A Multi-Institutional Study on the Safety and Efficacy of Specimen Morcellation After Laparoscopic Radical Nephrectomy for Clinical Stage T1 or T2 Renal Cell Carcinoma

Simon D. Wu, M.D.,¹ O. Alex Lesani, M.D.,¹ Lee C. Zhao, M.D.,¹ William K. Johnston, M.D.,¹ J. Stuart Wolf, Jr., M.D.,² Ralph V. Clayman, M.D.,³ and Robert B. Nadler, M.D.¹

Abstract

Introduction and Objective: Specimen morcellation during laparoscopic radical nephrectomy (LRN) for renal cell carcinoma (RCC) is controversial. We seek to evaluate the safety and efficacy of specimen morcellation and LRN for treatment of presumed malignant renal lesions.

Methods: We retrospectively reviewed all patients who underwent LRN at three academic institutions from 1996 to 2007. One hundred eighty-eight patients underwent specimen morcellation after LRN for enhancing solid or cystic renal masses.

Results: LRN was successfully performed on all the patients. Patient age ranged from 36 to 94. One hundred sixty-seven patients were in clinical stage T1, 19 patients T2, and unknown in two. The specimen was manually morcellated within a Cook Lap Sac or Endocatch II bag under laparoscopic or direct observation. On histological review of morcellated specimens, 165 patients were confirmed to have RCC, 17 had an oncocytoma, and 2 had benign cysts. At least 13 patients with RCC were pathologically upgraded to stage T3. Mean operative time was 225 minutes (range 94–650). Mean hospital stay was 2.5 days (range 1–8). In patients with RCC, 11 developed recurrent disease with mean follow-up of 21 months (range 0.3–111). In one patient, a port site recurrence occurred in concert with renal fossa and lymph node metastases.

Conclusions: Intracorporeal mechanical morcellation after LRN appears to be safe and effective in clinical stage T1 and T2 RCC. This supports the use of morcellation as an alternative for intact specimen removal in properly selected patients.

Introduction

Morcellation in conjunction with laparoscopic radical nephrectomy (LRN) has been an area of controversy since Clayman et al1 described the initial LRN with morcellation in 1991. It makes sense to use the existing ports to morcellate and extract the specimen and preserve the integrity of a minimally invasive laparoscopic operation. Critics counter that morcellation does not allow for adequate tumor staging and therefore may impact the ability to enroll patients in clinical chemotherapy trials. There also is a concern over intraabdominal, port site, and extraction site tumor seeding. In this multinstitutional study, we sought to evaluate the safety and efficacy of specimen morcellation in conjunction with LRN for presumed renal cell carcinoma (RCC).

Materials and Methods

Records of all patients who underwent LRN from 1996 to 2007 were retrospectively reviewed at three academic urology departments. All procedures using manual morcellation of kidneys suspected of containing clinical stage T1 or T2, N0 RCC were included in the analysis. Postoperative follow-up included physical exam, routine laboratory studies, as well as axial imaging with computed tomography or magnetic resonance imaging to evaluate for complications and recurrent or metastatic disease.

The specimen entrapment and morcellation technique varied between institutions but universally involved the basic principles of performing morcellation under direct and/or laparoscopic vision; this includes extensive draping around

¹Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, Illinois.
²Department of Urology, University of Michigan Medical Center, Ann Arbor, Michigan.
³Department of Urology, University of California Irvine Medical Center, Orange, California.
the port site through which the morcellated specimen is delivered to prevent tumor spill and dissemination. The techniques of specimen entrapment and morcellation utilized at Northwestern University have been previously described.² At the University of California, Irvine, morcellation is performed by placing the specimen into a LapSac (Cook Urological, Spencer, IN) that is delivered through the caudal most port site that has been enlarged to 20 mm. This is followed by a triple draping of the surgical field around the port site. The neck of the LapSac is covered by a sterile adhesive drape, a fenestrated absorbent towel, and a nephrostomy drape. The neck of the LapSac is passed through a hole in each of these drapes. These precautions are taken to help prevent potential wound contamination by any spilled tumor cells. The tumor is then manually morcellated using a Sopher gynecological ring forceps that has 14×45 mm reinforced jaws. After completion of morcellation, the surgeon and all other members of the surgical team who participated during morcellation regown and reglove.

The University of Michigan has utilized both an impermeable nylon sac (i.e., LapSac) with intracorporeal morcellation and later adopted the technique described by Landman et al,³ which entails placing the specimen in a self-opening plastic sac (Endo Catch II; Autosuture, Norwalk, CT) and lengthening a port site incision until the sac contents can be seen (typically 2–4 cm, depending on patient’s body wall thickness). Specimen morcellation is then performed under direct observation above the abdominal wall. A fenestrated drape is used to protect the port site from potential seeding. Once the specimen has been extracted, the incision is irrigated with 200 mL of sterile water after the surgical team regown and reglove. Table 1 compares the variations in morcellation technique among the three institutions.

Results

One hundred eighty-eight patients underwent LRN for renal lesions suspicious for clinical stage T1 and T2, N0, M0 RCC. Seventy-four patients were female (40%) and 113 male (60%). Mean age was 62.6 (range 24–94). Preoperative clinical staging was T1N0M0 in 167 (89%) patients and T2N0M0 in 19 (10%). Clinical staging information was not available for two patients (Table 2). None of the cases required conversion to an open procedure. Morcellation of renal tumor specimens occurred without spillage or perforation of the LapSac or EndoCatch II sack. Morcellation time was not assessed. Mean operating time was 225 minutes (range 94–650 minutes). No gross tumor spillage occurred and no perforation of entrapment sacks was noted during morcellation.

Average tumor size was 4.9 cm (range 1.5–16). Histologic review of morcellated specimens revealed that 165 (87%) patients had RCC, 17 (9%) had oncocytomas, 2 (1%) had benign cysts, and 1 had both transitional cell carcinoma and RCC. Thirteen (7%) patients had a pathologic upgrade to pT3 (Table 2).

Thirty patients (16%) experienced complications. Thirty-eight complications were reported overall (Table 3): 4 cardiac, 5 respiratory/thromboembolic events, 8 gastrointestinal, 14 renal/genitourinary, 2 neurologic, 4 postoperative bleeds, and 1 death. One extraction site wound infection occurred. One extraction site incisional hernia occurred. Mean hospital stay was 2.5 days (SD 1.6 days). Mean follow-up was 21.3 months (range 0–111). Out of 11 recurrences (5.8%), 10 were pulmonary or visceral recurrences and 1 in the tumor bed (Table 4). In one patient, a port site recurrence occurred in concert with renal fossa recurrence and lymph node metastases. There were no isolated port site recurrences. No cancer-related deaths occurred during follow-up period.

Discussion

Laparoscopic nephrectomy was originally described by Clayman et al1 in 1991. It was predicated on specimen morcellation to minimize employment of more invasive enlarged incisions on the abdomen. To that end, the LapSac and an electronic morcellator were developed. The latter is no longer commercially available. Since then laparoscopic radical or total nephrectomy has been widely accepted as an oncologically sound and safe technique.4–11 Advantages in analgesic use and recovery compared with open nephrectomy have been documented.6,8 Although the initial report of LRN described entrapment and morcellation of the kidney and tumor specimen, morcellation has not become a widely accepted practice.

From a technical standpoint, morcellation can be performed safely without increased risk of tumor spillage. First, the LapSac has been shown to be impermeable to tumor spillage. Urban and colleagues found no diffusion of bovine serum albumin, indigo carmine, or mouse bladder tumor cells into dialysate when LapSacs were used as a dialysis membrane.¹² Deployment of the LapSac can be simply accom-

Table 1. Morcellation Techniques Used at Respective Institutions

<table>
<thead>
<tr>
<th>Institution</th>
<th>University of California, Irvine</th>
<th>University of Michigan</th>
<th>Northwestern University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entrapment/extraction port site</td>
<td>Most caudal</td>
<td>Most caudal</td>
<td>Most caudal</td>
</tr>
<tr>
<td>Morcellation port site</td>
<td>Most caudal</td>
<td>Most caudal</td>
<td>Umbilical</td>
</tr>
<tr>
<td>Entrapment sac used</td>
<td>LapSac</td>
<td>LapSac/Endocatch II</td>
<td>LapSac secured to</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Endocatch II carrier</td>
</tr>
<tr>
<td>Morcellation port site incision length</td>
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<td>20–40 mm</td>
<td>20 mm</td>
</tr>
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<td>Fenestrated drape</td>
<td>Sterile towels</td>
</tr>
<tr>
<td></td>
<td>fenestrated absorbent towel</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>nephrostomy drape</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morcellation instrument</td>
<td>Sopher clamp</td>
<td>Sopher clamp</td>
<td>Ring forceps</td>
</tr>
</tbody>
</table>
is immune to perforation. Lastly adequate draping must be undertaken to prevent wound contamination, and all instruments, gowns, and gloves are changed at the end of morcellation before proceeding with the remainder of the surgery.  

Advantages in postoperative analgesic usage and convalescence are shown to favor laparoscopic over open nephrectomies. Nadler compared 33 patients who were prospectively enrolled and assigned in alternating fashion to receive hand-assisted, transperitoneal with morcellation or retroperitoneal laparoscopic nephrectomy. Intact specimen removal was performed in the hand-assisted and retroperitoneal groups. Patients who underwent morcellation had shorter hospital stays and time to normal daily activity. Camargo et al also demonstrated decreased narcotic requirement favoring morcellation versus intact specimen removal. Two studies that compared intact versus morcellated specimen removal showed no difference in postoperative status, but these studies were not randomized and had small numbers or did not compare similar populations.

Critics also cite port site and peritoneal seeding as reasons against performing morcellation. However, only several case reports have shown this. Barrett et al described a solitary port site recurrence at 25 months in a patient with an advanced and large specimen (pT3N0M0 grade 4, 862 gm). Two cases were reported by Castilho and associates. Both patients had pT1N0 grade 2 RCC that presented 5 and 12 months after LRN. Both patients presented with abdominal masses under the trocar sites and ascites. Risk factors cited as possibly contributing to recurrence included not using a LapSac specifically designed for morcellation, presence of ascites at time of nephrectomy, and unrecognized microperforations in the sack. Recent reviews on tumor spillage and port site metastases after open radical nephrectomy for RCC (0.4%). Nadler’s survey of over 2600 laparoscopic radical nephrectomies. Nadler compared 33 patients who were prospectively enrolled and assigned in alternating fashion to receive hand-assisted, transperitoneal with morcellation or retroperitoneal laparoscopic nephrectomy. Intact specimen removal was performed in the hand-assisted and retroperitoneal groups. Patients who underwent morcellation had shorter hospital stays and time to normal daily activity. Camargo et al also demonstrated decreased narcotic requirement favoring morcellation versus intact specimen removal. Two studies that compared intact versus morcellated specimen removal showed no difference in postoperative status, but these studies were not randomized and had small numbers or did not compare similar populations.

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staging based on axial radiographic imaging (i.e., computed tomography or magnetic resonance imaging) is accurate but may under- or stage tumors in 5% to 35% of cases. Distinguishing between T2 and T3a tumors may be especially problematic because of tumor size and lack of sensitive radiographic findings. Grade and histologic type can be reliably and accurately identified in morcellated specimens. Various methods of specimen preparation to enhance accuracy of pathologic evaluation after morcellation have been reported and demonstrate that accurate pathologic staging is possible. Indian Ink staining of the specimen after enrapment but before morcellation allows pathologic determination of surgical margin status. Needle core biopsy of intact specimen before morcellation is accurate in confirming histologic diagnosis. Pathologic staging may also be successfully accomplished when morcellation is performed through a slightly extended extraction incision allowing for removal of larger fragments. Additional prognostic factors such as microvascular invasion can be assessed in morcellated specimens, but renal sinus fat invasion may not be reliably determined. Renal sinus fat invasion, however, is often associated with other negative prognostic indicators (e.g., perirenal fat invasion, lymph node metastases) that may be reliably determined. Renal sinus fat invasion, however, is often associated with other negative prognostic indicators (e.g., perirenal fat invasion, lymph node metastases) that may be reliably determined. Further, systematic models of sampling morcellated specimens have been developed to determine the amount of tissue to be examined to arrive at the diagnosis with a given degree of certainty.

No clear evidence exists that pathologic staging information lost because of specimen morcellation affects clinical follow-up or survival. Specifically, recurrence-free survival, disease-free survival, and overall survival do not appear to be different between open and laparoscopic nephrectomy with morcellation. Reports of pathologic upstaging for clinical T1 RCC and its impact on prognosis have been conflicting at best. Roberts found that up to 31% of the patients diagnosed with clinical T1 RCC were upstaged to pathologic T3a. However, recurrence-free survival did not differ between patients with pT1 and pT3a (in this study, defined as microscopic perinephric fat invasion) RCC. This study implies that current tumor nodes metastasis staging for pT3a tumors with microscopic perinephric fat invasion may not always correlate with prognosis and absence of pathologic staging after morcellation may be, in some cases, more academic concern rather than a clinical one. Svatek and colleagues found that 9% of the clinical T1 RCC were upstaged pT3a (excluding adrenal involvement). Unlike the Roberts’ study, patients with clinical T1 tumors that were pathologically upstaged exhibited higher probability of disease recurrence and cancer-specific death. Finally, lack of durable and standardized adjuvant therapy also diminishes the impact of potential pathologic staging information lost with specimen morcellation. Even with advent of targeted antivascular agents in treatment of metastatic RCC, these agents are still under investigation for use in the adjuvant setting. Cohen and colleagues argue, however, that it is precisely for this reason patients should undergo intact specimen extraction to identify potential candidates to enroll in adjuvant therapy trials.

In our present multiinstitutional series, morcellation technique–related complications were rare, and the subsequent rare occurrence of metastatic disease could not be ascribed to morcellation. Operating time and length of hospitalization are also consistent with previously published LRN series. Thirty patients overall experienced complications (16%) that are consistent with reported laparoscopic nephrectomy series. One perioperative death occurred. This patient also had cardiopulmonary complications after a relatively lengthy case (365 minutes) during a prolonged hospitalization of 14 days. Interestingly, only one extraction site incisional hernia was reported (0.5%), despite upward force applied to the extraction site during the actual process of morcellation. This compares favorably to intact specimen extraction after laparoscopic nephrectomy that is associated with incisional hernias in up to 36% with a hand-assisted approach and also reported rates of trocar site hernias (0.02%–5%). Elashry et al found a 17% rate of incisional hernias (0.02%–5%). Further, patient characteristics (e.g., body mass index, comorbidities) were not evaluated; these characteristics certainly can influence outcomes. Clinical staging (e.g., nodal status, tumor size) and pathologic information were missing for some patients. Lastly, a comprehensive study evaluating the benefits of morcellation should also include functional

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
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<th>Tumor size (cm)</th>
<th>Pathologic stage upgrade</th>
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<th>Grade</th>
<th>Time to recurrence (months)</th>
<th>Location of recurrence</th>
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outcomes (i.e., postoperative pain scores, time to return to normal activity) in addition to oncologic ones.

Conclusions

Morcellation is a safe method of specimen extraction after laparoscopic total radical/total nephrectomy. Our data support that there is equivalent survival in the morcellated patient cohort compared with open nephrectomy. Concerns for inaccurate pathologic staging are offset by similar survival seen between open and laparoscopic nephrectomy with morcellation and the documented ability to obtain accurate histology, assess for lymphovascular invasion, and to still stage the disease given the size of morcellated pieces. It would appear that only in those cases that require very specific information about pathologic staging (e.g., research protocols—ASSURE, S-TRAC, SORCE; qualification for adjuvant therapies, determining more intensive surveillance schedules, possibility of upper tract urothelial carcinoma) should morcellation not be performed.

Disclosure Statement

Dr. Wolf—Terumo Corp, consultant; Gyrus-ACMI, lecturer.

Dr. Clayman—Cook Urological, Consultant/Advisor; Applied Urology, Investment Interest; Cook Urological Inc., Royalty Affiliation; Greenland Inc., Royalty Affiliation; Orthopedic Service Inc., (OSI) Royalty Affiliation; Galil Inc., Consultant/Advisor; Boston Scientific, Investigator; Karl Storz Inc., Consultant/Advisor.

Dr. Nadler—Intuitive Surgical (da Vinci), Consultant or Advisor; Angio Dynamics, Consultant or Advisor; Boston Scientific, Investigator; Karl Storz Inc., Consultant or Advisor; Vascular Technology Inc., Consultant/Advisor; Greenwald Inc., Royalty Affiliation; Applied Urology, Investment Interest; Cook Urological Inc., Royalty Affiliation; Galil Inc., Consultant/Advisor; Boston Scientific, Investigator; Gyrus-ACMI, lecturer.

References


Address correspondence to:
Robert B. Nadler, M.D.
Department of Urology
Northwestern University Feinberg School of Medicine
675 North St. Clair St.
Galter 20-150
Chicago, IL 60611
E-mail: r-nadler@northwestern.edu

### Abbreviations Used

- **EBL**: estimated blood loss
- **LRN**: laparoscopic radical nephrectomy
- **NA**: not available
- **RCC**: renal cell carcinoma
- **SD**: standard deviation
- **TCC**: transitional cell carcinoma