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Feasibility and Adequacy of Robot-Assisted Lymphadenectomy for Renal-Cell Carcinoma

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Abstract

Background and Purpose: The role of lymph node dissection (LND) for renal-cell carcinoma (RCC) is evolving. When clinically negative, nodal disease is rare, but LND remains important in selected patients. Earlier identification of micrometastasis may become beneficial with emerging systemic agents. The ability to perform an adequate LND laparoscopically is uncertain. Open surgical data suggest a minimum of 12 nodes needed to identify most nodal metastases. Robotics may improve adequacy of laparoscopic LND. We report our results with the first reported robot-assisted LND series for RCC.

Patients and Methods: Robot-assisted LND was performed in 36 patients with RCC by a single surgeon. For right-sided tumors, LND included paracaval, retrocaval, and interaortocaval nodes, and left-sided tumors included interaortocaval and periaortic nodes.

Results: Mean patient age was 58 years (22–79) with a mean body mass index of 32 kg/m^2 (20–54). Mean tumor size was 7.3 cm with 16 T_3 tumors, including 4 vena caval tumor thrombi. Mean time for LND was 31 minutes, and mean estimated blood loss was 74 mL with no transfusions. Discharge was postoperative day (POD) 1 in 94% and POD 2 in 6%. A mean of 13.9 nodes was obtained with 1 pN+ (2.8%) patient. Mean nodal yield from the first to second half of cases rose from 11 to 16.8 nodes ($P = 0.02$) with 77% having a minimum of 12 nodes in the second half.

Conclusions: Robot-assisted LND for RCC is feasible with adequate nodal yield. Increased yield in later cases may reflect a learning curve. The positivity rate was low as expected, but higher yield was obtained than in the limited laparoscopic literature.

Introduction

The role of lymph node dissection (LND) for renal-cell carcinoma (RCC) is controversial, with patient selection, benefit, and ideal extent of dissection all open to debate. There is no doubt that LND provides significant prognostic information when nodal positivity is identified,[1] but the expected rate of node positivity ranges widely between 5% and 38%,[2] likely because of variations in patient selection and variations in templates and techniques.

While the absence of a survival advantage in the largest randomized trial of LND for RCC to date (EORTC 30881) would argue against performing LND in all patients because of an only 3% rate of positivity that was identified in the studied population, which comprised mostly low-risk patients,[3] it cannot be concluded that, consequently, LND should never be performed.[4] Despite the limitations of evidence in favor of a survival benefit for LND in selected patients,[5–9] LND still plays an important diagnostic role in higher risk patients, which may become even more compelling in the era of improved systemic therapy for RCC.

Laparoscopy has gained widespread adoption in the surgical management of RCC, but if LND has any role in RCC, laparoscopy must either allow adequate ability to perform LND or not be offered to patients in whom LND may have benefit. The ability to detect node positive disease (and therefore likely the potential therapeutic benefit of LND, if any) is correlated to the number of lymph nodes removed.[10] To date, the sparse data in the literature regarding laparoscopic LND for RCC are insufficient to demonstrate the adequacy of laparoscopy for this application. We hypothesized that robotics may improve the ability to perform an adequate LND. We report our early results with the first such reported series of robot-assisted LND for RCC.

Patients and Methods

Between May 2008 and November 2010, 36 patients underwent retroperitoneal lymphadenectomy for RCC in conjunction with radical or partial nephrectomy by a single surgeon (RA) who is experienced in robot-assisted surgery, having performed several hundred procedures and more than

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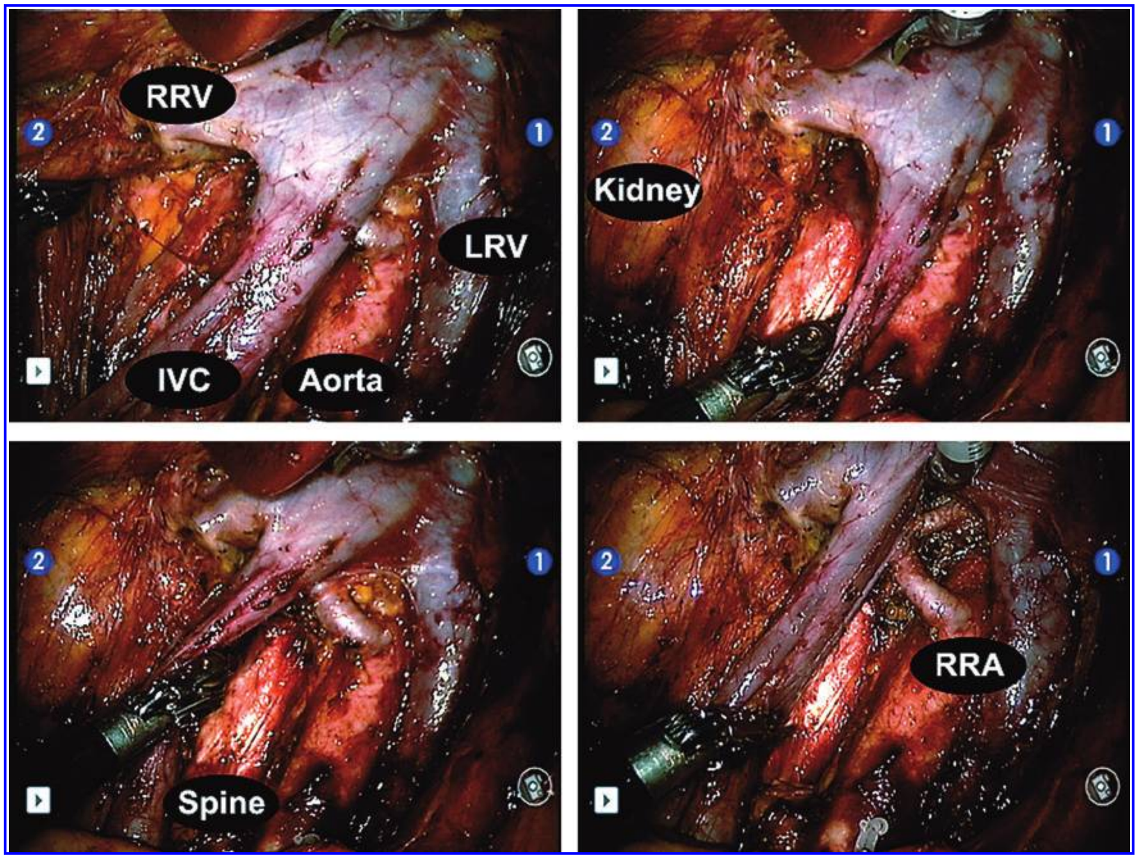

FIG. 1. Representative completed lymph node dissection after right partial nephrectomy illustrating right renal vein (RRV), left renal vein (LRV), inferior vena cava (IVC), spine visible on retraction of vena cava to both sides, and right renal artery (RRA) at the level of the aorta before crossing behind the vena cava.

100 renal procedures at inception. Preoperative, perioperative, and postoperative data were recorded prospectively with Institutional Review Board approval.

LND was performed selectively for assessment of feasibility, but all patients had tumors of at least 4 cm (including cystic RCCs), renal vein or vena caval tumor thrombus on preoperative imaging, or clinically enlarged nodes that were identified on preoperative imaging or intraoperatively. LND was omitted in patients when additional operative time was thought to be potentially harmful.

The lymphadenectomy performed in all cases included removal of all hilar nodes and nodes surrounding the ipsilateral great vessel. Therefore, for right-sided renal tumors, the LND included pericaval, retrocaval, and interaortocaval nodes (Fig. 1) and for left-sided renal tumors included preaortic, periaortic, and interaortocaval nodes.

All patients underwent mechanical bowel preparation, received enoxaparin prophylaxis immediately preoperatively, and were placed in full flank position for gravity retraction of intra-abdominal organs as routinely used by the surgeon for robot-assisted renal surgery even when LND is not performed. A periumbilical camera port site was routinely used. The robotic cautery scissors instrument and fenestrated bipolar forceps instrument were used in all LNDs using bipolar cautery to seal lymphatics and selectively placing robotic clips on larger lymphatics when deemed necessary. Lumbar vessels were managed by bipolar cautery or robotic clips or were left intact with splitting and rolling around them to keep the node packets intact for *en bloc* submission.

Nodes were extracted in one bag and submitted for pathologic evaluation as one specimen. Nodes were counted grossly in the pathology department by finger separation from fat before fixation for microscopic evaluation. No clearing techniques or solvents were used to identify lymph nodes. Microscopic evaluation on hematoxylin and eosin

Table 1. Preoperative and Intraoperative Patient Data by Primary Procedure Performed with Lymph Node Dissection

Procedure	*Radical nephrectomy (N = 33)*	*Partial nephrectomy (N = 3)*
Side renal mass L/R	14/19	0/3
BMI (kg/m^2) mean	32 (20–54)	28 (26–30)
Age (years) mean	60 (36–79)	41 (22–62)
IVC thrombus	4	0
Mean OR time (min)	203 (64–396)	231 (185–275)
Mean LND time (min)	31 (7.5–55)	32 (17–53)
EBL (mL)	67 (10–200)	133 (100–200)
No. of robotic ports used	1 to 4	3
No. of assistant ports	0 to 2	1

BMI = body mass index; IVC = inferior vena cava; OR = operative; LND = lymph node dissection; EBL = estimated blood loss.

Table 2. Postoperative Data by Primary Procedure Performed with Lymph Node Dissection

Procedure	*Radical nephrectomy (N = 33)*	*Partial nephrectomy (N = 3)*
No. clear-cell RCC	25	3
No. papillary RCC	5	0
No. chromophobe RCC	3	0
Mean largest dimension (cm)	7.7 (2.2[a]–18 cm)	3.5 (3.1[a]–4 cm)
Median Fuhrman grade	2 (1–4)	2 (1–3)
$pT_{1a}/pT_{1b}/pT_2$	5/6/6	3/0/0
pT_{3a}/pT_{3b}	10/6	0/0
Mean lymph nodes removed	13.7 (3–31)	15.3 (11–22)
No. patients with + lymph node	1 (3%)	0
Mean length of stay (d)	1.06 (1–2)	1.00 (1–1)
Mean follow-up (d)	523 (24–940)	488 (195–659)
LND complications	2 (6%)	0 (0%)

[a]All tumors >4 cm on preoperative imaging but may have been <4 cm on pathologic evaluation, particularly for primarily cystic tumors.
RCC = renal-cell carcinoma; LND = lymph node dissection.

staining by a pathologist confirmed the presence of lymphatic nodal tissue within each of the counted nodes and identified any tumor involvement. Neither pathologists nor gross room pathology staff members were aware of the study. All patients were routinely imaged with CT scanning at 6-month intervals for surveillance.

Results

A total of 33 patients underwent LND with radical nephrectomy, and 3 patients underwent LND with partial nephrectomy. Four patients had clinically enlarged nodes intraoperatively, and two had enlarged nodes on preoperative imaging. Mean patient age was 58 years (range 22–79 y) with mean body mass index of 32 kg/m^2 (range 20–54 kg/m^2) (Table 1). Mean pathologic tumor size was 7.3 cm with 16 T_3 tumors, including 4 vena caval tumor thrombi. Nineteen nephrectomies and all three partial nephrectomies were for right renal tumors.

The mean total operative time was 206 minutes (median 203 min) and was 187 minutes excluding partial nephrectomy procedures, caval thrombi, and two procedures where more than 1 hour was needed for laparoscopic lysis of adhesions. Mean and median time for the LND alone were both 31 minutes. Mean estimated blood loss for the entire procedures was 72 mL (range 10–200 mL).

No additional ports were needed for the LND over those used for the nephrectomy or partial nephrectomy. Twenty-two of 33 nephrectomy procedures were performed with three ports and no assistant port, 1 was performed as a single-incision robotic procedure, 2 added a robotic fourth arm port for caval thrombectomy, and the remaining 8 procedures had one or two assistant ports for suction or retraction. All partial nephrectomy procedures were performed with three robotic ports and one assistant port. A mean of 13.9 nodes was obtained overall with a median of 12.5 nodes (range 4–36 nodes) (Table 2). Mean nodal yield from the first 18 patients to the second half of cases rose from 11 nodes to 16.8 nodes ($P = 0.02$) with 77% of patients in the second half having a minimum of 12 nodes.

One (2.8%) patient was identified as having metastatic disease in 1 of 24 nodes and was one of the patients with caval tumor thrombus but did not have clinically enlarged nodes. Among the six patients with clinically enlarged nodes, none were found to have metastatic disease despite an average (and median) of 19 nodes removed in this group.

No patient needed blood transfusion. Discharge was POD 1 in 94% and POD 2 in 6% for a mean length of stay of 1.06 days (median 1 d). Mean follow-up after the date of surgery was 520 days (range 24–940 d). Only two complications related to the LND were identified during the follow-up period. An asymptomatic lymphocele that was found on surveillance imaging at 6 months developed in one patient, and one patient had a cautery injury to the small bowel during the LND from a defect in the insulation on the robotic scissor instrument that was repaired robotically.

Discussion

Lymphadenectomy at the time of radical or partial nephrectomy has demonstrated prognostic value,[1,2] but the therapeutic benefit remains uncertain. Evidence in favor of a therapeutic benefit is limited by small patient numbers, as would be expected given that those who would be cured by LND would be those with nodal involvement that is entirely resectable but in the absence of more distant metastasis. In his original description of LND for RCC, Robson and associates[5] reported a 35% 10-year survival in patients with nodal involvement, suggesting that LND can alter the course of pN+ patients. Similarly, Giuliani and colleagues[6] reported a 31.9% survival rate at 10 years after LND in pN+ patients without clinical evidence of metastasis. In a contemporary study of pN+ patients without clinical metastasis, Canfield and coworkers[7] reported 30% of patients without evidence of disease at a median of 17.7 months after extensive LND.

Clearly, the selected patient who stands to gain from LND and the population studied in EORTC 30881 are entirely

Table 3. Comparison of Current Series with Laparoscopic Lymph Node Dissection Experience in the Literature

Series	*Year*	*Technique*	N	*Mean no. LN (range)*	*% positive*	*Comment*
Busby[12]	2008	Lap	28	6 (1–31)	0%	LND for upper tract TCC
Chapman[13]	2008	Lap	50	7.8 (0–25)	10%	6.5% pN+ when clinically neg
Simmons[14]	2007	Lap	14	2.7 (1–9)	57%	All clinically N+ 1–2, hilar LND only
Rosoff[15]	2009	Lap	6	5 (2–10)	17%	All patients clinically N+
Current study	2011	Robotic	36	13.9 (4–36)	2.8%	6/33 clinically enlarged nodes

LN = lymph node; LND = lymph node dissection; TCC = transitional-cell carcinoma; Lap = laparoscopic.

different, because the majority of patients in this study were at low risk for nodal involvement: 70% had pT_2 or less tumors, median tumor size was 5.5 cm, and patients with clinically enlarged nodes preoperatively were excluded. There are as yet no randomized trials analyzing the therapeutic or diagnostic efficacy of LND specifically in patients at high-risk of nodal disease where such a population (one with a >3.3% incidence) might allow definitive identification of a survival advantage for LND. Nevertheless, the evidence available is adequate to justify LND in patients with locally advanced RCC, those with a radiologic or intraoperative finding of enlarged nodes, or as an adjunct to cytoreductive nephrectomy for additional debulking when possible,[2,11] and potentially in patients meeting other criteria such as tumor size >10 cm or evidence of tumor necrosis.[1]

The goal of our study was not to evaluate the therapeutic efficacy of LND, but rather to identify whether an adequate LND could be performed robotically. Given that there is a role for LND in selected patients but insufficient evidence supporting that an adequate LND can be performed with standard laparoscopy, we assessed the feasibility of a robotic approach with assessment of nodal yield as a primary end point. As a feasibility study, our patients undergoing LND had only to meet two criteria: Primary tumor >4 cm and ability to tolerate additional anesthesia time without concern. Therefore, the study group did not represent an ideal group uniformly at high risk for nodal involvement allowing study of therapeutic effect of LND. As expected, the pN+ rate among our patients was low, but the nodal yield and low complication rate achieved the intended goal.

Standardization of LND templates for RCC is lacking, but lymph node yield has been demonstrated to better identify pN+ status. Terrone and colleagues[10] reported a series of 608 LND at the time of open nephrectomy where the likelihood of detecting positive lymph nodes more than doubled when more than 12 lymph nodes were removed. The median number of nodes removed in pN+ patients was 11.5 nodes compared with 9 in pN_0 patients ($P < 0.01$).

The limited series in the literature reporting node yields with standard laparoscopy do not exceed a mean of 7.8 nodes[12–15] (Table 3). Chapman and associates[13] extended their LND template with experience in their series of 50 patients to achieve a mean of 12.1 nodes in their last 10 patients, although with chylous ascites in two patients necessitating drainage. Our nodal yield was achieved with as little potential artificial inflation possible by performing *en bloc* dissection, submission of nodes as one specimen, and blinding of pathology staff. We obtained a mean of 13.9 nodes overall, which increased to a mean of 16.8 nodes with 77% of patients having at least 12 nodes in the second half of the patient series after only 18 cases of experience. In addition, the complication profile with robot-assisted LND mirrored the relatively universal experience in open surgery of minimal morbidity or mortality associated with LND for RCC.[2]

Further investigations will be necessary to confirm our initial findings based on a small patient series as part of a feasibility study. Reproducibility by other surgeons and other institutions will be needed before definitive conclusions can be reached regarding the utility of robot assistance for LND in patients with RCC. The evolution of improved systemic therapies for RCC in an era of minimally invasive management of renal tumors may necessitate that earlier identification of micrometastatic disease through adequate LND not be sacrificed for the sake of smaller incisions, and robotic technology may eventually fill this need with further experience and study.

Conclusion

Robot assistance allows for a safe and effective LND during radical or partial nephrectomy for RCC. While positivity was low, adequate nodal yield demonstrates feasibility of the robotic approach and may allow a minimally invasive approach for patients who stand to benefit from LND but would otherwise need open surgery to accomplish it adequately.

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Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

CT = computed tomography
LND = lymph node dissection
RCC = renal-cell carcinoma