Extended Pelvic Lymph Node Dissection in Robotic-assisted Radical Prostatectomy: Surgical Technique and Initial Experience

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OBJECTIVES	To describe, and show in the accompanying video segments, a technique for extended pelvic
OBJEONVES	lymph node dissection (ePLND) in robotic-assisted radical prostatectomy (RARP) and report
	our clinicopathologic and perioperative outcomes. The extent of pelvic lymphadenectomy
	during radical prostatectomy has not been standardized. However, evidence demonstrates that an
	ePLND yields a greater number of positive nodes.
METHODS	A total of 32 patients with clinically localized prostate cancer underwent RARP with ePLND by
	a single surgeon (J.C.) between January and August 2008. The template for the ePLND included
	the obturator, hypogastric, external iliac, and common iliac lymph nodes up to the bifurcation
	of the aorta. Systematic review and grading of adverse events were performed.
RESULTS	The median number of lymph nodes retrieved was 18 (interquartile range [IQR] 12-28). Four
	patients (12.5%) had lymph node metastases. Of the 4 patients with lymph node metastases, 1
	patient (25%) had the involved lymph node exclusively in the common iliac region. Median
	operative time for the ePLND was 72 minutes (IQR 66-86). Median hospital length of stay was
	2.0 days (IQR 2.0-2.8). Graded complications included 13 grade 1 events and 1 grade 2 event,
	with 1 grade 1 event being considered related to ePLND. No clinically presenting lymphoceles
	or thrombotic events were encountered.
CONCLUSIONS	An ePLND during RARP is technically feasible and appears to have minimal morbidity. It
	produces a high lymph node yield and may result in improved pathologic staging. UROLOGY 75:
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Pelvic lymphadenectomy provides important information regarding pathologic stage and prognosis for prostate cancer. Although it is considered the most accurate staging method for lymph node metastases (LNM), there is no general consensus on the indication and anatomic limits of a pelvic lymph node dissection (PLND). There is concern that limiting the PLND may leave undetected LNM and understage the disease.¹⁻³ Accurate staging allows for an improved assessment of prognosis and aids in identifying men for consideration of adjuvant therapy.

Recent published studies suggest that an extended PLND (ePLND) increases lymph node yield and the retrieval of positive nodes.¹⁻³ Despite this possible bene-

Reprint requests: David S. Yee, M.D., M.P.H., Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 307 East 63rd St, 2nd Floor, New York, NY. E-mail: yeed1@mskcc.org fit, ePLND is not without associated costs. Associated costs include complications of pelvic lymphadenectomy that might occur more frequently with an extended dissection. Additional operative time and financial costs must also be taken into account.

We describe, and show in the accompanying video segments, a standardized approach for ePLND in roboticassisted radical prostatectomy (RARP). We also report the clinicopathologic and perioperative outcomes of our initial experience with ePLND during RARP.

MATERIAL AND METHODS

Patient Population

Between February and August 2008, a total of 32 patients with clinically localized prostate cancer were treated with RARP and ePLND by a single surgeon (JC). None of the patients had received preoperative radiation or androgen deprivation therapy. Institutional Review Board approval was obtained and patient data were collected and entered prospectively into an electronic database.

Clinicopathologic characteristics were evaluated, including the radical prostatectomy specimen, total lymph node count, and positive lymph node count with location. Perioperative

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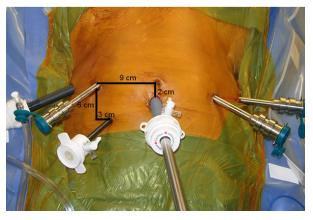


Figure 1. Port placement for extended pelvic lymph node dissection during robotic-assisted radical prostatectomy.

outcomes were also assessed, including estimated blood loss, ePLND operative time, total operative time, and complications. A retrospective review of charts, outpatient notes, and correspondence with local physicians was performed to determine all complications within 30 days of surgery. Complications were defined and graded according to an established 5-grade modification of the Clavien system.⁴ The ePLND-related postoperative complications were defined as clinically significant lymphoceles requiring hospitalization or intervention, deep venous thrombosis, pulmonary embolism, major vascular or ureteric injury, and sensory or motor neuropraxia. All patients were placed on a standardized perioperative care pathway, including deep venous thrombosis prophylaxis [sequential compression stockings and low molecular weight heparin (5000 IU dalteparin) subcutaneously daily until discharge].

Surgical Technique

All patients underwent transperitoneal RARP using the 4-arm da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA). The patient was positioned in steep Trendelenburg position with the arms tucked at the side and legs slightly spread to facilitate docking of the robot. Port placement was as follows: 12-mm laparoscope and assistant ports were placed supraumbilical and 2-4 cm cephalad to the left anterior superior iliac crest, respectively; two 8-mm robot ports were placed 2 cm below and 9 cm lateral to the camera port bilaterally; one 5-mm assistant port was placed 6 cm cephalad and 3 cm medial to the left lower quadrant 8-mm port; and the optional 8-mm port for the fourth arm was placed 2 cm cephalad to the right anterior superior iliac crest (Fig. 1).

The template of the ePLND included the obturator, hypogastric, external iliac, and common iliac nodal packets up to the bifurcation of the aorta as depicted in Figure 2. Specifically, the ePLND dissection included the lymphatic tissue overlying the hypogastric artery and the external iliac vein from the node of Cloquet distally to the bifurcation of the aorta proximally. Lymphatics within the obturator fossa were also removed, sparing the obturator nerve and vessels. The dissection was performed with bipolar forceps and monopolar scissors.

The ePLND was initiated by sharply incising the peritoneum over the proximal right common iliac artery. The dissection then proceeded distally on top of the common iliac artery to the medial border of the right ureter and the common iliac bifurcation (Video Clip 1). Next, the peritoneal incision was carried caudally along the medial aspect of the ureter while following the hypogastric artery to the level of the medial umbilical ligament (Video Clip 2). Lymphatic tissue was reflected medially away from the hypogastric vessels and ligated so as to free the right common and hypogastric nodal packets. The peritoneum was then incised up to the crossing vas deferens to remove lymphatics overlying the external iliac vessels to the node of Cloquet distally (Video Clip 3). Then, the dissection was carried medially over the external iliac vessels and directed toward the angle deep to the common iliac bifurcation to identify the obturator nerve. Subsequently, lymphatic tissue was removed within the obturator fossa while preserving the obturator nerve and vessels (Video Clip 4).

Dissection of the left common and hypogastric nodal packets used the same landmarks contralaterally and was best achieved by continuing the dissection from the aortic bifurcation under the sigmoid mesocolon to the left-sided structures (Video Clip 5). With this approach, care must be taken to identify the left ureter to prevent inadvertent injury. Occasionally, the left side required mobilization of the sigmoid colon to complete the dissection (Video Clip 6).

Pathologic Evaluation

The lymph node packets were routinely tagged and submitted in separate packages (ie, para-aortic, paracaval and precaval, right common iliac and presacral, right pelvic, left common iliac, left pelvic). Lymph node specimens were dissected and submitted whole (if small), bisected, or occasionally serially sectioned (if very large). After they were grossed, they were placed into 10% neutral buffered formalin. Within 4-8 hours they were loaded onto processors in which they were fixed in 2 cycles of formalin (10% neutral buffered) for 2 hours for each cycle (4 hour total). After being embedded in paraffin, slides were then stained with hematoxylin and eosin and examined microscopically. The radical prostatectomy specimens were examined in a whole-mount fashion. Specimens were assigned a Gleason grade and staged according to the 2002 TNM (tumornode-metastasis) clinical staging system. A positive surgical margin was defined as presence of tumor at the inked margin of the specimen regardless of whether additional tissue was resected.

Statistical Analysis

Descriptive statistics were calculated using SPSS version 15.0 (SPSS, Inc., Chicago, IL).

RESULTS

Table 1 lists clinicopathologic features of the 32 patients treated with RARP and ePLND. The median number of lymph nodes removed was 18 (interquartile range [IQR] 12-28). Positive nodes were found in 4 patients (13%), and the median number of positive nodes was 1 (range 1-3). Of the 4 patients with LNM, 1 patient (25%) had the involved lymph node exclusively in the common iliac region. LNM were in the hypogastric and common iliac region in 1 patient and in the external iliac region only in 2 patients. The patients with LNM had a preoperative probability of lymph node involvement between 3%-11%

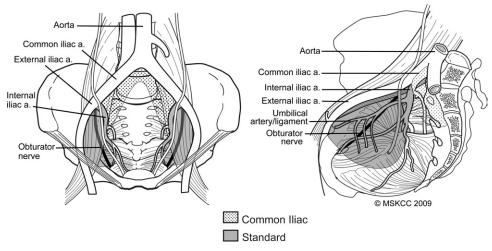


Figure 2. Standard and extended pelvic lymph node dissection templates. Reprinted with permission, Memorial Sloan-Kettering cancer center © 2009. All Rights Reserved.

Table 1. Clinical and pathologic characteristics of 32 patients undergoing extended pelvic lymph node dissection during robotic-assisted radical prostatectomy

No. Patients Age, median, years (IQR)	32 60 (55-66)
Preoperative PSA, median, ng/mL (IQR)	6.3 (4.9-8.1)
Clinical stage, n (%)	
T1a/b/c	20 (63)
T2a/b/c	12 (37)
Biopsy Gleason score, n (%)	
≤ 5	13 (41)
7	16 (50)
≥ 8	3 (9)
Extraprostatic extension, n (%)	10 (31)
Seminal vesicle invasion, n (%)	1 (3)
Positive surgical margin, n (%)	4 (12)
Preoperative probability of lymph node	
involvement, median	
Partin tables nomogram, % (range)	2 (0-6)
Kattan nomogram, % (range)	2 (2-4)
Lymph node metastasis, n (%)	4 (13)
Standard template, n (%)	2 (6)
Extended region only, n (%)	1 (3)
Both templates, n (%)	1 (3)
Retrieved nodes, median, n (IQR)	18 (12-28) 14 (8-20)
Standard template nodes, median, n (IQR)	14 (8-20)
Extended region-only nodes, median,	5 (2-10)
n (IQR)	000 (4 50 400)
Estimated blood loss, mL (IQR)	300 (150-400)
ePLND operative time, minutes (IQR)	72 (66-86)

IQR = interquartile range; PSA = prostate-specific antigen; ePLND = extended pelvic lymph node dissection.

and 2%-14% by the updated Partin tables and the Kattan nomogram, respectively.^{5,6}

The median operative time for the ePLND was 72 minutes (IQR 66-86), and the median total operative time was 298 minutes (IQR 282-330). Median estimated blood loss was 300 mL (IQR 150-400) and no blood transfusions were recorded. Median hospital length of stay was 2.0 days (IQR 2.0-2.8). In this cohort, 81% of patients had an American

Table 2. Complications occurring in patients after surgery

All complications, n (%)	11 (34)
Genitourinary (5 grade 1 and 1 grade 2)	6 (19)
Infectious (all grade 1)	5 (16)
Neurological (grade 1)	1(3)
Wound (grade 1)	1 (3)
Gastrointestinal (grade 1)	1(3)
ePLND-related complications, no. patients (%)	1(3)
Neurological (grade 1)	1 (3)

Association of Anesthesiologists score ≤ 2 . Median follow-up was 266 days (IQR 175-347).

A total of 14 complications occurring within 30 days after surgery in 11 separate patients were recorded and grouped into categories as outlined in Table 2. All but one of the complications were grade 1. Urinary tract infection (infectious complication) occurred in 5 patients. A wound complication (ie, drainage from umbilical port site at 1 week postoperatively) and a neurological complication (ie, temporary unilateral sensory neuropraxia lasting 3 days) occurred in 1 patient each. Constipation occurred in 1 patient and was defined as an inability to have a bowel movement by postoperative day 5 with no signs of ileus or small bowel obstruction. Six genitourinary complications were recorded, including 3 patients with urinary retention requiring Foley catheter placement, 2 patients with poor catheter drainage requiring irrigation, and 1 patient admitted for intravenous hydration and pain management from unilateral ureteral obstruction secondary to vesicourethral anastomosis edema (this last complication was grade 2). No lymphoceles presented clinically and no vascular injuries, thrombotic events, urine leaks, or deaths were seen.

COMMENT

The indication and extent of pelvic lymphadenectomy in prostate cancer varies widely among urologists. PLND has routinely been performed at radical prostatectomy to more accurately stage disease, and the presence of LNM is an adverse prognostic factor.⁷ Precise staging helps identify appropriate treatment and assess prognosis in prostate cancer.

The downward stage migration of prostate cancer resulting from the advent of prostate-specific antigen screening has led to an apparent decrease in the incidence of LNM. Contemporary radical prostatectomy series report LNM in approximately 5% of men,^{1,8} down from nearly 30% in the 1980s.⁹ This trend has led some surgeons to omit PLND in low-risk patients.^{10,11} Analysis of a community-based cohort demonstrated a decrease in pelvic lymphadenectomy overall, fuelled by sharp decreases in low- and intermediate-risk prostate cancer cases. Overall, PLND was performed in 94% of the men undergoing radical prostatectomy in 1992; by 2004, this figure had decreased to 80%. In patients who underwent PLND from 1992 to 2004, a mean of 5.7 lymph nodes (median 5.0) were removed.¹²

Pelvic lymphadenectomy is the most accurate staging method in prostate cancer, as conventional imaging techniques have proven insufficient.¹³ Given the poor sensitivity of radiographic imaging, several investigators have developed algorithms to predict lymph node status.^{5,6,11} Bluestein et al¹¹ combined serum prostate-specific antigen, primary Gleason grade, and clinical stage to identify patients at low risk for lymph node metastases. Cagiannos et al⁶ also constructed a predictive nomogram based on several preoperative variables to predict the probability of LNM. Most of these nomograms, however, are based on limited PLND data and include only the obturator fossa and the external iliac region.¹⁴ Recently, Briganti et al^{15,16} have published nomograms predicting the probability of LNM among patients undergoing ePLND. These nomograms are awaiting external validation.

The wide range observed in lymph node yield and incidence of positive nodes is not surprising given the existing differences in extent of PLND and technique. The exact nomenclature and anatomic boundaries of pelvic lymphadenectomy vary between institutions. Standardization of lymph node group terminology and templates are needed, both to allow the identification of best practices and to improve our ability to compare future studies on PLND in prostate cancer. Currently, dissection for our standard PLND includes the lymphatic tissue overlying the hypogastric artery and the external iliac vein to the obturator nerve, extending to the node of Cloquet distally to the bifurcation of the common iliac artery proximally. In ePLND, we extend this dissection proximally to include the lymphatic tissue medial to the common iliac artery up to the bifurcation of the aorta.

Anatomic studies have been performed to define the periprostatic subcapsular network that drains the prostate lymphatics. The network is composed of the ascending, lateral, and posterior groups. The ascending duct from the cranial prostate drains into the external iliac lymph nodes, the lateral duct drains into the hypogastric lymph nodes, and the posterior duct drains from the caudal prostate to the subaortic lymph nodes of the sacral promontory. The levels of lymph node drainage are segregated into hypogastric (primary), obturator (secondary), external iliac (tertiary), and presacral (quaternary lymphatics).^{17,18} Lymphatic crossover is common and no single sentinel lymph node has been identified.¹⁹

Recently, Mattei et al mapped the primary prostatic lymphatic landing sites based on single-photon emission computed tomography/computed tomography/magnetic resonance imaging (SPECT/CT/MRI) fusion imaging confirmed by ePLND. They found that the common iliac region was a primary landing site in 16% of lymph nodes.²⁰ Our study of 32 patients supports the common iliac region as a primary lymphatic landing site even in the absence of LNM distally. Of the 4 patients with LNM, 1 patient (25%) had an involved lymph node exclusively in the common iliac region and would have been understaged by a standard dissection template. This patient's preoperative predictive probability of lymph node involvement was just 2% based on the Kattan nomogram. Another patient in our study had LNM in both the common iliac and hypogastric regions.

Several studies have already demonstrated that ePLND increases lymph node yield and the retrieval of positive nodes.¹⁻³ The mean lymph node count ranges from 18-28 for ePLND compared with 9-11 nodes for limited PLND.¹⁻³ Heidenreich et al² found LNM in 26% of patients with ePLND (external iliac, hypogastric, obturator, common iliac, presacral regions) compared with 12% of patients with standard PLND (external iliac and obturator regions). Bader et al²¹ reported similar findings in 367 men treated with radical prostatectomy and ePLND, with 25% of patients positive for metastasis. Stone et al found that twice as many lymph nodes were removed with an extended PLND than with a standard laparoscopic PLND (mean 17.8 vs 9.3 nodes). They also reported a 23% incidence of LNM in men undergoing ePLND compared with 7% in men undergoing standard PLND.³ Our findings confirm that, compared with a standard PLND template, ePLND increased lymph node vield [from 14 to 18 nodes (unpublished data, 2008)].

The number of lymph nodes removed during pelvic lymphadenectomy serves as a surrogate measurement for the extent of PLND. Currently, the number of lymph nodes that should be removed to adequately stage prostate cancer is unknown. On the basis of lymphadenectomy data on 858 patients, Briganti et al²² suggested that at least 10 nodes should be assessed to accurately stage a patient. Barth et al²³ found that the rate of LNM was twice as high when 13 or more lymph nodes were removed compared with lower lymph node yields and recommended that at least 13 nodes should be removed for adequate prostate cancer staging. An autopsy study by Weingartner et al²⁴ suggested that removal of approxi-

mately 20 lymph nodes serves as a guideline for a sufficient PLND.

Whether pelvic lymphadenectomy has a therapeutic role in prostate cancer management remains unclear. As with other cancers, ePLND in prostate cancer may provide a survival advantage; however, the data presented is insufficient to address this issue. In a review of approximately 13 000 patients from the Surveillance Epidemiology and End Results database, Joslyn and Konety reported that a more extensive PLND improved diseasespecific survival even in patients with negative nodes.²⁵ However, the true therapeutic value of ePLND requires a large multi-institutional, prospective randomized clinical trial. Currently, the Association of Oncological Urology of the German Cancer Society has initiated a clinical phase 3 trial of limited PLND vs ePLND.¹⁴

Pelvic lymphadenectomy has potential morbidity: reported complication rates for men undergoing PLND historically range from 4% to 50%.²⁶ The morbidity associated with PLND may be associated with the extent of dissection. In a randomized prospective evaluation of extended vs limited PLND in patients with clinically localized prostate cancer, Clark et al²⁷ reported an overall complication rate of 10.5%, with 75% of complications occurring on the side of the patient where ePLND was performed. Briganti et al²⁸ also demonstrated an increased overall complication rate of 19.8% for ePLND vs 4.6% for a limited dissection, as well as a significantly higher lymphocele rate of 10.3% for ePLND. Conversely, Heidenreich et al² did not observe differences in complication rates between ePLND and standard PLND in 203 patients. In this study, the rate of obturator nerve injury was lower in the ePLND group compared with the standard PLND group (1.1% vs 2%).² In our series, all except 1 were grade 1 complications, most of which might be considered part of the normal postoperative course after radical prostatectomy. This, however, would deviate from Dindo and Clavien's recently replacing their terminology "normal postoperative course" with the new term "ideal postoperative course" (in which no complications are observed).²⁹ The only ePLND-related complication was temporary unilateral sensory neuropraxia in 1 patient (3%). There were no cases of clinically significant lymphoceles, which may be partially attributable to our transperitoneal approach.

PLND also has associated operative time and costs. Conventionally, the overhead costs are greater for laparoscopic lymphadenectomy than for its open counterpart, primarily due to longer operative time and equipment costs.³⁰ In our RARP study, our median operative time was 72 minutes (IQR 66-86) for ePLND compared with 47 minutes (IQR 66-86) for standard PLND (unpublished data, 2008). However, in our series, no additional instruments beyond the laparoscopic retrieval bags were required to complete the ePLND.

We acknowledge the limited number of patients and short follow-up in this study. The short follow-up time

CONCLUSIONS

We have described a standardized approach for a roboticassisted ePLND in prostate cancer. ePLND during RARP is technically feasible and appears to have minimal morbidity. It produces a high lymph node yield and may result in improved pathologic staging.

does not allow an adequate assessment of oncological

outcomes and longer follow-up will be needed to deter-

Acknowledgments. We acknowledge medical illustrator Terry Helms from Media Services at Memorial Sloan-Kettering Cancer Center for the figure depicting the standard and extended pelvic lymph node dissection templates.

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EDITORIAL COMMENT

In this issue of Urology, Yee et al describe a surgical technique of extended pelvic lymphadenectomy (EPLND) during robotic prostatectomy. The technique is similar to that described previously.¹ It is clear now that robotic techniques do not compromise on the ability to perform EPLND.

Editorializing on articles about surgical technique is somewhat awkward. Such articles advance the art of surgery. Although important, they fall in the category of expert opinion, level 5 evidence as classified by the Center for Evidence-Based Medicine. With apologies to felinophiles, there are many ways to skin a cat, and here are some tricks that we have picked up after performing EPLND on more than 500 patients with Gleason 8-10, T2, PSA > 10 (mean 20). These should also be considered "expert opinion."

- 1. The first step is to release the attachments of the sigmoid mesocolon and the right colon to the iliopsoas muscle as needed to get adequate exposure to the iliac vessels proximally.
- 2. The second step is to open the peritoneum and take down the bladder.
- 3. We find it helpful to transect the vasa to open up the pelvic area widely.
- 4. The 30° down-lens makes it easier for the surgeon to look over the retracted large bowel than the 0° lens does.

What about the science of surgery? Is an extended lymphadenectomy necessary in all patients? The fact that the wider the template used the greater will be the number of nodes removed is intuitive and inarguable. What is not clear is whether a wider dissection will result in greater cure rates. A multi-institutional randomized clinical trial would provide level 1a evidence of a therapeutic benefit or lack thereof. A prospective single institution cohort study with > 80% follow-up may yield level 1 b evidence. However, much of what exists in the published data are case series (level 4). The one retrospective cohort study from Johns Hopkins (level 2)² examined outcomes of 2 experienced surgeons, one who preformed EPLND, and one who performed limited node dissection (LPLND). Biochemical recurrence rates were similar in both groups, although, the recurrence rates were lower in a subset of patients who underwent EPLND. Such a subset analysis should be considered hypothesis generating, rather than conclusive. To our knowledge, no other authors have compared the 2 techniques in matched cohorts, much less with a randomized, prospective controlled study.

The down-side of EPLND is that at least in the hands of some (but not all) experienced surgeons, complication rates are higher in patients undergoing extended pelvic lymphadenectomy.^{3,4,5} In the absence of clear therapeutic benefit, the principle primum non nocere holds. Thus, our practice is to perform EPLND in "aggressive cancer" as defined earlier (level 5 evidence) and a limited internal iliac and obturator node dissection in patients with less aggressive cancer.⁶ With the latter approach, the positive node yield was 13-fold greater than with LPLND of the external iliac and obturator areas (Level 1 b evidence).

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