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REVIEW ARTICLE

Laparoscopic Partial Nephrectomy: Expanding Role in the Treatment of Localized Renal Cell Carcinoma

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ABSTRACT

Context: The increasing incidence of localized renal cell carcinoma (RCC) over the last three decades have been well evident and have called for different treatment modalities among which laparoscopic partial nephrectomy has evolved.

Objective: To review the development, techniques, outcomes and current status of laparoscopic partial nephrectomy for the treatment of renal tumors.

Materials and methods: A literature search of English-language publications was performed using the Medline database and website PubMed. Many papers were identified of which 64 papers were selected for review based on their contribution and relevance.

Conclusion: Laparoscopic partial nephrectomy provides perioperative results as well as intermediate and long-term oncologic and functional outcomes comparable with the reference standard (open partial nephrectomy) with significantly decreased patient morbidity. Today, the indications for laparoscopic partial nephrectomy have expanded to include larger, more complex and higher-stage tumors.

Keywords: Laparoscopic partial nephrectomy, Localized renal cell carcinoma, Partial nephrectomy, Nephron-sparing surgery.

INTRODUCTION

Renal cell carcinoma (RCC) accounts for nearly 3% of all adult malignancies. The incidence of renal cell carcinoma (RCC) has increased steadily between 1975 and 2002.[1,2] Incidence has increased most rapidly for localized tumors, probably because of improved noninvasive diagnostic imaging.[1] From 1988 to 2002, the average renal tumor size decreased from 67 to 59 mm, according to an analysis of data from the surveillance, epidemiology and end results (SEER) database. Analysis of a large European cohort showed that the general incidence of surgically removed renal cancers increased from 6.2 to 7.5 per 100,000 patients, the incidence of T1 tumors increased from 36.6 to 44.2% and advanced tumors decreased from 46.4 to 33.7% during the period 1995 to 2005.[3] The number of patients presenting with tumors < 4 cm increased from 30 to 39%. Improved survival in more recently diagnosed patients could be attributed to these trends.[2] Incidentally diagnosed small (≤ 4 cm) renal masses are currently the most commonly encountered renal tumors in urologic practice.[1] This has lead to an increased incidence of asymptomatic organ-confined small renal masses (SRMs).[1] A SRM is generally defined as a contrast-enhancing mass within the kidney with the largest dimension ≤ 4 cm.[4]

Although there is controversy on the mortality rate of RCC, cancer statistics shows that mortality rates are decreasing (38% in 1997 *vs* 25% in 2007).[5]

The current standard of care for clinically localized RCC is surgical, preferably with nephron-sparing surgery (NSS) because of the reported excellent oncologic outcome and overall survival. Active surveillance and minimally invasive ablative technologies have emerged as potential alternatives to surgery in selected patients.[6]

DISCUSSION

Active surveillance is considered an appropriate strategy for elderly patients or patients with significant comorbidities who are not good surgical candidates.[7,8] Gill et al recently suggested that active surveillance also seems a reasonable option for masses ≤ 1 cm in diameter, regardless of the patient's life expectancy.[4] Surveillance is currently not recommended in fit and young patients.[9] Surveillance requires excellent patient compliance and rigorous follow-up with contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI).

Energy ablative therapies for localized renal cell carcinoma, cryosurgery and radiofrequency ablation (RFA) by open, laparoscopic or percutaneous approaches are promising minimally invasive nephron-sparing treatment options for localized RCC for most small (mainly < 3.0 cm) low-grade renal tumors in patients who are at high surgical risk. Potential advantages of ablative procedures are reduced morbidity, shorter hospitalization, faster convalescence, preservation of renal function, lower costs, and the ability to treat patients who are at high-risk for surgery, but a primary concern is the higher local recurrence rate with cryoablation and RFA when compared with surgical excision.[11] A second concern is the controversy over the validity of the radiographic definition of postablative success.[12] Another weakness is the absence of histopathologic

confirmation of complete tumor destruction and negative surgical margins.[13] Finally, ablative procedures may preclude or complicate subsequent surgical salvage due to perinephric fibrosis.[13]

Other minimally invasive techniques, such as high-intensity focused ultrasound (HIFU), radiosurgical ablation (CyberKnife), microwave thermotherapy, laser ablation and pulsed-cavitational ultrasound should be considered experimental and pending to determine their oncologic and functional role in the management of localized RCC.

Radical nephrectomy has been the traditional approach for localized RCC in patients with a normal contralateral kidney. During the last decade, the status of radical nephrectomy has been questioned because of several factors including: (1) Equal oncologic efficacy as partial nephrectomy for renal tumors < 4 cm,[14,15] and tumors between 4 and 7 cm,[16,17] (2) increased incidental detection of SRMs (< 4 cm) with a significant proportion of benign tumors (up to 20%),[18] (3) possibility of late recurrence of RCC in the contralateral kidney, and (4) a higher risk of new-onset chronic kidney disease or worsening of chronic kidney disease following RN that leads to more cardiovascular events and worse survival.[19-22] Radical nephrectomy might no longer be regarded as the gold standard treatment for SRMs and should be reserved for patients with massive renal tumors in whom partial PN is not an option.[19]

Partial nephrectomy has the advantages of preservation of renal function, a reduced risk of chronic kidney disease and avoidance of overtreatment of benign renal masses by nephrectomy and better quality of life than after radical nephrectomy.[23] A significant concern with the use of partial nephrectomy for RCC is the potential risk of local recurrence in the ipsilateral kidney due to incomplete resection, but there are reports demonstrating low rates of recurrence following partial nephrectomy particularly when performed for tumors < 4 cm.[24] Many so-called local recurrences are not due to incomplete removal but are rather *de novo* tumors, such as multifocal papillary RCC. A second concern is the occurrence of positive surgical margins. It has been shown that a normal tissue margin of just 1 mm when performing partial nephrectomy may be sufficient to prevent local recurrence and disease progression from RCC.[24] During the last decade elective partial nephrectomy has become the gold standard for the treatment of T1a tumors (< 4 cm) in patients with a normal contralateral kidney.[15] When partial nephrectomy is performed in carefully selected patients in specialized centers, indications can be expanded to include, T1b tumors (4-7 cm).[13,16,17,25-33] Recently, a study revealed that partial nephrectomy can be safely performed and provide effective tumor control for selected patients with renal tumors ≥ 7 cm.[34]

Laparoscopic partial nephrectomy was first performed transperitoneally by Winfield et al[35] and retroperitoneally by Gill et al.[36] Advances in laparoscopic skills made it possible to transfer the techniques of open partial nephrectomy to laparoscopic partial nephrectomy to treat SRMs laparoscopically. In selected centers, laparoscopic partial nephrectomy today is an established alternative treatment for T1a tumors.[37] Laparoscopic partial nephrectomy can be performed retroperitoneoscopically or preferentially and transperitoneally. The choice of approach is based on the tumor location and size as well as the experience of the surgeon.[38,39] Ng et al compared transperitoneal and retroperitoneal laparoscopic partial nephrectomy and observed similar results in terms of analgesic use, blood loss and perioperative complications.[40] Laparoscopic partial nephrectomy has the advantages of reduced operative time, decreased operative blood loss and a shorter hospital stay compared with open partial nephrectomy,[41] but laparoscopic partial nephrectomy is technically demanding, and longer ischemic time and hemostasis concerns remain.

In a recent multicenter study, Gill et al compared the most recent 1039 patients undergoing open partial nephrectomy with the very initial 771 patients undergoing laparoscopic partial nephrectomy for a single renal tumor < 7 cm.[41] Postoperative renal function was similar (97.9% *vs* 99.6% functioning renal units after 3 months), but urologic complications were more common in the laparoscopic partial nephrectomy group [odds ratio (OR): 2.14; 95% CI, 1.39-3.31]. For postoperative hemorrhage, the OR was 3.51 (95% CI, 1.82-6.77), favoring the open partial nephrectomy group. However, equivalent functional and early oncologic outcomes were achieved.

In their retrospective analysis, Simmons et al evaluated the use of laparoscopic partial nephrectomy for tumors > 4 cm in size (n = 58).[42] There were no increased risks for positive margins or intraoperative or postoperative genitourinary complications for tumors > 4 cm when compared with two groups—one with tumor size < 2 cm (n = 89) and the other with tumor size 2 to 4 cm (n = 278).

The initial laparoscopic partial nephrectomy data indicated somewhat longer ischemia times compared with open partial nephrectomy. However, the increasing experience with laparoscopic partial nephrectomy and the development of an 'early unclamping' technique has significantly decreased ischemia times, allowing superior laparoscopic partial nephrectomy outcomes. Specifically, laparoscopic partial nephrectomy ischemia times have now been decreased by > 50%, to a mean of 14 minutes currently.[43-45] Most recently, Gill et al reported the initial experience of 'zero ischemia' laparoscopic partial nephrectomy, a technique that does not involve hilar clamping even for technically complex tumors. This novel technique involves two innovative concepts: (1) Anatomic microdissection to isolate and superselectively control tumor-specific tertiary or higher-order renal artery branches with neurosurgical micro-bulldog clamps and (2) adjunctive transient controlled reduction of blood pressure, if necessary.[46]

Gill et al recently reported a single-surgeon series of 800 laparoscopic partial nephrectomy cases encompassing a 9-year

period (1999-2008). The authors divided the entire cohort into three chronologic eras: Era I (1999-2003; n = 276), era II (2004-2006; n = 289) and era III (2007-2008; n = 235). In comparing eras I, II and III, tumors in the most recent era were larger (more commonly > 4 cm) and central, with peripheral masses < 4 cm less common ($p < 0.05$ for all). Despite this increasing tumor complexity, mean warm ischemia times were shorter in the most recent era: 32 minutes, 32 minutes and 14 minutes, respectively ($p < 0.0001$). Overall, postoperative and urologic complications were significantly lower in the most recent era. Finally, renal functional outcomes were superior in era III, as documented by a lesser percent decrease in estimated GFR (18%, 20% and 11% respectively).

Intermediate-term oncologic outcomes of laparoscopic partial nephrectomy are comparable with those achieved with open partial nephrectomy.[47] The rate of positive surgical margins after laparoscopic partial nephrectomy is similar to that observed with open partial nephrectomy.[48]

These contemporary data suggest that despite increasing tumor complexity, three key outcomes of contemporary laparoscopic partial nephrectomy (ischemia time, complications and renal function) have improved significantly. In experienced hands, laparoscopic partial nephrectomy now rivals open partial nephrectomy, albeit with vastly decreased patient morbidity. Laparoscopic partial nephrectomy delivers 5 and 7 years oncologic results similar to open partial nephrectomy.[49]

Absolute indications for laparoscopic partial nephrectomy include synchronous bilateral RCC, tumor in a solitary kidney or unilateral tumor with a poorly or nonfunctioning contralateral kidney, wherein radical nephrectomy would render the patient anephric.[50]

Relative indications exist where the contralateral kidney is at risk for future compromise: Hereditary RCC, genetic diseases with risk of metachronous kidney cancer, diabetes, hypertension, stone disease or renovascular disease. Elective indications for partial nephrectomy comprise renal tumors ≤ 4 cm or indeterminate cysts with malignant potential in the presence of a normal contralateral kidney.[50]

Increasing experience and advances in laparoscopic techniques have led to refinements in renal hilar control, tumor excision, pelvicaliceal repair and hemostatic reconstruction of the parenchymal defect.[51,52] With increasing experience, these indications have been extended to include tumors infiltrating well into the renal sinus, completely intrarenal tumors, hilar tumors, tumors in a solitary kidney, large tumors and tumors in the presence of renovascular disease.[53-57]

Current contraindications for LPN include a completely central intrarenal tumor, tumors with a caval thrombus and prior open kidney surgery. Morbid obesity and the presence of more than two tumors increase the technical difficulty of laparoscopic partial nephrectomy. Patients with a coagulopathy and platelet dysfunction must be approached with caution.[50]

In their first 200 laparoscopic partial nephrectomies, Ramani et al reported perioperative complications in 66 patients (33%).[58] Open conversion was required in two patients (1%). Reoperative laparotomy was necessary in four patients (2%). Overall, hemorrhagic complications occurred in 19 patients (9.5%). Urine leak occurred in nine patients (4.5%). Other urologic and nonurologic complications occurred in 4.5 and 15% respectively.

Presence of a solitary kidney, prolonged warm ischemia time, and increased intraoperative blood loss were found to be independent risk factors on multivariate analysis for the development of postoperative complications after laparoscopic partial nephrectomy.[59]

Robot-assisted partial nephrectomy allows magnified stereoscopic visualization and the use of articulated robotic instruments under precise control; reducing the technical challenges associated with tumor dissection and parenchymal reconstruction during laparoscopic partial nephrectomy. Although the first experiences of robot-assisted partial nephrectomy are encouraging, oncologic outcomes are still immature and larger series with longer follow-up are awaited to confirm the preliminary results.[60-62]

Renal biopsy; the impact of renal biopsy on treatment of small renal lesions is still controversial. Renal biopsy is only useful if the result will change the course of treatment. Because small, incidentally discovered renal lesions may be benign in a substantial percentage of patients, biopsy to confirm malignancy is important either prior to or at the time of utilization of minimally invasive ablation techniques.

In summary, the literature shows that biopsy of renal masses can provide an accurate differentiation between malignant and benign tissue in > 90% of cases. The rate of inconclusive biopsies ranges from 3 to 20%. Significant bleeding is unusual, and most biopsies are performed under CT guidance. Limitations of biopsy are hybrid tumors and cystic tumors where malignant tissue is hit by chance. Larger tumor size (< 4 cm) and a solid pattern are significant predictors of a diagnostic result for biopsies of renal tumors.[63] Tumor seeding after renal biopsy has a low incidence with overall estimated risk < 0.01%.[64] Accuracy and standardization of criteria for renal biopsy have to be further investigated, especially for nondiagnostic biopsies and the diagnosis of benign tumors.

Nearly 20 to 30% of all renal tumors that are subjected to NSS are actually benign on final histopathology. These patients could potentially avoid an operation and its associated morbidity if we had a consistent method to discriminate benign from malignant masses preoperatively. Optical coherence tomography (OCT) has been shown to provide an optical biopsy of tissues in various nonurologic fields. However, its potential application in the setting of laparoscopic partial nephrectomy is not currently clear.[50]

CONCLUSION

An increasing number of SRMs today are detected in asymptomatic patients by noninvasive abdominal imaging. Surgical removal is the standard of care for small renal tumors.

The choice of treatment for the patient with localized RCC needs to be individualized. Preservation of renal function without compromising the oncologic outcome should be the most important goal in the decision-making process.

Laparoscopic partial nephrectomy is technically challenging and requires advanced, time-sensitive laparoscopic skills. In experienced hands indications for LPN have expanded significantly and current emerging data indicate that in experienced hands, laparoscopic partial nephrectomy has shorter ischemia times, a lower complication rate, and equivalent long-term oncologic and renal functional outcomes, yet with decreased patient morbidity compared with open partial nephrectomy. Robotic partial nephrectomy is being explored at selected centers, and cryotherapy and radiofrequency ablation are options for carefully selected tumors. Active surveillance is an option for selected high-risk patients. Percutaneous needle biopsy is likely to gain increasing relevance in the management of small renal tumors.

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