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# 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

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#### **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 multiinstitutional 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

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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.<sup>2</sup> 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  $14 \times 45$  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,<sup>3</sup> 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  $T_1N_0M_0$  in 167 (89%) patients and  $T_2N_0M_0$  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 cancerrelated deaths occurred during follow-up period.

#### **Discussion**

Laparoscopic nephrectomy was originally described by Clayman et al<sup>1</sup> 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. <sup>4–11</sup> Advantages in analgesic use and recovery compared with open nephrectomy have been documented. <sup>6,8</sup> 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. Deployment of the LapSac can be simply accom-

Table 1. Morcellation Techniques Used at Respective Institutions

Institution	University of California, Irvine	University of Michigan	Northwestern University
Entrapment/extraction port site	Most caudal	Most caudal	Most caudal
Morcellation port site	Most caudal	Most caudal	Umbilical
Entrapment sac used	LapSac	LapSac/Endocatch II	LapSac secured to Endocatch II carrier
Morcellation port site incision length	20 mm	20–40 mm	20 mm
Draping	Clear plastic adhesive drape fenestrated absorbent towel nephrostomy drape	Fenestrated drape	Sterile towels
Morcellation instrument	Sopher clamp	Sopher clamp	Ring forceps

TABLE 2. PATIENT CHARACTERISTICS AND SELECT PERIOPERATIVE OUTCOMES

n       188         Mean patient age, year (SD)       62.6 (13.5)         Number of females (%)       74 (39%)         Mean tumor size, cm (SD)       4.9 (2.2)         Clinical T stage (%)       75 (40%)         T1a       75 (40%)         T1b       92 (49%)         T2       19 (10%)         NA       2 (1%)         Upstaged to pT3       13 (7%)         Fuhrman nuclear grade       1         I       88 (47%)         III       43 (23%)         IV       10 (5%)         NA       32 (16%)         Tumor histology (%)       32 (16%)         Clear cell RCC       137 (73%)         Papillary RCC       12 (6%)         Chromophobe RCC       13 (7%)         Sarcomatoid RCC       2 (1%)         Oncocytoma       17 (9%)         TCC       0 (0%)         Other       2 (1%)         Benign cyst       2 (1%)         NA       3 (2%)         Tumor recurrence (%)       11 (5.8%)         Mean time to recurrence, month       19.4
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Recurrence site
Morcellation port site 1
Other port site 0
Renal fossa 1
Pulmonary/visceral 10
Cancer related deaths 0
Mean follow-up time, month (SD) 21.3 (22.0)
Mean EBL, mL (SD) 200 (315)
OR time, minute (SD) 225 (80)
Mean length of stay, days (SD) 2.5 (1.6)

<sup>&</sup>lt;sup>a</sup>Patient had both clear cell and papillary RCC.

plished as described by User and Nadler.2 With this technique, a LapSac is secured to the frame of an Endocatch II device after the original specimen sack is removed. The LapSac is then rolled tightly and the compressed frame and sack are drawn back into the cannula of the device. The device then can be redeployed as usual. The University of Michigan uses the morcellation technique described by Landman et al.<sup>3</sup> Specimens are morcellated within an Endocatch II entrapment sack, which when compared with a LapSac is more flimsy. To ensure against tumor spillage, the authors modified their technique to widen the extraction incision to 3 cm and to only grasp and morcellate tissue that is protruding outside (i.e., extracorporeal) the wound. Endocatch II sack integrity was maintained in all cases, and no trocar site or local recurrences were noted in follow-up.<sup>3</sup> Proper technique is required in all cases with morcellation under direct and/or laparoscopic vision to prevent perforation of the sack, as neither sack

TABLE 3. COMPLICATIONS

Institution	Total
Patients with complications (%)	30 (16%)
Complication type	, ,
Cardiac/MI/arrhythmia	4 (11%)
Respiratory/PE/DVT	5 (13%)
Gastrointestinal	8 (21%)
Urologic/renal	14 (37%)
Neurologic	2 (5%)
Postoperative bleed	4 (11%)
Death	1 (2%)
Total no. of complications	38 (100%)

MI = myocardial infarction; PE = pulmonary embolism; DVT = deep vein thrombosis.

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.<sup>13</sup>

Advantages in postoperative analgesic usage and convalescence are shown to favor laparoscopic over open nephrectomies. All 15 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 17 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 11 or did not compare similar populations. 18

Critics also cite port site and peritoneal seeding as reasons against performing morcellation. However, only several case reports have shown this. Barrett et al<sup>19</sup> 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. 20,21 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 seeding and port site metastases in urologic laparoscopy have shown this to be rare in the context of nephrectomy and morcellation done for presumed RCC. 22-25 In Micali's survey of over 2600 laparoscopic radical nephrectomies, no tumor seeding was noted.<sup>22</sup> Certainly, these numbers compare favorably with that of incisional scar metastases after open radical nephrectomy for RCC (0.4%).<sup>24</sup> In our multiinstitutional study, one port site metastases developed in concert with renal fossa and lymph node recurrence. Ten out of the 11 recurrences were either pulmonary or visceral in location. This is also consistent with reported

Concern remains, however, regarding loss of pathologic staging with specimen morcellation.<sup>26</sup> Preoperative

<sup>&</sup>lt;sup>b</sup>Patient had both papillary RCC and TCC.

NA = not available; SD = standard deviation; RCC = renal cell carcinoma; TCC = transitional cell carcinoma; EBL = estimated blood loss.

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TARTE A	DATENTEC	TATTETT	RECURRENT	DICEACE
I A RI F 4	PATIENTS	WITH	KECHRRENT	LUSEASE

Age	Gender	Clinical stage	Multiple tumors	Tumor size (cm)	Pathologic stage upgrade	Histology	Grade	Time to recurrence (months)	Location of recurrence
78	M	T1b	No	6	_	Clear cell	2	18.8	Lung
39	F	T1b	Yes	5	_	Clear cell	4	1.5	Lung
51	M	T1b	No	5	_	Clear cell	2	37.1	Lung
54	M	T1b	No	6.8	_	Clear cell	4	42.7	Brain
75	F	T1a	No	2.5	_	Clear cell	3	7.5	Bone
61	M	T1b	No	5.5	_	Clear cell	3	45.7	Lung
76	M	T1a	No	3.5	_	Clear cell	2	29.5	Larynx
61	F	T2	No	8	T3a	Clear cell	4	6.3	Lung
40	M	T2	No	7.3	ТЗа	Clear cell	3	7.3	Renal fossa, port site, lymph node
65	F	T2	No	8	T3a	Clear cell	3	10.9	Contralateral kidney
80	F	T2	No	13	T3a	Clear cell	4	5.7	Abdomen and bone

staging based on axial radiographic imaging (i.e., computed tomography or magnetic resonance imaging) is accurate but may under- or overstage tumors in 5% to 35% of cases.<sup>27</sup> Distinguishing between T2 and T3a tumors may be especially problematic because of tumor size and lack of sensitive radiographic findings.<sup>28</sup> Grade and histologic type can be reliably and accurately identified in morcellated specimens.<sup>27,29</sup> Various methods of specimen preparation to enhance accuracy of pathologic evaluation after morcellation have been reported and demonstrate that accurate pathologic staging is possible.<sup>29</sup> Indian Ink staining of the specimen after entrapment but before morcellation allows pathologic determination of surgical margin status.<sup>30</sup> Needle core biopsy of intact specimen before morcellation is accurate in confirming histologic diagnosis.<sup>31</sup> Pathologic staging may also be successfully accomplished when morcellation is performed through a slightly extended extraction incision allowing for removal of larger fragments.<sup>3</sup> Additional prognostic factors such as microvascular invasion can be assessed in morcellated specimens, but renal sinus fat invasion may not be reliably determined. 9,29,32 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.<sup>29,33,34</sup> 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.<sup>35</sup>

No clear evidence exists that pathologic staging information lost because of specimen morcellation affects clinical follow-up or survival. 4,5,7,8,13,14,36 Specifically, recurrence-free survival, disease-free survival, and overall survival do not appear to be different between open and laparoscopic nephrectomy with morcellation. <sup>7–9,14</sup> Reports of pathologic upstaging for clinical T1 RCC and its impact on prognosis have been conflicting at best. 36,37 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.<sup>36</sup> 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 an academic concern rather than a clinical one. Svatek and colleagues<sup>37</sup> 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.<sup>37</sup> 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.<sup>38</sup> Cohen and colleagues<sup>39</sup> 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. 4,5,7,8 Thirty patients overall experienced complications (16%) that are consistent with reported laparoscopic nephrectomy series. 4-6,8,13 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<sup>16</sup> and also reported rates of trocar site hernias (0.02%–5%).40 Elashry et al41 found a 17% rate of incisional hernias when the intact specimen was extracted from a lower flank port-connecting incision.

Weaknesses of this study are the lack of prospective randomized comparison of intact versus morcellated specimen removal. 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

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; Greenwald Inc., Royalty Affiliation; Orthopedic Service Inc., (OSI) Royalty Affiliation; Galil Inc., Consultant/Advisor; Boston Scientific, Investigator; Vascular Technology Inc., Consultant/Advisor; Karl Storz Inc., Consultant/Advisor.

Dr. Nadler—Intuitive Surgical (da Vinci), Consultant or Advisor; Angio Dynamics, Consultant or Advisor.

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### **Abbreviations Used**

EBL = estimated blood loss

LRN = laparoscopic radical nephrectomy

NA = not available

RCC = renal cell carcinoma

SD = standard deviation

TCC = transitional cell carcinoma