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Laparoscopic Surgery in Urological Oncology: Brief Overview

Jose R. Colombo Jr, Georges P. Haber, Mauricio Rubinstein, Inderbir S. Gill

Section of Laparoscopic and Robotic Surgery, Glickman Urological Institute, The Cleveland Clinic Foundation, Cleveland, Ohio, USA

ABSTRACT

The authors report the experience of a high-volume center with laparoscopic surgery in urological oncology, as well as a review of other relevant series. Laparoscopic outcomes in the treatment of adrenal, kidney, upper tract transitional cell carcinoma, bladder, prostate, and testicular malignancy are described in this review. Specific considerations as complications and port-site recurrence are also addressed. The authors concluded that the intermediate-term oncological data is encouraging and comparable to open surgery.

Key words*: urological neoplasms; treatment; laparoscopic surgery; complications*
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INTRODUCTION

Initially described for the treatment of kidney cancer (1), laparoscopic approach has rapidly evolved in the urological oncologic field. This relatively new surgical technique is part of the urologist's armamentarium in treating adrenal, upper tract transitional cell carcinoma, bladder, prostate, and testicular malignancy. The laparoscopic technique duplicates open surgery oncological principles, associating the benefits of minimally invasive approach. Herein, the authors present their experience in laparoscopic surgery for urological cancer at The Cleveland Clinic, and review other relevant series.

KIDNEY CANCER

Laparoscopic radical nephrectomy (LRN) is considered the standard treatment for most patients with renal malignancies that are not eligible to nephron-sparing surgery. Major advantages of LRN over open radical nephrectomy include decreased perioperative morbidity, lower blood loss, shorter hospital stay, and quicker convalescence (2,3). Reports available in literature have showed comparable results between laparoscopic and open radical nephrectomy, with projected 5-year cancer-specific survival of 87% to 98% in the laparoscopic series, and overall survival of 81% to 94% (4-8) (Table-1). In 63 consecutive patients undergoing LRN at our institution, estimated 7-year overall and cancer-specific survival was 72% and 90%, similarly to a contemporary series of open radical nephrectomy.(9) For T1 tumors (≤ 7 cm) the estimated 7-year cancer-specific survival in the laparoscopic group was 97% vs. 96% in the open group ($p = 0.84$), and for T2 tumors (> 7 cm) the estimated 7-year cancer-specific survival in the laparoscopic group was 66% vs. 87% in the open group ($p = 0.26$). No contralateral

Table 1 – *Laparoscopic radical nephrectomy oncological outcomes.*

Author	N	Follow-up (years)	Blood Loss (mL)	Operative Time (hours)	Hospital Stay (days)	Estimated 5-year Cancer-Specific Survival
Dunn et al. 2000 (3)	44	2.1	N/A	5.5	3.4	91%
Chan et al. 2001 (4)	66	2.9	280	4.2	3.8	95%
Ono et al. 2001 (5)	102	2.4	254	4.7	N/A	95%
Portis et al. 2002 (6)	64	4.5	219	N/A	4.8	98%
Saika et al. 2003 (7)	195	3.3	248	4.6	N/A	87%
Permpongkosol et al. 2005 (8)	121	6	280	4.2	3.8	94%*
Colombo et al. 2006 (9)	48	5.4	179	2.8	1.4	91%*

*Adapted from Colombo et al. (9); * actual 5-year survival; N/A: not available.*

recurrence was found during the follow-up in this series, this is likely due to the relative small number of patients, low positive margin rate, and small incidence of multifocality. Renal function in this series, decreased significantly after radical nephrectomy; however, this was not affected by the surgical approach.

Retroperitoneal is our preferred access, except in cases of larger tumors (> 10 cm) and previous retroperitoneal surgery. Prospective randomized studies comparing the transperitoneal and retroperitoneal approaches concluded that there is no statistical difference between the techniques (10,11).

For appropriate histopathological analysis, the specimen is always extracted intact in an adequate laparoscopic bag. Financial analysis performed at our institution concluded that laparoscopic radical nephrectomy is 12% less expensive than open radical nephrectomy once the learning curve is reached (12).

In patients with metastatic renal cell carcinoma, the laparoscopic cytoreductive nephrectomy can be performed with low morbidity, smaller blood loss, and shorter hospital stay. The minimally invasive technique may shorten the interval between the nephrectomy and start of systemic therapy (13).

Partial nephrectomy for renal cancer was initially indicated for patients with compromised renal function, solitary kidney, and bilateral tumor. Since, long-term oncological outcomes haven been demonstrated as equivalent to radical nephrectomy while preserving renal function (14), indications of partial nephrectomy has expanded to patients with normal contralateral kidney. Laparoscopic partial nephrectomy (LPN) has emerged as a minimally invasive alternative to partial nephrectomy in order to minimize the morbidity of the open procedure (15). LPN was limited to patients with small, superficial, solitary, and peripheral tumors. With increasing experience, LPN is now performed for larger, central and hilar tumors. In our study with 100 patients, each with at least 3-years follow-up, overall survival was 86% and cancer-specific survival was 100% (16). Fifty of these patients, have reached 5-years follow-up, with overall and cancer-specific survival of 84% and 100%, respectively (17) (Table-2). Hilar clamping is used to provide a bloodless field during tumor excision and pelvicaliceal repair. The impact of hilar clamping was evaluated and no clinical sequelae were observed with warm ischemia smaller than 30 minutes (18). Similar perioperative complication rate was found after LPN in patients with abnormal renal function (serum creatinine ≥ 1.5 mg/dL comparing to patients with normal renal function (19). While comparing the percentage decreasing in renal function, evaluated by serum creatinine and glomerular filtration rate, there was no significant difference between patients with abnormal and normal renal function. In this study, solitary kidney was an independent risk factor for hemodialysis.

***Table 2** – Partial nephrectomy series oncological outcomes.*

Author	N	Approach	Follow-up (months)	Tumor Size (cm)	Overall Survival	Cancer-Specific Survival
Lerner et al. 1996	185	Open	44	4.1	77%	89%
Belldegrun et al. 1999	146	Open	57	3.6	86%	93%
Hafez et al. 1999	485	Open	47	2.7	81%	92%
Moinzadeh et al. 2006 (16)	100	Laparoscopic	42	3.1	86%	100%
Lane & Gill 2006 (17)	50	Laparoscopic	62	3.0	84%	100%

Adapted from Lane & Gill (17).

ADRENAL CANCER

Although laparoscopic approach has become the gold standard for benign surgical adrenal disorders such as Cushing's disease, aldosteronoma, and pheochromocytoma, only few reports addressing laparoscopic surgery for adrenal malignancy are available. In our institution more than 330 laparoscopic adrenalectomies were performed. Our experience with 31 patients with adrenal malignancy showed an estimated 5-year survival of 40%. In this study, local recurrence occurred in 7 patients (23%), and these patients had significantly decreased 3-year survival compared to those without local recurrence (16.7% vs. 66%, p = 0.016). The survival rate was not associated with gender, age, tumor size, or laparoscopic approach employed. There was no difference in survival for patients with solitary metastasis to the gland compared to those with primary adrenal malignancy. In this series, the 5-year survival was similar in patients with an adrenal tumor smaller than 5 cm vs. 5 cm or greater (36% vs. 46%, p = 0.43) (20). These results can be favorably compared to those in a prior open series with 37 patients undergoing open adrenalectomy for non-primary adrenal malignancy, with a 5-year actuarial survival of 24% (21). The suspicion of peri-adrenal infiltration is a contraindication for laparoscopic adrenalectomy. Tumor size per se is not a contraindication, although we generally limit laparoscopic adrenalectomy to tumors in the 10 cm range. Intraoperative concern regarding the adequacy of wide excision should lead to open conversion.

BLADDER CANCER

Radical cystectomy is the gold-standard treatment for organ confined muscle invasive or high-grade superficial recurrent bladder cancer (22). Laparoscopic approach for radical cystectomy is relatively new, and studies available in the literature show encouraging perioperative and short-term oncological data. Urinary diversion can be performed either intracorporeally ("pure laparoscopic") or through a 5-7 cm mini-laparotomy incision ("laparoscopic assisted"). A series with 37 patients undergoing laparoscopic radical cystectomy in our institution with a mean follow-up of 31 months (1-66 months) showed an estimated 5-year overall and cancer-specific survival of 58% and, 68%, respectively (23). Both overall and cancer-specific survivals were superior in organ confined vs. non-organ confined disease and node-negative vs. node-positive disease. Overall survival was superior when an extended lymphadenectomy (median number of nodes = 21) is performed, compared to patients undergoing limited template lymphadenectomy (median number of nodes = 6). Cancer-specific survival trended towards to a slightly improvement; however, this did not reach statistical significance, likely due to smaller number of patients (Table-3). When comparing "pure laparoscopic" technique to "laparoscopic-assisted" technique we found that the morbidity of laparoscopic radical cystectomy is largely due to the urinary diversion procedure. Our data support the extracorporeal performance of the bowel work and ureteroileal anastomoses.

Table 3 – *Sub-group analysis of overall and cancer-specific survival in 37 patients undergoing laparoscopic radical cystectomy.*

Final Pathology	N	Mean Follow-up (months)	Overall Survival	Cancer Specific Survival
pT1	11	27	61%	100%
pT2	12	36	91%	100%
pT3	10	29	45%	85%
pT4	4	28	25%	66%
p Value			0.08	0.21
Organ confined	23	32	77%	100%
Non-organ confined	14	28	31%	76%
p Value			0.01	0.03
Concomitant CIS	8	25	41%	55%
No CIS	24	33	81%	100%
p Value			0.03	0.002
pN0	30	32	74%	100%
pN1	7	27	25%	33%
p Value			0.02	0.002

Adapted from Haber & Gill (23); CIS = carcinoma in situ.

Laparoscopic-assisted radical cystectomy is technically more efficient, associated with a quicker recovery profile, and decreased complication rate (24) (Table-4).

PROSTATE CANCER

Radical prostatectomy has been shown to improve cancer-specific survival in the context of a randomized trial (25). The laparoscopic approach offers the advantage of magnification of the surgical field, allowing a clear operative field with better view during the dissection of the neuro-vascular bundles and urethro-vesical anastomosis. Transrectal real-time Doppler ultrasound is routinely performed in our institution during the procedure to identify the neuro-vascular bundle and the prostatic edges. This technique decreased significantly the overall positive margin rate (29% vs. 9%, $p < 0.001$), and predicted the presence of pT_2 and pT_3 disease in 85% and 85% of cases, respectively (26). In a series of 1000 laparoscopic radical prostatectomies published by Guillonneau et al. (27), the positive margin rate was 6.9%, 18.6%, 30% and 34% for pT2a, pT2b, pT3a, and pT3b, respectively. Overall 3-year biochemical progression-free survival was 90.5%, ranging from 44% to 91% according to the pathological stage. Rassweiler et al. (28) published their early 180-case experience with 16% of positive margins, and 95%biochemical progression-free survival. Early oncological results of laparoscopic radical prostatectomy are comparable to the open approach, but studies with long-term follow-up are still lacking.

Salomon et al. (29) reported a potency and continence rate of 59% and 90%, while. Guillonneau et al. (30) reported a potency and continence rate of 85%, and 82% after a period of 12 months (Table-5).

Table 4 – *Laparoscopic radical cystectomy with urinary diversion. Pure laparoscopic vs. laparoscopic assisted.*

Urinary Diversion	Pure Laparoscopic	Laparoscopic Assisted	p Value
Number	17	20	
Operative time (hours)	9.38	7.35	< 0.001
Blood Loss (cc)	788	472	0.01
Transfusion	4	1	0.10
Oral Intake (days)	6	2.8	0.01
Ambulation (days)	16.8	2.46	0.02
Major complications	29.4%	5%	0.04
Late complications	17.6%	20%	0.86

Adapted for Haber et al. (24)

UROTHELIAL CANCER

Laparoscopic nephroureterectomy with en bloc bladder cuff for upper tract urothelial carcinoma appears to have similar oncological outcomes comparing to open nephroureterectomy, regarding positive margin rate, and bladder, local and distant recurrences (31). Operative time and perioperative complication rate are equivalent, with less blood loss, less analgesic use, and shorter hospitalization, avoiding the usual two incisions of the open nephroureterectomy (31,32). At least five methods for controlling the distal ureter and bladder cuff were described, including endoscopic, laparoscopic and open. The most commonly used is the open technique, through a low Gibson incision. This method avoids patient repositioning, minimizing tumor spillage with ureteral clipping early in the procedure, right after renal hilum control. To decrease the presence of ureteric stump, it is recommended to dissect laterally to the bladder until visualization of the ureteral hiatus, performing the resection of bladder cuff under direct vision (32).

Matin & Gill (33) reported a different recurrence and survival rates related to the surgical technique employed to control the distal ureter and bladder cuff. The cystoscopic detachment and ligation of the bladder cuff was significantly associated to a better survival when compared to the laparoscopic extravesical stapling with cystoscopic deroofing and fulguration of the intramural ureter.

In a multicenter study with 116 patients undergoing laparoscopic nephroureterectomy for upper tract transitional cell carcinoma, the mid-term results were comparable to the open series (34). The 2-year overall survival according to the pathologic

Table 5 – *Laparoscopic radical prostatectomy series oncological outcomes.*

Author	N	Gleason Score	PSA (ng/mL)	Positive Margins		Biochemical Progression-Free			
				pT2	pT3	pT2a	pT2b	pT3a	pT3b
Guillonneau et al. 2003 (27)	1000	N/A	10	6-18%	30-34%	91.8%	88%	77%	44%
Rassweiler et al. 2005 (28)	500	6	11.7	7.4%	31.8%	95.9%		88%	
Solomon et al. 2002 (29)	137	5.7	11.6	21.9%	40.8%	90.4%		56.8%	

N/A: not available.

grade was 88%, 90%, 80% and 90% for grade I, II, III, IV, respectively. The 2-year cancer-specific survival was 89% for pT1, 86% for pT2, 77% for pT3, and 0% for pT4. Although long-tem follow-up data is not available yet, the mid-term data support the use of minimally invasive technique to treat upper tract transitional cell carcinoma.

TESTICULAR CANCER

When indicated, standardized retroperitoneal lymph node dissection (RPLND) can be performed for Stage I and low-volume Stage II disease using laparoscopic access, even after chemotherapy. Both staging and therapeutic techniques are currently performed with minimal morbidity (35,36). The long-term results reported by Steiner et al. (36) are similar to the open series. In this study, the antegrade ejaculation was preserved in 98% of patients, with significantly lower morbidity.

RPLND after chemotherapy represents a technical challenge. The complication rate for this procedure is still high, and it should be performed by only very experienced laparoscopic surgeons (37). Janetschek et al. described their experience with 35 patients undergoing postchemotherapy laparoscopic RPLND, with chylous ascites occurring in 6 cases. In their institution, a preoperative low-fat diet is now used 1 week before and 2 weeks after the surgery (38).

CONSIDERATIONS

Perioperative Complications

Analyzing 1867 laparoscopic procedures for urological malignancy at our institution, the perioperative complication rate was 12.3% (95% CI 10.9 to 13.8) (39). Intraoperative complications occurred in 4.9% (95% CI 4.0 to 6.0), including hemorrhage (3.6%), and visceral injury (1.2%). Because of these complications, 18 (0.9%) cases were converted to open procedure. Postoperative complications have been noted in 162 (8.6%) cases, and the most common were hemorrhage in 52 (2.7%), acute renal failure in 16 (0.8%), and pneumonia, pulmonary embolism, pulmonary edema, atrial fibrillation in 7 (0.3%) cases each. Perioperative mortality occurred in 8 cases (0.4%). Radical cystectomy (adj. OR 4.9, 95% CI 1.3 to 8.0; $p < 0.001$), length of surgery greater than four hours (adj. OR 2.5, 95% CI 1.7 to 3.8; $p < 0.001$), partial nephrectomy (adj. OR 2.4, 95% CI 1.5 to 3.8; $p < 0.001$), and serum creatinine ≥ 1.5 mg/dL (adj. OR 2.1, 95% CI 1.0 to 4.3; $p = 0.04$) were found as independent predictors for perioperative complication. The length of hospitalization increased directly proportional to the number of complications ($p < 0.001$).

Literature supports the importance of experience of the surgeon and hospital-volume in the treatment of cancer. Begg et al. (40) found that perioperative mortality in complex open oncologic procedures is lower when performed by surgical team with higher volume. In study addressing exclusively open radical prostatectomy (41), the same author concluded that postoperative complication rate is significantly reduced when the operation is performed in a high-volume hospital and by an experienced surgeon. In our study, surgeon's experience was not an independent predictor for perioperative complication ($p = 0.07$), although we identified a trend pointing to it. After 50 cases of laparoscopic surgeries for urological malignancy the adjusted odds ratio was 0.97. When increasing this experience to 100 cases and 500 cases, the odds ratio were 0.96 and 0.80, respectively. We believe that multicentric studies with a larger number of procedures would show the same result for laparoscopic procedures as well.

Port-Site Recurrence

Port site metastasis, intraperitoneal dissemination, and local recurrence represent a major concern when laparoscopic approach is employed. Port-site recurrence is influenced by local and systemic immunological status, tumor behavior and technical factors (42). Activation of cytokines (IL-1 and IL-6), C-reactive protein, and polymorphonuclear leukocytes occur in a smaller level after a laparoscopic procedure compared to similar open procedure (42,43). Some studies showed a better preservation

of cell-mediated immunity after laparoscopic surgery (44,45). However, these benefits are not applied to the peritoneal level, possibly related to the hypoxic environment due to pneumoperitoneum pressure and secondary effect of the carbon dioxide in the peritoneal macrophage response (35-37).

In a series with over 1000 laparoscopic cases, Rassweiler et al. (42) found eight cases of local recurrence and 2 port sites metastasis. In the multicentric study by Micali et al. (46) with 10912 laparoscopic surgeries for cancer, 10 cases of port seeding, and 3 cases of peritoneal tumor spreading were found. Aggressiveness of tumor, deficient immunological state of the oncological patient, and poor oncological principles related to specimen extraction are responsible for these rare events (42,46).

In attempting to minimize the risks for port-site and local recurrence, tumor violation and spillage should be avoided by using the appropriated surgical technique, including the use of impermeable bags during specimen extraction, and removal of tumor-contaminated instruments from the operative field after the target-organ entrapment.

CONCLUSION

Although long-term oncological outcomes are not available for the majority of genitourinary malignancies treated by the laparoscopic approach, the intermediate-term data are encouraging and comparable to open surgery. Multicentric studies with longer follow-up are necessary to validate this relatively new surgical approach.

CONFLICT OF INTEREST

None declared.

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Correspondence address:
Dr. Inderbir S. Gill
Section of Laparoscopic and Robotic Surgery
The Cleveland Clinic Foundation
9500 Euclid Av, A100
Cleveland, OH 44195, USA
Fax: +1 216 445-7031
E-mail: gilli@ccf.org