nephrectomy among 4 groups: laparoscopic nephrectomy for T1 lesions, laparoscopic nephrectomy for T2 lesions, open nephrectomy for T1 lesions, and open nephrectomy for T2 lesions. In comparing the 2 laparoscopic groups, their data showed no significant difference in number of intraoperative complications, number of postoperative complications, rate of conversions to open surgery, opioid analgesic requirements, length of hospital stay, or time to return to normal activity. The only significant difference between the 2 laparoscopic groups was the amount of blood loss (200 mL for the T2 group versus 100 mL for the T1 group). Although this was a statistically significant difference, the authors describe its clinical significance as negligible. This study also demonstrated the benefits of laparoscopic nephrectomy over open nephrectomy for larger tumors. The laparoscopic T2 group had significantly shorter operative time, less blood loss, decreased analgesic requirements, shorter hospital stay, and a more rapid convalescence in comparison with the open T2 group.[11]

Table 2.
Patient Status at Mean Follow-up of 29.5 Months (Range 10–70)

Disease Status	
No Evidence of Disease	22 (73)
Alive With Disease	5 (17)
Died of Disease	1 (3)
Died Without Disease	2 (7)
% 2.5-yr Survival	
Overall	90
Cancer-specific	97
Recurrence-free	80
Recurrences by Pathologic Stage (%)	n (%)
T2	0/18 (0)
T3 (both a and b)	5/11 (45)
T3a	4/9 (44)
T3b	1/2 (50)
T4	1/1 (100)

Malaeb et al[8] showed similar advantages for hand-assisted laparoscopic nephrectomy over the open approach for T2 renal masses. Although a smaller study in terms of patient numbers (9 hand-assisted vs 10 open), the hand-assisted laparoscopy group had statistically significant advantages in terms of intraoperative blood loss, operative time, length of hospital stay, analgesic requirement, and time to regular diet. Hemal et al[1] also demonstrated operative and postoperative advantages for laparoscopic versus open nephrectomy with similar findings to the above studies, although the laparoscopic group had significantly longer operative time. Furthermore, these patients were followed for a mean of almost 5-years and the long-term outcomes compared. The laparoscopic group was followed for an average of 51.4 months, and the open group for an average of 57.2 months. The 5-year overall, recurrence-free, and cancer-specific survival were similar for the 2 groups.[1] Most recently, Berger et al[12] compared perioperative data for a series of laparoscopic radical nephrectomies. The large tumor group (≥7 cm, 40 patients) had significantly greater EBL, longer operative time, and a trend toward a greater increase in postoperative creatinine than those patients in the small tumor group (<7 cm, 124 patients). All other perioperative measures were not significantly different. Furthermore, at a mean follow-up time of 22 months, only one recurrence developed in the large tumor group compared with no recurrences in the smaller tumor group.[12]

In this series, we report on 30 cases of renal masses ≥7 cm managed by LRN or HALRN. The mean operative time was 175.7 minutes, and the mean EBL was 275.5 mL. The mean hospital stay was 2.4 days. No intraoperative complications occurred (including vascular or intestinal injury). Four minor postoperative complications occurred (13% of cases), including 2 cases of ileus that resolved with conservative management, one superficial surgical site infection treated with intravenous antibiotics, and one delayed

bleed. The delayed bleed presented as a decrease in hemoglobin at the initial follow-up (7 days postoperatively) in the patient with T4 disease. The patient was admitted and transfused 2 units of blood. A CT scan with intravenous and oral contrast was performed that revealed a retroperitoneal hematoma. The patient responded to the transfusion, and a conservative approach was taken for management.

A number of studies have compared the postoperative and short-term outcomes of laparoscopic nephrectomy with the traditional open approach.[2,3,8,11–13] The data presented in this paper are consistent with the findings of those authors demonstrating similar operative time, reduced blood loss, fewer complications, and shorter hospital stay compared with open radical nephrectomy.

At a mean follow-up of 30 months, 22 patients (73%) showed no evidence of disease, and 5 patients (17%) were alive with disease. One patient (3%) died of complications related to renal cell carcinoma, and 2 patients (7%) died from other causes. The one positive margin was in a patient with T4 disease extending into the psoas muscle. This was not suspected on preoperative MRI. Even with the addition of the hand-assist device, the patient had a positive posterior margin. Furthermore, this patient had positive lymph nodes. The patient died of disease with multiple sites of metastasis 13 months after surgery. In the cohort of patients who were alive with disease (n=5), 4 had evidence of pulmonary nodules suspicious for metastatic disease while one had an enhancing liver lesion that was biopsy-proven metastatic RCC. Four of these 5 patients had suspicious radiographic findings of metastatic disease prior to nephrectomy and thus, in actuality, underwent a cytoreductive nephrectomy. All 5 patients are currently on adjuvant RCC immunotherapy protocols.

Disease recurrence appeared to be stage-dependent with none of the pathological stage T2 lesions demonstrating recurrence within the first 2 years. The higher stage lesions had a higher rate of recurrence with 5 out of 11 of the T3 lesions (45%) and the one T4 lesion (100%) demonstrating recurrence within the first 2 years. Again, it is important to note that 4 of 5 pT3 recurrences had suspicion of metastatic disease prior to nephrectomy. Of note, none of these recurrences occurred at a port site or in the nephrectomy bed.

Other studies have investigated the effect of tumor size on the oncologic efficacy of laparoscopic nephrectomy.[1,4–6,14] The intermediate-term oncologic outcome demonstrated in this paper is consistent with previous findings, both for laparoscopic and open series. This supports the notion that recurrence of RCC is dependent on the stage of the disease at the time of resection, and not the surgical approach used to extirpate the lesion.[15,16]

Hand-assisted laparoscopic nephrectomy was utilized in 7 cases; 4 were based on preoperative decision and 3 were from intraoperative conversion. Six of the 7 cases were right-sided tumors. Indications for preoperative HALRN selection included tumor size >10 cm, BMI>30, or both of these. Of the 3 intraoperative conversions, one was needed to "milk" back tumor thrombus in a patient with pT3b disease suspected preoperatively, one was for T4 disease where a posterior plane behind the right kidney could not be developed (due to tumor invasion into the psoas muscle), and one was for a 9-cm left-sided lesion with dense adhesions to the tail of the pancreas. Unfortunately, the study size was too small to accurately provide preoperative predictors for HALRN conversion. However, we hope these added details will facilitate the decision-making process prior to surgery.

There were 2 cases of venous tumor thrombus (T3b). One case of pT3b was suspected preoperatively. As discussed above, this case required conversion to HALRN in order to "milk" the thrombus towards the specimen side of the resection prior to firing the GIA stapler. The other case of pT3b demonstrated invasion into distal branches of the renal vein. This was not suspected until final pathologic reading and was managed by the standard procedure.

A regional lymphadenectomy (left nephrectomy=hilar and para-aortic nodes; right nephrectomy=hilar and paracaval nodes) was performed in cases of preoperative lymphadenopathy (n=4 cases) or intraoperative findings of suspicious lymph nodes (n=2 cases). In total, 6 patients underwent lymphadenectomy with an average yield of 5 lymph nodes (range, 2 to 10). The one patient with T4 disease had positive lymph nodes; the remaining cases were negative.

From a technical perspective, the large size of these masses necessitated certain adjustments in surgical technique. To create more working space, the laparoscopic ports were placed inferiorly and medially in comparison with the approach for smaller lesions. Furthermore, several cases required placement of a hand-assist device to aid in mobilization of the kidney and to facilitate extraction of the specimen.

Some concerns still remain for the laparoscopic removal of larger renal tumors. These include technical feasibility issues (visibility, working space), increased surgical morbidity, completeness of resection, increased vascularity of

larger lesions, and the possibility of tumor seeding. Some of these questions have already been answered. Some are answered by this study and studies like it. Others will not be answered until we have much longer follow-up data for these patients.

We recognize several limitations in this study. First, our 2-surgeon group did not have a contemporary open radical nephrectomy series to which we might compare our laparoscopic results. The most notable limitations, however, are that our study is a retrospective, single-institution study with small patient numbers and limited follow-up. A larger, prospective study would not only increase our sample size, but also enable us to draw more meaningful conclusions about the relative perioperative benefits of laparoscopic surgery for management of larger renal masses. Longer follow-up would allow us to more accurately determine whether laparoscopic nephrectomy has the same long-term oncologic benefit as open radical nephrectomy. Unfortunately, the data we have available provide a mean follow-up time of only 2.5 years. Nevertheless, we have elected to include patients with shorter follow-up to emphasize the feasibility of the laparoscopic operative approach for such advanced renal tumors. Prior studies have highlighted longer follow-up, albeit with less extensive disease.[1] Our goal was to provide data on both successful completion of the procedure as well as oncologic outcomes. As such, our mean follow-up is shorter than follow-up in several of the other studies.

CONCLUSIONS

Laparoscopic radical nephrectomy for large tumors is a technically challenging operation. However, in experienced hands, LRN is a reasonable therapeutic option for the management of large, advanced RCC lesions. Patients experience benefits of less blood loss, shorter hospitalization, and a more rapid convalescence. Patients who undergo laparoscopic nephrectomy still suffer from recurrences of RCC, though at a similar rate and distribution as those who underwent open surgical resection. Thus, it appears that individual tumor biology rather than the surgical approach best determines the chances of cure.

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