Laparoscopic and Partial Nephrectomy

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ABSTRACT
Radical nephrectomy is the gold standard curative operation for patients with localized renal cell carcinoma (RCC). Since its introduction in 1990, laparoscopic radical nephrectomy is being increasingly done at numerous institutions worldwide. In the hands of experienced laparoscopic urological surgeons and with adherence to established principles of open radical nephrectomy, laparoscopic radical nephrectomy is now a standard of care for patients with T1–3a N0 M0 RCC. Intermediate-term outcome data indicate equivalent cancer-free survival to open radical nephrectomy in such cases. Nephron-sparing surgery (NSS) is now an established approach for patients with localized RCC when there is a clinically relevant need to preserve renal function. NSS is also indicated in patients with a single, small, unilateral, localized RCC when the opposite kidney is completely normal. The technical success rate with NSS for RCC is excellent, and long-term patient survival free of cancer is comparable with that obtained after radical nephrectomy. We recently reviewed the results of NSS in 107 patients with localized sporadic RCC treated at the Cleveland Clinic before 1988 who were followed up for a minimum of 10 years. Long-term preservation of renal function was achieved in 93% of patients, and the 10-year cancer specific survival rate was 73%. Although open surgical partial nephrectomy remains the gold standard for nephron-sparing treatment of RCC, laparoscopic partial nephrectomy is now available in selected cases. The optimal indications for laparoscopic NSS are in patients with a relatively small and peripheral renal tumor. In such cases, laparoscopic NSS is proving to be an effective, minimally invasive therapeutic approach with respect to renal functional outcome, with additional advantages of reduced postoperative narcotic use, earlier hospital discharge, and a faster convalescence. The laparoscopic approach is associated with longer warm ischemia time, more major intraoperative complications, and more postoperative urological complications. Continued efforts are required to develop laparoscopic renal hypothermia techniques and to facilitate intrarenal suturing while minimizing the warm ischemia time.

INTRODUCTION
Epithelial tumors of the kidney represent nearly 3% of all solid neoplasms. Renal cell carcinoma (RCC) accounts for approximately 85% of newly diagnosed renal malignancies, occurring at an estimated rate of 4.4 to 11.1/100,000 person-years (1). Data from the United States Surveillance Epidemiology and End Results program show a steady rise in RCC rates of 2.3 to 4.3% annually between 1975 and 1995 (1). This increase can be attributed in part to early detection through the increasing utilization of noninvasive imaging techniques, although incidental detection alone cannot fully explain the upward trend. Surgical resection remains the standard treatment for RCC. The concept of wide excision of the affected kidney outside its investing (Gerota’s) fascia to include the perirenal fat and ipsilateral adrenal gland has dictated surgical thinking and management of this tumor for more than a half a century. Compared with simple nephrectomy, this approach was favored because of the recognition that extrarenal involvement of the adjacent perirenal fat and adrenal gland may contribute to surgical failure, thus necessitating the maintenance of anatomic planes of resection to obtain the widest surgical margin possible. Today, a better understanding of the biology of RCC, standardized staging, and changing patterns of presentation for patients with this tumor permit a refined management approach that may comprise observation, radical nephrectomy, or nephron-sparing therapy.

RADICAL NEPHRECTOMY
Radical nephrectomy is the gold standard curative operation for patients with localized RCC. The preoperative evaluation of patients with RCC has changed in recent years because of the advent of new imaging modalities such as ultrasonography, computed tomography (CT), and magnetic resonance imaging. In most patients, these noninvasive modalities can be used to do a complete preliminary evaluation. Renal arteriography is no longer routinely necessary before performing radical nephrectomy. All patients should undergo a metastatic evaluation, including a chest X-ray examination, abdominal CT scan, and occasionally a bone scan, which is only necessary in patients with bone pain or an elevated serum alkaline phosphatase level.

Radical nephrectomy encompasses the basic principles of early ligation of the renal artery and vein, removal of the kidney outside Gerota’s fascia, removal of the ipsilateral adrenal gland, and performance of a complete lymphadenectomy from the crus of the diaphragm to the aortic bifurcation. Perhaps the most important aspect of radical nephrectomy is removal of the kidney outside Gerota’s fascia, because capsular invasion with perinephric fat involvement occurs in 25% of patients. Recent studies suggest that removal of the ipsilateral adrenal gland is not routinely necessary unless the malignancy either extensively...
involves the kidney or is located in the upper portion of the kidney. Although lymphadenectomy allows for more accurate pathologic staging, the therapeutic value is controversial, and there remains a divergence of clinical practice among urologists with respect to this aspect of radical nephrectomy.

Technique and Results of Laparoscopic Radical Nephrectomy. Since its introduction in 1990, laparoscopic nephrectomy is being increasingly done at numerous institutions worldwide. At the Cleveland Clinic, laparoscopic radical nephrectomy is preferentially done by the retroperitoneal technique. Retroperitoneoscopy offers several advantages, including expeditious access to the renal artery and vein, which allows for early ligation; the need for only three laparoscopic ports; extrafascial mobilization and intact extraction of the kidney; and avoidance of the peritoneal cavity, which allows for earlier recovery of intestinal function than with the transperitoneal technique.

Whether done retroperitoneally or transperitoneally, laparoscopic radical nephrectomy must duplicate established open surgical oncological principles. These include early sequential control of the renal artery and vein before tumor manipulation, wide specimen mobilization external to Gerota’s fascia, avoidance of any specimen traumatization or rupture, and intact specimen extraction with documented negative surgical margins on histopathologic analysis. In the hands of experienced laparoscopic urological surgeons, it is currently possible to achieve these goals in properly selected patients with localized RCC.

We recently reviewed our initial experience with 100 retroperitoneal laparoscopic radical nephrectomies at the Cleveland Clinic (2). In the 100 patients (mean tumor size, 5.1 cm), mean surgical time was 2.8 hours, blood loss was 212 mL, specimen weight was 554 g, and hospital stay was 1.6 days. Complications occurred in 14 patients (14%), three (3%) of whom were major and 11 (11%) minor. Two patients (2%) had their nephrectomies converted to open surgery. There was no perioperative mortality. During a mean follow-up of 16.1 months, there was no local or port-site occurrence; two patients developed metastatic disease with one death in 11 months. All laparoscopic specimens were extracted intact, and surgical margins were negative for cancer in all 100 patients.

Current Indications for Laparoscopic Nephrectomy. In the hands of experienced laparoscopic urological surgeons and with adherence to established principles of open radical nephrectomy, laparoscopic radical nephrectomy may now be considered a standard of care for patients with T1–3aN0M0 RCCs. Intermediate-term outcome data indicate equivalent cancer-free survival to open radical nephrectomy in such cases.

Currently, open radical nephrectomy remains the preferred technique for patients with RCC and any of the following characteristics: (a) major venous or vena caval involvement, (b) local tumor invasion, (c) massive tumor size, and (d) gross lymphadenopathy. In these settings, the ability of laparoscopic radical nephrectomy to achieve complete tumor excision is not established. In addition, most patients with metastatic RCC who require cytoreductive nephrectomy are better served with an open surgical approach. Preliminary data with laparoscopic nephrectomy in such cases have shown prolonged operative times, substantial morbidity, and a high open conversion rate.

Laparoscopic Radical Nephrectomy: Morcellation versus Intact Extraction. Laparoscopic radical nephrectomy with specimen morcellation for extraction continues to be practiced at some centers. Nevertheless, we believe that intact specimen extraction in an impermeable sac is preferable for several reasons. From a technical standpoint, this is easily done through a muscle-splitting extension of one of the port-site incisions or more recently through a low Pfannenstiel incision. Intact extraction enables accurate study of the surgical margins and pathologic staging of the tumor. Prognosis and follow-up of patients with RCC depends on tumor size, stage, grade, microvascular invasion, and completeness of tumor resection. Relevant information obtained from accurate histopathologic study of the intact specimen is used for prognostication of individual cases and formulation of stage-dependent postoperative surveillance protocols. Although pathologic staging does not currently affect postoperative treatment regimens, this will likely change in the near future with the advent of effective adjuvant systemic immunotherapy.

Intact specimen extraction does not seem to increase incisional morbidity. In the analysis by Ono et al. (3) of 60 patients, intact extraction was done in 26 patients undergoing transperitoneal (n = 11, group 1) or retroperitoneal (n = 15, group 2) laparoscopic nephrectomy. Fractionated specimen extraction was done in the most recent 34 patients undergoing transperitoneal laparoscopic nephrectomy (group 3). There was no significant difference in postoperative analgesia, convalescence, or complications among the 3 groups. Similarly, on comparing patient outcome among various centers worldwide, no significant differences are apparent in patient morbidity between intact extraction versus morcellation. Specifically, mean specimen weights, analgesic requirements, hospital stay, and convalescence seem comparable between the intact extraction and morcellation groups. In addition, the technique of tumor morcellation entails an additional 30 to 45 minutes of operative time. The only discernible rationale for morcellation is the minor cosmetic advantage of avoiding a small 4- to 6-cm incision. I believe that the important information afforded to the patient and the surgeon by accurate pathologic examination of the intact specimen, coupled with a reduced operative time, far outweighs this trivial cosmetic issue.

PARTIAL NEPHRECTOMY OR NEPHRON-SPARING SURGERY

Indications. Standard indications for nephron-sparing surgery (NSS) fall into three categories: absolute, relative, and elective. Absolute indications for NSS include circumstances where radical nephrectomy would render the patient anephric, with subsequent immediate need for dialysis. This encompasses patients with bilateral RCC or RCC involving a solitary kidney, whether resulting from unilateral renal agenesis, prior removal of the contralateral kidney, or irreversible impairment of contralateral renal function. Patients with bilateral synchronous renal tumors also have an absolute indication for NSS, and an attempt should be made to preserve as much functioning parenchyma as possible. Preservation involves performing bilateral partial nephrectomy when feasible, usually as a staged procedure with the less involved side done first. When partial ne-
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Relative indications for NSS include patients with unilateral RCC and a functioning opposite kidney, when the opposite kidney is affected by a condition that might threaten its future function, such as calculus disease, chronic pyelonephritis, renal artery stenosis, ureteral reflux, or systemic diseases such as diabetes and nephrosclerosis. In such patients, the risks and benefits of NSS must be considered in the context of the general clinical status, including age, comorbidities, risk of disease progression, and the possibility that these conditions will negatively affect remaining renal function.

Relative indications for NSS also include patients with hereditary forms of RCC such as von Hippel-Lindau disease, where there is a high likelihood of subsequent lesions developing in the remaining renal parenchyma. The natural history of RCC in patients with von Hippel-Lindau differs from sporadic RCC in that the diagnosis is made at a younger age, and there usually are multiple bilateral renal tumors. In patients with von Hippel-Lindau or other hereditary renal malignancies, NSS is offered based on the genetic predisposition to recurrence and the importance of preserving renal function.

Elective indications for NSS include patients with localized unilateral RCC and a normal contralateral kidney. Recent studies have clarified the role of NSS in such patients. With evolving longer-term data, a size criterion has gained gradual acceptance for elective NSS. Data from our institution, as well as from the Mayo Clinic and Memorial Sloan-Kettering Cancer Center, indicate that radical nephrectomy and NSS provide equally effective curative treatment for such patients who present with a single, small (<4 cm), and clearly localized RCC (4–6).

Although the long-term functional advantage of NSS when there is a normal opposite kidney remains to be shown definitively, the benefits of maximal nephron preservation may include a decreased risk of progression to chronic renal insufficiency and end-stage renal disease. In recent studies by McKiernan et al. (7) from Memorial Sloan-Kettering Cancer Center and Lau et al. (8) from Mayo Clinic, patients who underwent radical nephrectomy were compared with patients who underwent elective NSS. Each institution’s groups were well matched for age, grade, stage, tumor size, preoperative creatinine level, and year of surgery. Although they identified no significant difference in cancer-free survival, Lau et al. (8) showed that at 10 years, renal insufficiency (defined as an increase in serum creatinine to >2 mg/dl) was significantly different between the groups, occurring in 12.4% of radical nephrectomy cases compared with only 2.3% of NSS cases. Similarly, McKiernan et al. (7) found that the chance of progression to renal insufficiency was significantly higher in the radical nephrectomy group. In both groups, differences in functional renal reserve were thought to be responsible for these findings. Therefore, given the excellent short-term and long-term results of elective NSS for cancer control and the increasingly recognized functional benefits of this approach, patients with a single, small, unilateral, localized RCC may now be considered suitable candidates for NSS even when the opposite kidney is completely normal.

Preoperative Evaluation. Evaluation of patients with RCC before NSS must include a detailed history and physical examination and a laboratory evaluation, including serum creatinine measurement, liver function tests, and urinalysis or urine dipstick check, to screen for preoperative proteinuria. Radiographic testing is used to rule out locally extensive or metastatic disease, including chest X-ray examination and abdominal CT, as well as possible bone scan and chest or head CT, depending on the clinical circumstances.

However, NSS is technically challenging and requires a more detailed understanding of renal anatomy than en bloc removal of the kidney by radical nephrectomy. Knowledge of the relationship of the tumor to the collecting system and adjacent normal parenchyma and of the renal and tumor vascular supply is essential for preoperative planning. Therefore, more extensive and invasive preoperative imaging studies are often necessary before NSS. These studies include renal CT, arteriography, and occasionally venography. Arteriography has been used to delineate the intrarenal vasculature and may aid in excision of the tumor while minimizing blood loss and injury to normal adjacent parenchyma. It is most useful for nonperipheral tumors encompassing ≥2 renal arterial segments. Selective renal venography is done in patients with large or centrally located tumors to evaluate for the presence of intrarenal venous thrombosis and to assess adequacy of venous drainage of the planned renal remnant. These studies provide a two-dimensional map to aid complete excision of tumors, assess arterial and venous involvement, and plan complex reconstruction of the renal remnant. However, these studies yield only limited information on the anatomic spatial relationships among the tumor, normal renal parenchyma, collecting system, and vascular supply. Furthermore, the risks and costs of conventional arteriography or venography are not insignificant.

CT is widely accepted as the preferred imaging technique for detecting and staging RCC because of the low cost, high accuracy, and ready accessibility. Advances in helical CT image acquisition and computer technology allow production of high-quality three-dimensional images of the renal vasculature and soft tissue anatomy. The latest development in three-dimensional imaging is volume rendering, which allows real-time interactive stereoscopic viewing and presents complex anatomy not possible with conventional axial CT. By combining helical CT and three-dimensional volume rendering, a single noninvasive preoperative test has the potential to provide all of the critical information needed for planning and intraoperative management of renal mass lesions. New volume-rendering software allows real-time interactive stereoscopic viewing of these images and provides a topographical map of the renal surface and multiplanar views of the intrarenal anatomy. This permits evaluation of the complex renal anatomy with a single, unified study in a format that is familiar to the surgeon and consistent with intraoperative findings, thereby obviating the need for mental reconstruction of several two-dimensional imaging studies. A detailed prospective study at the Cleveland Clinic showed the utility of three-dimensional volume-rendering CT in accurately depicting the renal parenchyma and vascular anatomy.
necessary for the performance of NSS (9). The data from three-dimensional CT integrate essential information from angiography, venography, excretory urography, and conventional two-dimensional CT into a single preoperative staging test that diminishes the need for more invasive imaging. The use of a 3- to 5-minute videotape in the operating room provides concise, accurate, and immediate three-dimensional information to the surgeon during the dissection, allowing him or her to anticipate the subtleties of the anatomy. The three-dimensional volume-rendered CT has become the imaging modality of choice before NSS, allowing hilar dissection, tumor removal, and reconstruction to proceed quickly and confidently.

Clinical Results of Open NSS. The technical success rate with open NSS for RCC is excellent, and long-term patient survival free of cancer is comparable with that obtained after radical nephrectomy. Table 1 lists results of open NSS for RCC in >1262 patients described in the literature since 1990. The reported mean cancer-specific survival for all patients undergoing open NSS for localized RCC is 88 to 97.5%. Mean follow-up for these studies ranged from 4 to 6 years.

Recently, Fergany et al. (17) reviewed the results of open NSS done at the Cleveland Clinic in 107 patients with localized sporadic RCC treated before 1988 who were followed up for a minimum of 10 years or until death. Tumors were symptomat ic in 73 patients (68%), and indications for surgery were imperative in 96 (90%). Cancer-specific survival was 88.2% at 5 years and 73% at 10 years, and 26% of the patients died of metastatic disease. Long-term preservation of renal function was achieved in 93% of patients. Cancer-specific survival for tumors 4 cm or smaller was 98% at 5 years and 92% at 10 years regardless of the indication for partial nephrectomy. Important negative predictors of survival included high tumor grade, high tumor stage, bilateral disease, and tumors larger than 4 cm. These data are consistent with other shorter-term, previously published series that confirm that tumor stage, grade, and size remain the most important prognostic indicators determining outcome after NSS.

On the other hand, there are no significant biological differences between centrally versus peripherally located small, solitary, unilateral RCCs, and treatment with NSS or radical nephrectomy is equally effective regardless of tumor location in these patients.

LAPAROSCOPIC PARTIAL NEPHRECTOMY

The technique of laparoscopic partial nephrectomy for treatment of RCC is in its developmental stages. Until recently, the cumulative reported experience comprised fewer than 100 cases, and these were confounded by a lack of standardized technique and variable experience. Although both intraperitoneal and retroperitoneal laparoscopic partial nephrectomies have been successfully done, it has been difficult to reproduce the essential elements of open partial nephrectomy with contemporary laparoscopic instrumentation. Despite advanced techniques, including the use of a harmonic scalpel and biological tissue adhesives such as fibrin glue, laparoscopic partial nephrectomy has resulted in longer operative times and higher complication rates than open partial nephrectomy.

Recently, Gill from Cleveland Clinic described the technique of and reported on the largest single institutional experience with purely laparoscopic partial nephrectomy for renal tumor. Procedurally, the focus is to duplicate established open techniques of oncological NSS. The key technical steps include preoperative ureteral catheterization; preparation of the renal hilum; renal mobilization preserving the perinephric fat covering the tumor; laparoscopic flexible ultrasonography; scoring of the renal parenchyma along the proposed line of resection; administration of intravenous mannitol; transient clamping of the renal artery and vein; excision of the tumor with an approximate 0.5 cm margin using cold Endoshears and/or hot J-hook electrocautery; suturing of the collecting system, if necessary; and suture repair of the parenchymal defect using surgical bolsters and mattress sutures.

We recently compared the perioperative outcomes after laparoscopic and open NSS for patients with solitary renal tumors smaller than 7 cm at the Cleveland Clinic (18). Since September 1999, 100 consecutive patients underwent laparoscopic partial nephrectomy for a sporadic single renal tumor smaller than 7 cm at the Cleveland Clinic. A contemporary cohort of 100 consecutive patients with similar inclusion criteria underwent open NSS since April 1998. Because our laparoscopic technique was based on our established open surgical principles, both approaches were similar, including transient renal vascular control, sharp tumor excision in a bloodless field, pelvicalical repair when necessary, suture ligation of transected intrarenal blood vessels, and suture repair of the renal parenchymal defect over a bolster. Demographic, intraoperative, postoperative, and short-term follow-up data were retrospectively compared between the two groups.

Median tumor size was 2.8 cm in the laparoscopic group and 3.3 cm in the open group ($P = 0.005$). There were significantly more tumors larger than 4 cm in the open group ($P < 0.001$). There were more patients with a solitary kidney in the open surgical group ($P = 0.002$). More patients in the open

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<th>Outcome in patients undergoing nephron-sparing surgery for localized renal cell carcinoma</th>
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group underwent NSS for a malignant tumor (P = 0.002). Comparing the laparoscopic versus open groups, median surgical time was 3 vs 9.9 hours (P = 0.01), blood loss was 125 vs 250 mL (P < 0.001), and mean warm ischemia time was 27.8 vs 17.5 minutes (P < 0.001), respectively. In the laparoscopic and open groups, median analgesic requirement was 20.2 vs 252.5 mg of morphine sulfate equivalents (P < 0.001), hospital stay was 2 vs 5 days (P < 0.001), and convalescence averaged 4 vs 6 weeks (P < 0.001). Median preoperative serum creatinine (1.0 vs 1.0 mg/dl, P = 0.52) and postoperative serum creatinine (1.1 vs 1.2 mg/dl, P = 0.65) levels were similar between the groups. No kidney was lost because of warm ischemic injury. Three patients in the laparoscopic group had a positive surgical margin compared with none in the open groups (3% vs 0%, P = 0.10). Laparoscopic NSS was associated with a higher rate of major intraoperative complications (5% vs 0%, P = 0.02). There were no significant differences in overall postoperative complications; however, renal or urological complications were more common in the laparoscopic group (11% vs 2%, P = 0.01).

From this study, we concluded that open surgical partial nephrectomy remains the established standard for nephron-sparing treatment of renal tumors. When applied to small renal tumors, the laparoscopic approach, however, is associated with longer warm ischemic time, more major intraoperative complications, and more postoperative urological complications. Our data also suggest that more deliberate efforts to obtain a wider surgical margin are necessary with the laparoscopic approach. Nevertheless, our data show that laparoscopic NSS is emerging as an effective minimally invasive therapeutic approach with respect to renal functional outcome, with additional advantages of reduced postoperative narcotic use, earlier hospital discharge, and a faster convalescence. Continued efforts are required to develop laparoscopic renal hypothermia techniques and to facilitate intrarenal suturing while minimizing the warm ischemia time.

OPEN DISCUSSION

Dr. W. Marston Linehan: What is your thinking about where we are today with cryotherapy? Is it your opinion that cryotherapy is conventional therapy or it should only be done in a controlled setting? Take, for example, type 2 papillary carcinomas. If we start doing cryotherapy or radiofrequency ablation on these, not knowing the histology, I would start to get a little nervous.

Dr. Andrew Novick: I am deeply concerned about the manner in which these new technologies are being implemented across the world. As far as I am concerned, the gold standard of treatment for localized renal cell carcinoma is surgical excision with either total or partial nephrectomy with a margin of normal tissue. These ablative approaches are very intriguing, but they are all biologically unproven. They are developmental and should only be applied in settings where they pose the smallest risk for the patient.

Dr. Michael Atkins: Do you think that there is a need to know the pathology before planning these types of surgeries?

Dr. Novick: There’s a great need to know that information. Even in the most favorable group for partial nephrectomy, patients with a single tumor smaller than 4 cm. We have some local recurrences. We have some patients who develop metastatic disease, even in that favorable group. We know from our data of several hundred patients that if you take 100 patients with small renal cell cancer, 90% of them will have low-grade, low-stage tumors. But there is a 10% subset that will be grade 3 or 4 that may have T3a or T3b disease. Some time ago we used fine needle aspiration biopsies and cytomorphologies on small tumors to see if we could identify the grade, and we looked at other biological markers. It doesn’t work. It is a hit-or-miss technique, and you miss the tumor as often as you get it.

Dr. Atkins: Are you doing frozen sections on the tissue that comes out and potentially converting a laparoscopic approach to an open approach?

Dr. Novick: We do a frozen section, but at that point the operation is done, and we don’t change the procedure.

Dr. Tim Eisen: As a nonsurgeon, in a partial nephrectomy, how do you estimate what a safe margin of normal tissue is?

Dr. Novick: The surgical adage used to be that you need to have a 1-cm margin of normal tissue around the tumor. We’ve looked at this and there needs to be a margin of normal tissue all around the tumor, but the width of the margin is not relevant. When we’ve looked at our long-term results, patients with a 1-mm margin do as well as those with a 1-cm margin. The important point is to be sure that you have a margin of normal tissue. It doesn’t matter how large it is. We use three-dimensional CT scanning to visualize exactly where the tumor is, and I try to take a margin of 3 to 4 mm. If it ends up being 1.5 mm in a couple of locations, that’s fine.

Dr. Linehan: In the patient who has a high-grade tumor, some recommend taking out the whole kidney to avoid recurrence.

Dr. Novick: Maybe local recurrence isn’t the only issue with a high-grade tumor. When we do a partial nephrectomy, we are manipulating the whole kidney and the tumor much more with blood supply intact than when we do a radical nephrectomy. When we do a radical nephrectomy, we clamp the artery and the vein before we do anything. Maybe that added manipulation is promoting dissemination of cancer cells.

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