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Impact of surgeon and volume on extended lymphadenectomy at the time of robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium (IRCC)

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Conflict of Interest
Khurshid A. Guru is a Cofounder/Board member of Simulated Surgical Systems.

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Abstract

Objective—• To evaluate the incidence of, and predictors for, extended lymph node dissection (LND) in patients undergoing robot-assisted radical cystectomy (RARC) for bladder cancer, as extendedLND is critical for the treatment of bladder cancer but the role of minimally invasive surgery for extended LND has not been well-defined in a multi-institutional setting.

Patients and Methods—• Used the International Robotic Cystectomy Consortium (IRCC) database.

• In all, 765 patients who underwent RARC at 17 institutions from 2003 to 2010 were evaluated for receipt of extended LND.

• Patients were stratified by age, sex, clinical stage, institutional volume, sequential case number, and surgeon volume.

• Logistic regression analyses were used to correlate variables to the likelihood of undergoing extended LND.

Results—• In all, 445 (58%) patients underwent extended LND.

• Among all patients, a median (range) of 18 (0–74) LNs were examined.

• High-volume institutions (≥100 cases) had a higher mean LN yield (23 vs 15, $P < 0.001$).

• On univariable analysis, surgeon volume, institutional volume, and sequential case number were associated with likelihood of undergoing extended LND.

• On multivariable analysis, surgeon volume [odds ratio (OR) 3.46, 95% confidence interval (CI) 2.37–5.06, $P < 0.001$] and institution volume [OR 2.65, 95% CI 1.47–4.78, $P = 0.001$) were associated with undergoing extended LND.

Conclusions—• Robot-assisted LND can achieve similar LN yields to those of open LND after RC.

• High-volume surgeons are more likely to perform extended LND, reflecting a correlation between their growing experience and increased comfort with advanced vascular dissection.

Keywords

lymphadenectomy; bladder cancer; cystectomy; robotics

Introduction

Open radical cystectomy (RC) with pelvic lymph node dissection (LND) is the standard of care for treatment of invasive carcinoma of the bladder [1]. Regional LND may not only be diagnostic, but also therapeutic, in patients with locally advanced bladder cancer [2]. Studies have suggested up to a 36% improvement in 5-year survival in patients who underwent LND in limited nodal disease [3]. About 25% of patients will have pathological evidence of LN metastases at the time of RC [4–6]. Many analyses since then have suggested that cancer-specific and recurrence-free survival depend on the extent of surgical removal of local and regional disease [4].

Robot-assisted RC (RARC) has developed as a minimally invasive alternative to open RC for invasive bladder cancer [7–9]. While RA surgery becomes incorporated into urological oncology, there is still lack of data on oncological outcomes, including LN yield, surgical margins, and long-term survival after RARC [10].

In an effort to establish standards for surgical quality, Herr and the Bladder Cancer Collaborative Group [11] proposed standards for RC and LND, including a median of 10–14 LNs retrieved. There is data to indicate that the performance and LN yield of LND in RC are improving significantly over time [12]. Several studies suggest different thresholds for LN yield to prolong survival in the open RC literature [13]. Preliminary data have shown that comparable LN yields can be achieved in RARC [14,15]. Studies also show that a learning curve exists for LN yield [16] and the likelihood of receiving LND [14]. Single-institution series of RARC reported a high likelihood of patients receiving extended LND [17,18], but these results have not been reported in multi-institutional series. Therefore, we retrospectively studied a multi-institutional, prospectively maintained, international database to identify the LN yield, incidence of, and predictors for, extended LND in patients undergoing RARC for locally invasive bladder cancer.

Patients and Methods

The present study was a retrospective review of the prospectively maintained Institutional Review Board-approved database (I 97906) of the International Robotic Cystectomy Consortium (IRCC), the database encompasses a mixture of academic and private centres comprising patients treated with RARC for clinically localised bladder cancer from 2003 to 2010.

Clinical and pathological data were available from 765 patients who underwent RARC by one of 43 surgeons at 17 institutions. Patients in the group ranged in age from 28 to 90 years of age and 161 (21%) were women. Clinical features evaluated included age, gender, pathological stage, surgeon volume, institution volume, sequential case number, LN status, and LN yield.

LNs were evaluated according to the routine pathological methods at the participating institutions. Centralised review of pathology was not performed. Patients were divided into two groups for further analysis; those who underwent extended LND and those who underwent either standard or no LND. Institutions were surveyed about boundaries of the standard and extended LND, which are reported in Table 1. All pathological specimens were reviewed by individual institutional pathologists using the American Joint Committee on Cancer TNM staging system relevant to the time of diagnosis.

The primary outcome measures were the incidence of and predictors for extended LND in patients undergoing RARC. Groups were defined by gender, age groups (≤60, 61–70, 71–80, ≥81 years), preoperative T stage (≤T1 or carcinoma *in situ*, T2, ≥T3), pathological T stage (≤T2, T3, T4), case number (1–10, 11–25, 26–50, ≥51), surgeon volume (1–10, 11–50, ≥51), institution volume (≤100 or >100), and LN status (positive or negative).

Logistic regression analyses were used to evaluate predictors of undergoing an extended LND. Variables that were significantly associated ($P < 0.05$) with the likelihood of undergoing extended LND on univariable analysis were included in the multivariable model.

Results

In all 765 patients, who underwent RARC and had data on extent of LND, were included in this study. The mean (range) age was 67 (28–90) years and 161 patients (21%) were female. In all, 316 of patients (46%) had an American Society of Anesthesiologists score of ≥3. The mean (range) operative duration was 421 (157–862) min, the mean (range) estimated blood loss was 479 (50–3900) mL, and the median (interquartile range) hospital stay was 8 (6–13) days. In all, 445 patients (58%) underwent extended LND, 304 patients (40%) underwent standard LND, and 16 patients (2%) did not undergo LND. The mean (range) LN yield was 18 (0–74). In all, 596 patients (78%) underwent LND (LN yield ≥ 10) as defined by Herr et al. [11]. When stratified by type of LND, 68% and 88% of patients underwent standard and extended LND, respectively, and had ≥10 LNs removed. Overall, 198 patients (27%) had positive LNs. In all, 311 patients (41%) had a pathological stage of ≥pT3. In extended LND, the mean LN yield was 21 and in standard LND, the mean LN yield was 13 ($P < 0.001$; Table 2). In all, 90 patients (52%) who had continent diversion had an extended LND vs 353 (61%) of those who had an ileal conduit. Meanwhile, 66% and 65% of patients who had intracorporeal and extracorporeal diversion, respectively, had an extended LND.

The performance of extended LND was significantly associated with sequential case number, surgeon volume, and institution volume (Table 3). By the 51st case, patients were 4.4-times more likely to undergo extended LND (95% CI 2.86–6.93, $P < 0.001$). High-volume surgeons (>50 cases) were 9.5-times more likely to perform an extended LND (95% CI 4.50–20.2, $P < 0.001$). High-volume institutions (≥100 cases) were almost 10-times more likely to perform an extended LND (95% CI 6.07–16.6, $P < 0.001$).

On multivariable analysis, institutional volume and sequential case number remained as significant predictors of extended LND (Table 4). High-volume institutions (≥100 cases) were 3.46-times more likely to perform extended LND.

Discussion

Regional LND at the time of RC has been shown to enhance local disease control, prevent local recurrence, and improve overall survival [3]. Studies have shown that removing more

LNs improves overall survival and also correlates with a higher LN positivity rate [4]. This leads to more accurate staging and can guide adjuvant treatment. In a multi-institutional study of open RC, 9% of patients had no LNs removed during RC, and 37% had a limited LND (obturator region only) [19]. In the present series, 26 patients (3.4%) had no LNs removed or had no data about LN yield, and 78% of patients underwent LND (defined as ≥10 LNs removed).

Previous data from the IRCC on RARC and LND reported that the median LN yield was 17 and that 83% of patients underwent LND (defined as a LN yield of ≥10) [14]. Since then, six institutions and >700 patients have been added to the IRCC database. In addition, data about the extent of LND was obtained. Data about the extent of LND was available for 765 patients, of whom 455 (58%) underwent extended LND. Given the multi-institutional nature of the IRCC, a survey regarding boundaries of LND was sent to all IRCC institutions (Table 1). All responding institutions defined an extended LND as extending at least up to the aortic bifurcation ± the presacral LNs.

The mean number of LNs removed in the present series was 18. This is similar to large open RC series, where mean LN counts have ranged from 14 to 40 [20,21]. In our IRCC data, the mean number of LNs removed was 13 and 21 in standard and extended LND, respectively. This compares favourably to the collaborative group report by Herr et al. [11], which reported a mean LN yield of 13 and 26 for standard and extended LND, respectively. Nix et al. [15] reported no difference in mean LN yield between open RC and RARC (18 vs 19 LNs, respectively) in a prospective randomised single-centre non-inferiority study. Recently, Davis et al. [22] performed a second-look open LND by expert surgeons after completion of RALND. They reported that 80% of patients had either no residual tissue or some residual tissue without identification of LNs despite lengthy procedure times taken to search for LN tissue.

We found that the performance of an extended LND was significantly associated with surgeon volume and institution volume. On multivariable analysis, each increase in surgeon volume (1–10, 11–50, and ≥51 cases) was associated with a 3.5-fold increase in the likelihood of undergoing extended LND. This finding became more striking if the surgeon volume was stratified using a case number of 50 as a threshold (i.e. volume 1–50 vs ≥51). In this analysis, high-volume surgeons were 20- and 36-times more likely to perform extended LND on univariable and multivariable analysis, respectively (data not shown). This finding is similar to large open RC series, in which high-volume surgeons usually have improved outcomes over low-volume surgeons [23].

Receipt of an extended LND was significantly associated with high-volume institutions (≥101 cases). On multivariable analysis, high-volume institutions were >2.5-times more likely to perform extended LND than low-volume institutions. Similar findings have been validated in large multi-institution open RC series [24]. This can be explained by the fact that high-volume institutions probably have the experience, and availability of services, to be able to carry out a complex operation. In addition, it intuitively makes sense that high-volume surgeons are more likely to operate at high-volume institutions.

LN yield can vary based on pathological evaluation. The method by which LNs are submitted for pathological review can affect the number of reported LNs (*en bloc* vs separate packets) [21]. Pathological evaluation was not centralised within the IRCC, and the method of submitting LNs to pathology was not captured in the IRCC database.

The present study is the first of its kind with a large overall cohort comparable with contemporary open series. The present study has limitations inherent to the retrospective and observational data approach. First, due to the many surgeons and variability of practice type and location involved in this cohort, selection and reporting bias may have been present that could affect the results. Second, review of operative data was not centralised, and there was probably variability in specimen review. In addition, pathological evaluation was not centralised in the present cohort. Third, the number of patients varied widely among the 17 institutions studied. The outcomes from this cohort may have been influenced by institutions with higher volumes.

In conclusion, RA extended LND is feasible and follows the oncological principles of open extended LND. High-volume institutions and higher surgeon volume significantly predicted the performance of an extended LND in the present cohort.

Abbreviations:

IRCC	International Robotic Cystectomy Consortium
(RA)LN(D)	(robot-assisted) lymph node (dissection)
(RA)RC	(robot-assisted) radical cystectomy

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What's known on the subject? and What does the study add?

- Lymph node dissection and it's extend during robot-assisted radical cystectomy varies based on surgeon related factors.
- This study reports outcomes of robot-assisted extended lymphadenectomy based on surgeon experience in both academic and private practice settings.

Table 1

Institution reported boundaries of LND*.

Region	Standard LND	Extended LND
Obturator	Yes	Yes
Hypogastric	Yes	Yes
External iliac (up to crossing of ureter)	Yes	Yes
Common iliac	No	Yes
Up to aortic bifurcation	No	Yes
Above the inferior mesenteric artery	No	1/19 institutions
Presacral	No	10/19 institutions

*Two institutions did not provide details on LND definitions.

Table 2

The patients' characteristics.

Variable	Value
Age, years:	
Mean (SD)	67 (11)
Median (range)	67 (26–90)
BMI, kg/m^2:	
Mean (SD)	27.5 (5.2)
Median (range)	27 (13.6–48)
ASA score:	
Mean (SD)	2.4 (0.7)
≥3, n (%)	316 (46)
N (%):	
Prior abdominal surgery	326 (49)
Preoperative chemotherapy	76 (13)
Preoperative radiation	13 (2)
Clinical stage:	
Ta, Tis	47 (8)
T1	156 (26)
≥T2	405 (66)
Pathological tumour stage:	
pT0	83 (11)
Organ-confined	361(47)
Extravesical	311 (42)
No. positive LNs	198 (27)
Overall LN yield:	
Mean (SD)	18 (11)
Median (range)	16 (0–74)
Standard LND:	
Mean (SD)	13 (8)
Median (range)	13 (0–54)
Extended LND:	
Mean (SD)	21 (11)
Median (range)	20 (1–74)

Table 3

Extended vs no/standard pelvic LND.

	No/standard pelvic LND, n (%)	Extended pelvic LND, n (%)	Total, n (%)	OR (95% CI)	*P*
Age group, years:					
≤60	94 (29)	120 (27)	214 (28)	Reference 1.0	
61–70	108 (34)	147 (33)	255 (33)	1.07 (0.74–1.54)	0.732
71–80	98 (31)	135 (30)	233 (31)	1.08 (0.74–1.57)	0.691
≥81	19 (6)	41 (9)	60 (8)	1.69 (0.92–3.10)	0.090
Sex:					
Male	259 (81)	345 (78)	604 (79)	Reference 1.0	
Female	61 (19)	100 (22)	161 (21)	1.23 (0.86–1.76)	0.254
Preoperative T stage:					
≤T1 or CIS	103 (37)	100 (30)	203 (33)	Reference 1.0	
T2	142 (52)	197 (59)	338 (56)	1.43 (1.01–2.03)	0.045
≥T3	30 (11)	36 (11)	66 (11)	1.24 (0.71–2.16)	0.456
Case number:					
1–10	85 (26)	67 (15)	152 (20)	Reference 1.0	
11–25	98 (31)	95 (21)	193 (25)	1.23 (0.82–1.97)	0.342
26–50	84 (26)	97 (22)	181 (24)	1.46 (0.95–2.26)	0.084
≥51	53 (17)	186 (42)	239 (31)	4.45 (2.86–6.93)	<0.001
Surgeon volume, n:					
1–10	19 (7)	29 (7)	48 (7)	Reference 1.0	
11–50	230 (86)	153 (34)	383 (54)	0.44 (0.24–0.80)	0.008
≥51	18 (7)	262 (59)	199 (39)	9.53 (4.50–20.2)	<0.001
Institution volume, n:					
≤100	298 (92)	259 (58)	557 (73)	Reference 1.0	
≥101	22 (7)	186 (42)	208 (27)	9.72 (6.07–16.60)	<0.001
Pathological stage:					
≤T2	197 (63)	247 (56)	444 (59)	Reference 1.0	
T3	79 (25)	146 (33)	225 (30)	1.47 (1.06–2.05)	0.022
T4	37 (12)	49 (11)	86 (11)	1.05 (0.66–1.68)	0.818

	No/standard pelvic LND, n (%)	Extended pelvic LND, n (%)	Total, n (%)	OR (95% CI)	*P*
LN status:					
Negative	228 (75)	320 (72)	548 (73)	Reference 1.0	
Positive	75 (25)	123 (28)	198 (27)	1.16 (0.84–1.63)	0.360

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Table 4

Multivariable analysis – predictors of extended LND.

Variable	**OR (95% CI)**	***P***
Surgeon volume	3.46 (2.37–5.06)	<0.001
Institutional volume	2.65 (1.47–4.78)	0.001
Sequential case number	1.15 (0.96–1.38)	0.120