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Role of Pelvic Lymph Node Dissection during Radical Cystectomy

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Abstract

Radical cystectomy is considered the standard treatment for Muscle-Invasive Bladder Cancer (MIBC). However, a percentage of patients (up to 25%) who undergo this procedure are found to have metastatic lymph node deposits during the surgery. In such cases, the 5-year survival rate is reported to be around 25% to 30%. Performing Pelvic Lymph Node Dissection (PLND) during radical cystectomy can provide valuable prognostic information, including details about the disease extent, lymph node density, and spread of metastatic lymph nodes beyond their capsules. The National Comprehensive Cancer Network guidelines recommend the inclusion of PLND, covering the common iliac lymph nodes, in order to accurately stage MIBC.

Besides its diagnostic value, several studies have highlighted the potential therapeutic benefits of PLND. Clinical trials have shown that PLND cohorts generally exhibit better oncological outcomes compared to non-PLND cohorts, irrespective of the pathological nodal status. This advantage is attributed to the removal of metastatic and micrometastatic tumor cells present within the lymph nodes. Despite the diagnostic and therapeutic significance of PLND in MIBC, there is ongoing debate regarding the optimal PLND approach. Currently, extended PLND is recommended for diagnostic purposes, but its therapeutic effectiveness has not been consistently demonstrated in recent preliminary randomized controlled trials.

This manuscript has addressed the appropriate extent of PLND during radical cystectomy, considering its diagnostic and therapeutic importance. Based on the available evidence and randomized trials, we propose a suitable range for PLND.

Keywords: Bladder cancer; Lymph node dissection; Radical cystectomy

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Introduction

In 2018, Bladder Cancer (BCa) was the eleventh most common cancer worldwide, resulting in 549,393 new cases and 199,922 deaths [1]. Furthermore, BCa was diagnosed in 81,190 people in the United States and 4,379 people in South Korea, resulting in 17,240 and 1,438 deaths in the said countries, respectively. For cross-country comparison, the incidence rate per 100,000 people in the United States was 35.8 men and 8.8 women, which was higher than that in South Korea- 13.8 men and 3.3 women [2,3].

Depending on the stage, BCa is divided into Non-Muscle Invasive Bladder Cancer (NMIBC) and Muscle-Invasive Bladder Cancer (MIBC). MIBC invades beyond the muscularis propria with no distant metastasis. Approximately 25% of BCa are diagnosed as MIBC; the 5-year survival rate without treatment is <15% [4,5].

The standard treatment for MIBC is radical cystectomy and Pelvic Lymph Node Dissection (PLND). Preoperative cisplatin-based combination chemotherapy is recommended for patients eligible to receive cisplatin [6]. When MIBC is treated by radical cystectomy and PLND without the administration of preoperative neoadjuvant chemotherapy, approximately 50% of patients with MIBC are diagnosed with pTis-T2, pN0, with a 5-year survival rate of 75%, 20% with pT3-T4a, pN0, and 20% with pTany, pN1-N3 with a 5-year survival rate of 25% [7-9]. Micrometastases cause most recurrences after surgery, and radical cystectomy and PLND have excellent local treatment effects [10-12].

On pathological examination, up to 8% of patients with NMIBC and 30% of patients with MIBC and without clinical signs of nodular disease have positive lymph nodes (N+) [13-16]. Recurrence-Free Survival (RFS), Overall Survival (OS), and Cancer-Specific Survival (CSS) rates have shown clinically significant differences between radical cystectomy combined with LND and radical cystectomy alone. Over approximately 5 years, a 9% decrease in RFS/OS was observed in PLND [17-20].

Because the number of lymph node metastases with local progression is the most important risk factor for determining OS, CSS, and RFS, an extended LND can provide more accurate information for establishing a prognosis [21-23]. Prolonged LND may indirectly improve survival by inducing adjuvant chemotherapy in patients with pN+ disease [24,25].

There are some controversies about the efficacy of extended LNDs in improving cancer outcomes. Recent phase 3 RCTs have not demonstrated a benefit for cancer, despite retrospective studies demonstrating improved survival after extensive LND. It is still unclear whether a suitable PLND template exists [24]. Current guidance is imprecise because of these ambiguities. Although most guidelines recommend that bilateral LND should be performed during radical cystectomy; however, the anatomical extent is not specified [6,26,27].

Based on the current evidence, this review aimed to examine the findings from a diagnostic and therapeutic perspective and recommended the appropriate extent of PLND at the time of radical cystectomy in MIBC.

History of PLND

After Bardenheuer pioneered radical cystectomy in Germany in 1887 [28], Whitmore and Marshall, during radical cystectomy in 1962, proposed the extent of PLND; they proposed that the proximal boundary should be the mid portion of the common iliac arteries and the ureter (mid portion of the common iliac arteries), the distal boundary should be the inguinal ligament of Cooper, and the lateral boundary should be the lateral boundary of the iliac artery [26]. Since then, various PLND templates have been proposed. Leissner et al. [29] proposed a limited PLND (lPLND) which involved making a small incision into the bilateral obturator fossa, the distal part of the common iliac artery as the proximal boundary, the inguinal ligament as the distal boundary, the genitofemoral nerve externally, and the lymph nodes between the bladder walls medially. They also suggested that the standard PLND (sPLND) should encompass the aorta from its proximal border to its distal extent, the femoral generative nerve to the outside, the circumflex iliac vein to the distal border, and the extended PLND to remove the lymph nodes between the posterior internal iliac vessels. A super-extended PLND (sePLND) that resects to the origin of the Inferior Mesenteric Artery (IMA) at the proximal boundary was proposed.

In 2012, Roth et al. [22] published a study on the extent of PLND in patients with unilateral BCa. Before radical cystectomy in 40 patients with unilateral BCa, a radioactive isotope, technetium, was injected into the contralateral bladder wall using a flexible cystoscope. During surgery, radioactive lymph nodes were detected with γ probe, and after surgery, the collected lymph nodes were re-examined using γ camera. Contralateral lymphatic drainage was found in approximately 40% of patients, indicating that contralateral lymphatic drainage (crossover) is a common phenomenon in the BCa and that radial lymph nodes would have been missed in approximately 40% of patients if only unilateral PLND was performed, providing evidence for bilateral PLND.

Skinner reported that some BCa patients with pelvic lymph node metastasis could be treated with only radical cystectomy and PLND [23]. He reported that sePLND involving LNs of the common iliac vessels and distal aorta and vena cava could improve survival without increasing morbidity or mortality associated with radical cystectomy.

The NCCN Guidelines recommend performing bilateral PLND involving LNs of the common iliac, internal and external iliac artery, and obturator artery during radical cystectomy for MIBC [6]. In addition, when lymph node metastasis is confirmed after PLND, it is recommended to consider adjuvant radiotherapy or chemotherapy if neoadjuvant chemotherapy has not been performed.

The current guidelines recommend preoperative Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) for lymph node staging. These methods use dimensional criteria for lymph node classification [30,31]. Using these criteria, CT showed a sensitivity of 30% to 75% and a specificity of 50% to 100% [32,33]. Over-staging occurs in approximately 8% of cases, while under-staging occurs in approximately 30% [33]. The presence of micrometastases in non-enlarged lymph nodes is the cause of this high rate of false-negative results for N+.

MRI functions similarly to CT scanning, with a mean sensitivity of 56% and specificity of 94% [15]. When dealing with non-enlarged lymph nodes, fluorodeoxyglucose Positron Emission Tomography (PET)/CT is significantly less sensitive than tomography in ruling out lymph node involvement. The use of reactive lymph nodes is limited owing to physiological excretion through the urinary tract and false positives [34]. In determining whether N+ was present, Coline PET/CT did not demonstrate superior accuracy to conventional imaging [35]. Efforts to use radio- and fluorescence-guided surgeries have failed. Even when combined, both methods have been shown to have low specificity and high sensitivity [36].

LND persists to be the best method for nodal staging, despite the unreliability of the current imaging methods. Lymphatic bladder drainage has been the subject of several mapping studies, and previous studies reported that >30% of N+ were located between the temporal iliac bifurcation and the IMA [29].

A systematic review reported that up to 41% of N+ is above the common iliac bifurcation [37]. Roth et al. [38] reported that 8% of patients had N+ above the aortic bifurcation. Tarin et al. [39] showed that lymph node disease exceeded this level in at least 13% of pT2 patients. Several studies [29,39,40] have shown that 2% to 6% of patients have N+ only in the true pelvis (skip metastases).

Because there is strong evidence that a PLND could not eliminate lymph node metastases in a large proportion of patients, several operators have attempted to improve survival by performing super-extended LNDs.

Appropriate Extent of PLND for Diagnostic Intent at the Time of Radical Cystectomy in Muscle-Invasive Bladder Cancer

Lymph node metastasis is crucial in determining the staging and treatment plan for patients with MIBC. According to the international BCa nomogram consortium, when radical cystectomy and PLND were performed without neoadjuvant chemotherapy, lymph node metastases were found in approximately 25% of patients, and the median survival time was 19 months [24]. In 2004, Nishiyama et al. [25] presented the results of a retrospective study of 1,131 patients who underwent radical cystectomy at 32 hospitals in Japan between 1990 and 2000. PLND was performed on 1,013 patients, and lymph

Table 1: Comparison of LEA and SWAG S-1011 trials.

	LEA	SWOG S1011
Start date	Feb. 2006	Aug. 2011
Completion date	Aug. 2015	Aug. 2022 (Estimated)
Eligibility	T1-4a	T2-4a
Neoadjuvant chemotherapy	Not allowed	Allowed (56%)
Planned randomization	400	564
Randomization timing	Before surgery	Intraoperative
Randomized (n)	433	620
Intent to treat	362	Estimate 576
LND control arm	Limited	Standard
ePLND	IMA	Aorta bifurcation up to IMA
Primary endpoint	Recurrence-free survival at 5 years	Recurrence-free survival
Effect size	15% (from 50% to 65%)	10% improvement (from 55% to 65%) at 3 years
Power	90%	85%
Hazard ratio	0.8	0.72

node metastasis was confirmed in 162 patients (16.0%). Through multivariate analysis, lymph node involvement and PLND were reported as independent prognostic factors associated with survival along with gender, clinical stage, and pathological stage; only 20% to 30% of lymph node-positive patients reported long-term survival [41].

Leissner et al. [29] published a prospective multicenter mapping study in 2004 to identify the appropriate range of PLND for a more accurate diagnosis of pelvic lymph node metastasis, investigating the lymphatic drainage pattern of BCa. SePLND was performed in all patients scheduled for radical cystectomy, and pelvic lymph node metastasis distribution was examined. This study found that 44% of pelvic lymph node metastases were in the proximal direction of the common iliac bifurcation. Notably, 6.9% of lymph node metastases were observed in the common iliac node without lymph node metastasis in the distal direction of the common iliac bifurcation. For patients with a single lymph node metastasis, the authors reported that PLND for diagnostic purposes should include at least the common iliac lymph nodes, as lymph node metastasis was not observed in the proximal direction of the aortic bifurcation.

Roth et al. [38] injected radio labeled tracer into six sites within the bladder of 60 patients without tumors scheduled to undergo radical cystectomy to identify the primary lymphatic drainage location of the bladder. The bladder lymphatic drainage was evaluated using single photon emission Computed Tomography/CT, intraoperative gamma probe, and postoperative backup ePLND tissue using a gamma camera. They reported that 19% of radioactive nodes were detected in the proximal common iliac bifurcation. If an lPLND, including only obturator fossa and closure, was performed, 50% of radioactive nodes were removed. The authors found that the number of lymph nodes varies among patients, making it difficult to evaluate the quality of PLND based on the number of lymph nodes removed. Second, primary lymphatic drainage of the bladder is widely distributed in the pelvis, requiring bilateral PLND. However, if radioactive nodes were detected at the proximal uretero iliac junction, which only occurred in 8% of cases, lymph node dissection at the upper level of the uretero iliac junction was unnecessary as it may only involve unnecessary risks without diagnostic utility. Third, the study demonstrated the importance of meticulous dissection of the inner side skip metastases, isolated from the internal iliac vessels. However, according to Tarin et al. [39], skip metastases or isolated lymph node metastases at the proximal common iliac bifurcation were found in 7% of BCa patients. Furthermore, a prospective multicenter mapping study reported that skip metastases accounted for 6% of approximately 600 lymph node metastases [29].

As prognostic factors for patients with lymph node metastasis after radical cystectomy, it was reported that the presence or absence of lymph node metastasis in the iliac bifurcation, the number of removed lymph nodes, or the extent of PLND, the total number of lymph node metastases (tumor burden), the volume of lymph node metastases, the lymph node metastasis density (number of metastatic lymph nodes/number of removed lymph nodes), and extra nodal growth were identified. In multivariate analysis, extra nodal growth was the strongest predictor [29].

Appropriate Extent of PLND for Curative Intent at the Time of Radical Cystectomy in Muscle-Invasive Bladder Cancer

Many retrospective studies reported that PLND affects prognosis. Herr et al. [42] analyzed data from 637 MIBC patients who underwent radical cystectomy and PLND to investigate the correlation between surgical and pathological variables and 5-year disease-specific survival and local recurrence. The results showed that pathological stage and lymph node involvement were important variables for tumor-specific survival. In particular, even in lymph node-negative patients, if more lymph nodes were removed along with negative surgical margins, tumor-specific survival (continuous, P=0.001; RR=0.87; categorical, P=0.01; RR=0.51) improved and local recurrence decreased (continuous, P=0.000, RR=0.89). Subsequent meta-analyses have equally demonstrated that ePLND improves Disease-Free Survival (DFS) even in lymph node-negative patients [43]. These results can explain why 10% to 35% of patients with no lymph node metastasis on pathological examination may have micrometastasis when RT-PCR is performed [11]. The most effective method for analyzing the impact of PLND on prognosis is prospective multicenter studies. However, if these results are unavailable, secondary analysis of existing prospective multicenter studies can provide higher levels of evidence.

Table 2: Clinical outcomes of ePLND.

	Type of PLND	Boundary
Whitmore & Marshal [20]		Prox.: midportion of the common iliac arteries
		Distal: inguinal ligament
		Lateral: lateral margin of external iliac arteries
		*Including the nodes in the obturator region and the fossa of Marcille
Leissner et al. [21]	sePLND	Prox.: inferior mesenteric artery
		Distal: pelvic floor
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: pelvis and rectum nerve
	ePLND	Prox.: distal aorta
		Distal: circumflex iliac vein
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: pelvis and rectum nerve
	sPLND	Prox.: common iliac artery
		Distal: inguinal ligament
		Medial: bladder wall
		Lateral: genitofemoral nerve
	lPLND	obturator nerve
SWOG 8710 [41]	lPLND	*Included only nodes sampled medial to the external iliac vein and obturator nodes
	sPLND	*Included the distal common iliac, external iliac, obturator, and hypogastric nodes.
Cleveland clinic [45]	lPLND	Prox.: bifurcation of the iliac vessels
		Distal: circumflex iliac vein
		Medial: obturator nerve
		Lateral: genitofemoral nerve
Bern university [45]	sPLND	Prox.: crossing of the ureters with the common iliac arteries
		Distal: inguinal ligament
		Medial: bladder wall
		Lateral: genitofemoral nerve
USC university [46]	sePLND	Prox.: inferior mesenteric artery
		Distal: circumflex iliac vein and Cloquet's node
		Lateral: genitofemoral nerve and the pelvic side wall
		Post.: obturator fossa with full exposure of the intrapelvic course of the obturator nerve (Marcille's triangle) and the internal iliac vessels
		*Also included removal of lymphatic tissue along the common iliac vessels, the distal vena cava/aorta to the IMA takeoff and complete dissection of the presacral space from the bifurcation of the aorta into the sacral fossa
LEA trial [18]	ePLND	Prox.: inferior mesenteric artery
		Distal: pelvic floor
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: pelvis and rectum nerve
	lPLND	Prox.: bifurcation of internal and external iliac artery
		Distal: pelvic floor
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: obturator nerve
		*Excluded the deep obturator nodes

SWOG S1011 trial [52]	ePLND	Prox.: aorta bifurcation up to inferior mesenteric artery
		Distal: pelvic floor
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: pelvis and rectum nerve
	sPLND	Prox.: bifurcation of internal and external iliac artery
		Distal: pelvic floor
		Medial: bladder wall
		Lateral: genitofemoral nerve
		Post.: obturator nerve
Bern university [46]	ePLND	Prox.: up to level between mid and upper third of common iliac vessels
		Distal: circumflex iliac vein and Cloquet's node
		Medial: tissue medial to internal iliac vessels
		Lateral: genitofemoral nerve and the pelvic side wall
		Post.: obturator fossa with full exposure of the intrapelvic course of the obturator nerve (Marcille's triangle) and the internal iliac vessels

In 2004, Herr et al. [44] analyzed the SWOG 8710 Randomized Neoadjuvant MVAC Chemotherapy Trial, which demonstrated the effectiveness of neoadjuvant chemotherapy using MVAC for MIBC. Sixteen percent of the patients in this study either received lPLND or did not receive PLND. Post-analysis showed that both lymph node-positive and negative patients who received sPLND had a significant decrease in local recurrence and improvement in 5-year survival rates, regardless of whether they received neoadjuvant chemotherapy, compared to patients who received lPLND (p=0.01, <0.001, respectively). Furthermore, this study found negative surgical margin, resecting ten or more lymph nodes, and neoadjuvant chemotherapy as significant survival and local recurrence predictors.

Various researchers have proposed the appropriate extent of PLND during radical cystectomy. Many retrospective studies have reported a correlation between the number of removed lymph nodes and improved disease-free and cancer-specific mortality as surrogate markers for optimal PLND [42,45-47]. Some authors have proposed removing a minimum number of lymph nodes for appropriate PLND [45,46,48]. However, the total number of removed lymph nodes is influenced by factors such as the extent of PLND, the surgeon's technique, the pathologist's efforts, patient diversity, and the use of LN-revealing solutions [49,50]. Therefore, the anatomical definition of PLND still holds significant importance (Table 1).

In 2008, Dhar et al. [51] reported a retrospective study of the clinical outcomes of ePLND at the University of Bern and lPLND at the Cleveland Clinic (Table 2). The authors reported that the lymph node metastasis rate was twice as high in the ePLND group than in the lPLND group. The 5-year DFS period of patients with pelvic lymph node metastasis was superior in the ePLND group, with 35% compared to 7% in the lPLND group. The authors reported that lPLND was associated with higher local progression rates and worse prognosis in patients with and without lymph node metastasis and that ePLND could lead to more accurate staging and improved survival rates in patients with localized BCa and BCa with pelvic lymph node metastasis. In 2011, Skinner et al. [52] compared the clinical outcomes of ePLND (primarily performed at the University of Bern) and standard extended PLND (sePLND, primarily performed at the University of Southern California) (Table 2). There was no significant difference in 5-year DFS (40% *vs.* 42%, p=0.55) and OS (34% *vs.* 38%, p=0.44) between ePLND and sePLND. The authors concluded that removing lymph nodes outside the pelvic area did not affect the oncological outcome, as patients with lymph node metastasis outside the pelvic area generally had a poor prognosis.

According to several meta-analyses up to 2018 [44,53,54], ePLND appeared to be better than sPLND in terms of accurate staging and improved survival. However, these results were based on non-randomized retrospective study data, and the limitations of previous studies must be considered. Therefore, prospective randomized clinical trials must clearly identify patients who can benefit from ePLND and prove its therapeutic impact.

For the first time, the results of the prospective, multi-institutional, randomized, 3-arm German LEA trial 18 were reported to evaluate the therapeutic effects of ePLND and lPLND in radical cystectomy [40]. Patients with locally resectable T1G3 or T2-T4aM0 were randomly allocated to either the ePLND group (boundary: Figure 1A, refer to Table 2) or the lPLND group (boundary: Figure 1B-1, refer to Table 2). The primary endpoint was DFS, and the secondary endpoints included CSS, OS, and complications. From February 2006 to August 2010, 401 patients were randomized (ePLND: 198, lPLND: 203). The number of target patients was set, assuming the removed lymph nodes would be >15% higher in the ePLND group than in the lPLND group. The median number of removed lymph nodes was 31 in the ePLND group and 19 in the lPLND group. ePLND did not demonstrate higher efficacy than lPLND in oncologic outcomes (5-year RFS 65% *vs.* 59%; Hazard Ratio (HR)=0.84 (95% Confidence Interval 0.58-1.22); p=0.36), CSS (5-year CSS 76 % *vs.* 65 %; HR=0.70; p=0.10), and OS (5-year OS 59% *vs.* 50%; HR=0.78; p=0.12).

Regarding complications, lymphedema of Clavien grade 3 or higher within 90 days after surgery was more frequently reported in the ePLND group. There was no difference between the two groups in other comparative items (30-day and 90-day mortality, major complications of Clavien grade 3 or higher). Additionally, the rate of lymph node metastasis was higher in the lPLND group than in the ePLND (28% *vs.* 22%), which differed from the expectation that more lymph node metastasis would be diagnosed in the ePLND group. However, there are several considerations in applying the results of this prospective randomized study to clinical practice. First, 14% of T1G3 patients were included in the patient cohort. Lymph node

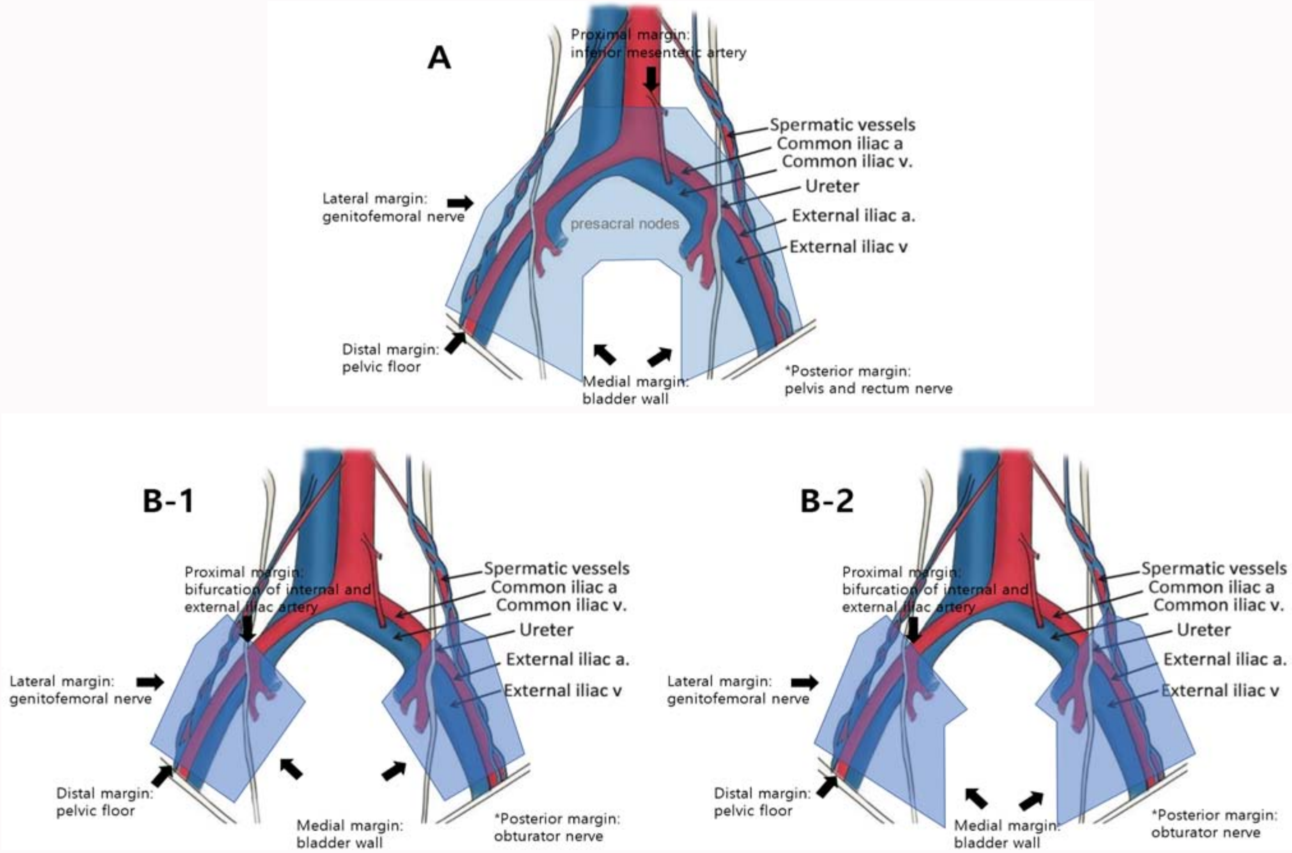

Figure 1: (A) Boundary of extended pelvic lymph node dissection for LEA and SWAG S-1011 trials, (B-1) Boundary of limited pelvic lymph node dissection for LEA trials, and (B-2) Boundary of standard pelvic lymph node dissection SWAG S-1011 trials.

metastasis is relatively rare in T1G3 patients, and the recurrence rate is generally lower than that of MIBC patients, which may dilute the effect of ePLND. Second, it is reasonable to consider that the IPLND group underwent sPLND. External and internal iliac nodal and obturator nodal dissections were included, and the number of removed lymph nodes was similar to the median number of known sPLND, which was 19 nodes [55,56]. Third, the target number of patients was inadequate because the criterion for improvement in 5-year RFS was too high, requiring more than 15% in the ePLND group compared to the lPLND group, which reduced the power of the test. The difference in 5-year RFS rates between ePLND and sPLND was reported to be 7% in several meta-analyses, and a sample size of >2,000 patients (1,225 patients per group; total of 2,250 patients) is required to demonstrate statistical significance with 80% power [57]. Fourth, only patients who did not receive neoadjuvant chemotherapy were included in the clinical trial to make the study population more homogeneous. However, neoadjuvant chemotherapy was administered as the standard treatment for MIBC patients. The exclusion of these patients from the study is significantly different from actual clinical practice, making it difficult to apply the study results directly to clinical practice. Despite these potential limitations, the LEA trial is the only prospective randomized phase 3 study comparing ePLND with lPLND in BCa. It emphasizes the importance of accurate patient selection and determination of the target number of patients when planning similar studies.

As an ongoing prospective study, there is a multi-institutional, randomized phase III study led by the SWOG group, called the SWOG S1011 trial [58], to compare the therapeutic effects of sPLND and ePLND in radical cystectomy. The study includes patients with T2-4a who received neoadjuvant chemotherapy. To control for confounding variables related to surgery, the study only included surgeons who have performed at least 50 radical cystectomies over the past 3 years and at least 30 per year. During radical cystectomy, one group underwent ePLND, and the other underwent sPLND (Figure 1A, 1B-2) (Table 2), and randomization was conducted during surgery. The primary endpoint was DFS, and the secondary endpoints were OS and morbidity. The study was designed to have 85% power to demonstrate statistical significance assuming the number of patients enrolled was sufficient to show a 10% improvement in 5-year DFS with ePLND compared to sPLND. From August 2011 to August 2022, 658 patients were randomized, and recruitment was completed earlier than expected in April 2017. The final results are currently being awaited during follow-up observation.

There are several differences to note when comparing the LEA trial and SWOG S1011 trial. First, the LEA trial included T1 BCa (T1-4a) patients, while the SWOG S1011 trial excluded them (T2-4a). Second, while the LEA trial did not include patients who received neoadjuvant chemotherapy, the SWOG S1011 trial enrolled 56% of patients who had undergone this treatment prior to surgery. This should be considered when interpreting the results of the SWOG S1011 trial, as there may be a lower likelihood of lymph node metastasis in the group that received neoadjuvant chemotherapy. Third, the range of the experimental group (ePLND) differed between the LEA trial (IMA) and the SWOG S1011 trial (aorta bifurcation up to IMA). The control group in the LEA trial received lPLND (proximally by the bifurcation of the internal and external iliac artery, distally by the pelvic floor, laterally by the genitofemoral nerve, and dorsally by the obturator nerve/excluded the deep obturator nodes). However, the control group in the SWOG S1011 trial received sPLND (proximally by the bifurcation of the internal and external iliac artery, distally by the pelvic floor, laterally by the genitofemoral nerve, and dorsally by the obturator nerve).

Conclusion

In MIBC, lymph node metastasis is important for determining adjuvant therapy, predicting prognosis, and deciding the interval for follow-up investigations. Bilateral PLND should be performed for diagnostic and staging purposes during radical cystectomy. The diagnostic PLND should include ePLND encompassing the common iliac lymph nodes, and PLND beyond the pelvic area may only carry unnecessary risks without diagnostic utility.

Many retrospective studies have reported that PLND impacts the prognosis of patients with lymph node involvement and those without lymph node involvement. However, there is still insufficient evidence to support the therapeutic role of ePLND, and there is controversy over the optimal range of PLND. The therapeutic role of ePLND and PLND after neoadjuvant chemotherapy should be waited for the results of the ongoing prospective study, the SWOG S1011 trial.

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