Acta Clin Croat (Suppl. 2) 2024; 63:35-39
doi: 10.20471/acc.2024.63.s2.5

Original Scientific Paper

THE ROLE OF LYMPHADENECTOMY IN RADICAL PROSTATECTOMY

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SUMMARY – The accuracy of evaluating lymph node invasion (LNI) in patients with prostate cancer (PC) can still be best achieved through pelvic lymph node dissection (PLND). The occurrence of LNI during radical prostatectomy (RP) with limited PLND (lPLND) is approximately 1-3%. This study presents the frequency of LNI in a cohort of patients with RP who underwent lPLND at our medical institution. Our patients primarily received open retro-pubic RP as a treatment for clinically localized PC. They were categorized into two groups based on whether they underwent PLND or not. We compared the clinical and pathological characteristics of both groups. There were 196 patients who underwent PLND and 149 patients who did not have PLND performed. On average, 4.19 lymph nodes were removed per patient. The incidence of positive nodes was found to be 8.7%. There was no lymphocele formation recorded in study cohort. The rate of positive nodes and the corresponding median number of nodes removed in our study were approximately the same as results reported in literature for lPLND. Although the consensus for extended PLND has been reasonably established, it still remains unclear which template is the most valuable for patients, and oncological benefits seem to be very limited.

Key words: *prostate cancer; radical prostatectomy; pelvic lymph node dissection*

Introduction

In 2022, prostate cancer (PC) ranked as the second most prevalent cancer among men, with nearly 1.4 million new cases reported globally. Furthermore, it stood as the fifth major contributor to cancer-related fatalities in men worldwide, resulting in approximately 375,000 deaths[1]. After confirmation of PC, a clinical staging of disease must be performed. Approximately 80% of patients with PC are diagnosed with organ-confined disease, 15% with regional metastasis, and 5% with distant metastasis[2]. Evaluating the presence of lymph node invasion (LNI) holds significant importance due to its negative impact on prognosis, specifically concerning biochemical recurrence and overall survival. Preoperative methods such as abdominopelvic CT scan or MRI are commonly utilized to assess LNI before surgery. Novel diagnostic techniques are also being investigated, such as PET-CT with different radiotracers. The improvement in diagnostic techniques of LNI has been notable, but there are still no satisfactory sensitivity and specificity levels[3]. Consequently, pelvic lymph node dissection (PLND) remains the most reliable method for accurately staging lymph node metastasis. However, the therapeutic benefits of PLND are still uncertain. This procedure carries potential risks of peri- and postoperative complications, longer operative time, and increased morbidity (4). Among the reported complications, lymphocele, which refers to the accumulation of lymphatic fluid in the retropubic space, is the one most commonly observed[5]. Various established risk factors associated

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with lymph node invasion (LNI) include preoperative PSA levels, clinical T stage, primary and secondary Gleason scores, and the percentage of positive biopsy cores. These factors are incorporated into several nomograms designed to predict the likelihood of LNI[6]. Nomograms are valuable tools that aid in decision-making and provide estimates of the probability of LNI. According to the guidelines of the European Association of Urology, extended PLND (ePLND) is recommended for patients with a predicted probability exceeding 5% according to the Briganti nomogram[7]. Incidence of LNI at RP depends on the extent of PLND. Incidence for limited PLND (lPLND) is around 1-3%, whereas for more extensive PLND it is up to 10% (8). In this study, we report the incidence of LNI in a patient cohort with RP who underwent lPLND at our institution.

Methods

A retrospective study was conducted at a single institution, encompassing the period from January 2020 to December 2021. The study focused on 345 patients who primarily underwent open retro-pubic radical prostatectomy as a treatment for clinically localized prostate cancer (PC). Based on the surgeon's judgment, the patients were divided into two groups: those who underwent pelvic lymph node dissection (PLND) (PLND group, n=196) and those who did not undergo PLND (no-PLND group, n=149). In the PLND group, the dissection boundaries included the area extending medially and caudally to the external iliac vein, encompassing the tendinous arch of the levator ani muscle and internal obturator muscle. This approach corresponds to a limited pelvic lymph node dissection (lPLND). All specimens were analyzed by a uropathologist. The diagnosis of cancer was established by transrectal needle biopsy. Prostate biopsies were not performed in a single institution. Evaluation of local tumor stage was established by digital rectal examination and was classified using clinical TNM classification. Preoperative serum samples of PSA were collected prior to prostatic manipulation. A lymphocele was recorded if it caused pelvic pain, leg edema, leg pain, or deep vein thrombosis.

Statistical analysis was performed using StatsoftStatistica v. 2.4.

Results

The total RP cohort consisted of 345 patients. Mean patient age was 67.3 years (range 49-76). A total of 196 (56%) patients underwent PLND (PLND group), and PLND was omitted in 149 (44%) patients (no-PLND group). The mean number of removed lymph node was 4.19 (median 4). Positive lymph nodes were found in 17 patients (8.7%). Patients treated with lPLND had significantly higher PSA (median 14.5 vs. 7.4, p<0.001), higher clinical stage tumor (clinical T2-T3: 84.2% vs. 31.5%, p<0.001), and higher biopsy ISUP grade group at diagnosis (grade group 3-5: 33.2% vs. 7.4%, p<0.001) compared with patients in whom PLND was omitted. Moreover, patients who underwent lPLND had significantly higher pathological tumor stage (T3-T4: 39.3% vs. 7.4, p<0.001) and higher ISUP group grade after RP (grade group 3-5: 60.2% vs. 23.5%, p<0.001) compared with patients without lPLND. There was no lymphocele formation recorded in the study cohort. Characteristics of the evaluable study cohort group are summarized in **Table 1**.

Discussion

Evaluation of LNI has been an essential component of the staging for patients with diagnosed localized prostate cancer. In certain cases, the presence of lymph node metastasis can contribute to a higher rate of biochemical recurrence following radical prostatectomy[3]. The prevalence of LNI correlates with tumor stage, biopsy tumor grade, and serum PSA levels. Different radiologic techniques such as CT and MRI are included to establish preoperative assessment of lymph nodes. Despite the uncertainties and potential risks associated with pelvic lymph node dissection (PLND), it remains the most accurate staging procedure for detecting lymph node invasion (LNI) and is considered a recommended approach for patients with intermediate or high-risk prostate cancer (PC). This procedure carries a risk of complications and should be avoided if the risk of LNI is low[7]. Patients should be carefully selected using available guidelines and predictive tools such as Briganti nomogram, Partin tables, Roach formula, etc. Another problem regarding PLND is its extent. The majority of studies have indicated that pelvic lymph node dissection (PLND) and the extent of dissection are associated with poorer intraoperative and perioperative outcomes. However, the current literature does not provide conclusive evidence regarding a direct therapeutic effect[4]. The European Association of Urology (EAU) recommends the use of extended pelvic lymph node dissection (ePLND), while the American Urological Association (AUA) and the National

Table 1. Baseline characteristics of study cohort

	lPLND	no-lPLND	p-value
Median age, yr (IQR)	66 (49-76)	68 (57-76)	
Median preoperative PSA, ng/ml (IQR)	14.5 (2.6-56.5)	7.4 (2.0-20.1)	p<0.001
Biopsy ISUP grade group, n (%)			
1	22 (11.2)	73 (49)	
2	109 (55.6)	65 (43.6)	p<0.001
3	48 (24.4)	11 (7.4)	
≥4	17 (8.8)	0	
Clinical tumor stage, n (%)			
T1c	31 (15.8)	102 (68.5)	
T2a	57 (29)	30 (20.1)	p<0.001
T2b	45 (22.9)	12 (8.1)	
T2c	61 (31.1)	5 (3.3)	
T3a	2 (1.2)	0	
T3b	0	0	
N stage, n (%)			
N0	179 (91.3)		
N1	17 (8.7)		
Median number of nodes removed, n (IQR)	4.19 (0-15)		
Number of positive nodes removed, n (%)			
0	179 (91.3)		
1	14 (7.1)		
2	3 (1.6)		
Lymphocele formation	0		
Final ISUP grade group, n (%)			
1	0	17 (11.4)	
2	78 (39.8)	97 (65.1)	
3	93 (47.4)	34 (22.8)	p<0.001
≥4	25 (12.8)	1 (0.7)	
Pathological tumor stage, n (%)			
T2	119 (60.7)	138 (92.6)	
T3a	34 (17.3)	9 (6)	p<0.001
T3b	43 (22)	2 (1.4)	
T4	0	0	

Institute for Health and Care Excellence (NICE) do not provide specific recommendations regarding the preferred approach to pelvic lymph node dissection (PLND)[3]. Some data suggest that ePLND may be necessary during radical prostatectomy to detect hidden metastases and could potentially have a positive impact on disease progression and long-term disease-free survival[9]. However, a randomized clinical trial conducted

by Touijer et al. did not find a significant difference in biochemical recurrence-free survival between patients who underwent ePLND and those who underwent limited PLND[10]. While there is a general consensus in favor of ePLND, the optimal template for performing this procedure remains uncertain. The oncological benefits of ePLND also appear to be limited in terms of improving patient outcomes[4]. Incidence of LNI at RP depends on the extent of PLND. The rate of positive nodes in our study was 8.7%, which is higher than observed in the literature for lPLND (8.7% vs. 1-6% for the incidence of positive nodes)[5,11-13]. The corresponding median number of nodes removed is approximately the same as results reported in other studies (4 vs. 3-8 nodes retrieved)[5,8,10,11,13]. It is important to note that prostatectomy ISUP grade group in this study did not differ significantly from the previously mentioned studies[5,8,10,11,13].

Postoperative complications are in positive correlation with the extent of dissection template. Patients who underwent ePLND were found to have a higher incidence of lymphoceles compared with those who underwent lPLND[4]. No lymphocele formation was recorded in our study cohort.

The limitations of this study were primarily related to its retrospective nature, which prevented us from analyzing all known clinically relevant factors for patients in our cohort. Another problem in this study was related to prostate biopsies. They were not performed in single institution, and specimens were not always analyzed by a uropathologist, but were sometimes by instead analyzed a general pathologist. This could have had an impact on the biopsy grade group. This is important, since the surgeon's decision to perform PLND is based on the characteristics of the patient before the operation. However, all RP specimens were analyzed by uropathologists at our institution. Given the tertiary care center nature of our institution, all the surgeons and uropathologists that contributed to the data in this study benefited from a high level of expertise and standardized protocols.

In conclusion, the incidence of LNI in the patient cohort with RP who underwent lPLND at our institution did not differ significantly from the results of other studies.

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Sažetak

ULOGA LIMFADENEKTOMIJE U RADIKALNOJ PROSTATEKTOMIJI

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Disekcija zdjeličnih limfnih čvorova (DZLČ) je još uvijek najprecizniji postupak utvrđivanja metastaza u limfnim čvorovima (LČ) kod bolesnika s karcinomom prostate (KP). Učestalost metastaza u LČ kod radikalne prostatektomije (RP) za ograničenu DZLČ je oko 1-3%. Cilj ove studije je prikazati incidenciju metastaza u LČ u skupini bolesnika kojima je bila učinjena RP i koji su bili podvrgnuti ograničenoj DZLČ u našoj ustanovi. Pacijenti su liječeni otvorenom retropubičnom RP za klinički lokalizirani KP. Pacijenti su stratificirani u dvije skupine: skupina kojima je rađena DZLČ i skupina kojima nije rađena. Uspoređene su kliničke i patološke karakteristike obje skupine.

Ograničena DZLČ je učinjena kod 196 pacijenata dok u 149 pacijenata nije učinjena. Broj izvađenih LČ je 4.19. Incidencija pozitivnih LČ je 8.7%. U istraživanoj skupini nije nađena limfokela.

Učestalost metastaza u LČ kod RP ovisi o opsegu same DZLČ. Stopa incidencije pozitivnih čvorova te medijan broja uklonjenih čvorova u našoj studiji je približno isti kao i u drugim studijama koje su proučavale ograničenu DZLČ. Iako se smatra kako je proširena DZLČ zlatni standard, još uvijek nije sasvim jasno utvrđeno koja vrsta DZLČ je najpogodnija za pacijente pošto su onkološki benefiti dosta ograničeni.

Ključne riječi: *karcinom prostate, radikalna prostatektomija, zdjelična limfadenektomija*