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UROONCOLOGY

Systematic Review

Is extended pelvic lymph node dissection for prostate cancer the only recommended option? A systematic over-view of the literature

Genişletilmiş pelvik lenf düğümü diseksiyonu prostat kanseri için önerilen tek seçenek mi? Literatürün sistematik gözden geçirilmesi

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ABSTRACT

Objective: Pelvic lymph node dissection (PLND) is performed alongside radical prostatectomy as the most accurate method of staging prostate cancer. Yet the potential therapeutic benefits of lymphadenectomy are yet to be confirmed.

Material and methods: A PubMed database search was performed to identify all papers comparing techniques for PLND or none. The primary outcome measure was long term oncological outcomes. Studies looking at men with clinically localized prostate cancer at the time of radical prostatectomy who received no adjuvant treatment were included. Previous reviews and single case reports were excluded. The subsequent available papers were then systematically reviewed.

Results: Limited PLND provides no benefit in low risk prostate cancer and is unlikely to provide a therapeutic benefit in higher risk groups either when compared with no PLND. Extended PLND may provide some therapeutic benefit, particularly in patients with occult metastases; however, the evidence base for this is not particularly strong and may be down to statistical phenomena.

Conclusion: When performed in prostate cancer patients, PLND should be extended, as it is a more accurate staging tool and may provide therapeutic benefit to some patients. However, to properly assess this, randomised controlled studies need to be performed in this area.

Keywords: Pelvic lymph node dissection; prostatectomy; prostate cancer; systematic review; outcomes.

ÖZ

Amaç: Radikal prostatektomiyle birlikte prostat kanserini evrelendirmenin en doğru yöntemi olarak pelvik lenf düğümü diseksiyonu (PLND) uygulanmaktadır. Buna rağmen lenfadenektominin potansiyel terapötik yararları henüz doğrulanmamıştır.

Gereç ve yöntemler: PLND teknikleri uygulanmış ve uygulanmamışları karşılaştıran makalelerin tümünü saptamak için bir PubMed veri tabanı araştırması yapılmıştır. Birincil sonuç ölçümü uzun vadede onkolojik sonuçlardı. Radikal prostatektomi sırasında adjuvan tedavi görmemiş klinik açıdan lokalize prostat kanserli erkekleri inceleyen çalışmalar bu derlemeye dahil edilmiştir. Önceki derlemeler ve tek olgu raporları çalışmaya alınmamıştır. Daha sonra ulaşılan makaleler de sistematik olarak gözden geçirilmiştir.

Bulgular: Düşük riskli prostat kanserinde sınırlı PLND herhangi bir yarar sağlamadığı gibi PLND olmamış hastalara göre daha yüksek risk gruplarında da terapötik yarar sağlaması mümkün değildir. Genişletilmiş PLND özellikle okült metastazları olan hastalarda bir miktar terapötik yarar sağlayabilir. Ancak bu tespite ilişkin kanıtların dayanağı özellikle güçlü olmadığı için istatistiksel anlam da taşımayabilir.

Sonuç: Prostat kanseri hastalarında uygulandığında, daha doğru bir evrelendirme aracı olduğu ve bazı hastalarda terapötik yarar sağlayabildiği için PLND'nin uygulama sahası genişletilmelidir Ancak, bu hususu uygun biçimde değerlendirmek için bu alanda randomize kontrollü çalışmaların yapılması gerekir.

Anahtar kelimeler: Pelvik lenf düğümü diseksiyonu; prostatektomi; prostat kanseri; sistematik gözden geçirme, sonuçlar.

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Introduction

In the management of prostate cancer (PCa), the role of pelvic lymph node dissection (PLND) at the time of radical prostatectomy has long been debated. Whilst it is reasonably well established as the best method for accurate staging of PCa[1], its role in treatment and whether it has any therapeutic benefit is still widely contested.[2] It has been proposed that lymphadenectomy may remove undetectable micrometastases and therefore potentially improve survival.[3] Yet the extent of PLND varies greatly between surgeons and centres, with some performing a limited PLND (lPLND), confined to the external iliac and obturator fossa areas, and others choosing an extended PLND (ePLND). Even then debate consider variability exists in the definition of ePLND with some surgeons removing the external iliac, hypogastric and obturator nodes and other including the pre sacral and pre sciatic nodes.[4] Risk of lymph node metastasis in PCa largely depends on the patient's risk group patients at the time of diagnosis.[5] In lower risk patients it is often felt that the risks of performing PLND outweigh any potential cases. Furthermore in comparison to other malignancy such as breast, a greater variation in the routes of lymphatic spread of cancer is found.[6] The goal of this review is to assess any available papers that look at comparing the effects of PLND on the outcomes of PCa treatment.

Material and methods

A series of PubMed searches were carried out between November and December 2015 using combinations of the following terms; pelvic lymph node dissection, lymphadenectomy, prostatectomy, prostate cancer, outcome, survival, and treatment. Filters were applied to exclude any studies not done in humans. The reference lists from any selected papers were also searched for relevant papers that may have been missed by the initial searches.

Papers for inclusion would look at men with clinically localized primary PCa at the time of radical prostatectomy. The papers would need to show a direct comparison between ePLND and lPLND, or between either of these and no dissection at all. lPLND was defined as removal of the exernal iliac and obturator nodes, and ePLND as the removal of these plus either the hyposgastic, pre-sciatic or pre-sacral nodes or any combination thereof. Patients would need to have not received any adjuvant therapy during the period of the study. Randomised controlled trials and prospective or retrospective analyses looking at men with PCa from all risk groups as stratified by D'Amico[5] would be included. All previous reviews were automatically excluded, as were single case reports, editorial pieces and titles that were not available in English or simply not available.

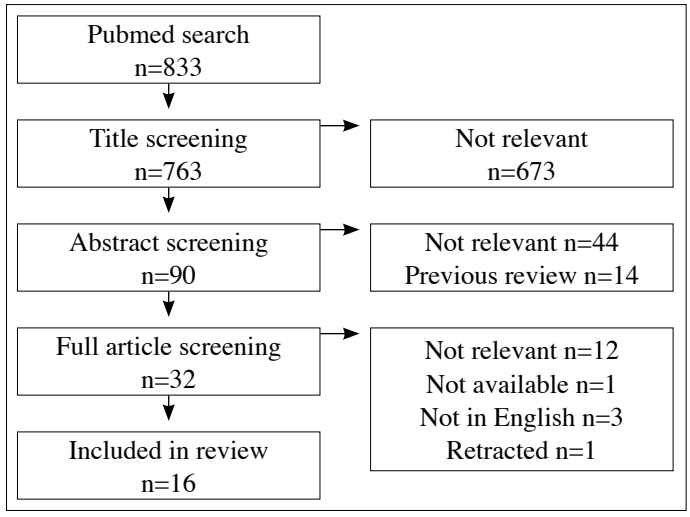

Figure 1. PRISMA flow diagram

The outcome measures of interest were: biochemical recurrence (BCR), defined as a prostate specific antigen reading of 0.2 or greater following radical prostatectomy, cancer specific survival (CSS). These were chosen as CSS would be the most definite way of assessing the outcome of therapy, but given the long follow up time required BCR could be used as an indicator of disease progression. The search technique is summarised in Figure 1.

Results

In total, sixteen studies were identified that compared PLND in terms of outcome. Twelve articles made a direct comparison between defined extents of PLND. Of these, seven[7-13] compared lPLND with no dissection at all and the remaining five[14-18] compared ePLND and lPLND, with one study[18] also including no PLND. In some of the studies, the term standard PLND was used but in these cases the extent matched that of lPLND and so will be referred to as lPLND here. Of the twelve, five were exclusively looking at patients in the low risk group, two looked at those at intermediate and high risk, one in exclusively high risk patients and one across all risk groups.

The remaining four[19-22] studies from the total of sixteen used the number of lymph nodes removed as a surrogate for the extent of dis section and were deemed to have a suitable format for inclusion in the review.

It is worth noting that there was one paper[23] that was included after the literature search but it had actually been retracted due to misconduct by one of the authors and was no longer available. A significant degree of clinical and methodological heterogeneity was seen across all studies which prevented pooled analysis of the results. Throughout the studies, there was a great degree

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Table 1. Summary data of all comparative studies

Paper	Year	Comparison	Total Pts	ePLND/ equivalent	lPLND/ equivalent	No PLND	Risk Groups	FU	BCRFS ePLND	BCRFS lPLND	BCRFS No PLND	p
Bivalacqua et al.[17]	2013	ePLND vs. lPLND	4265	2279	1986	-	All	126	30.1% @5 yrs	7.1% @5 yrs		0.018*
Kim et al.[16]	2013	ePLND vs. lPLND	464	170	294	-	Int. & High	36	77.8% @3 yrs	73.5% @3 yrs		0.497
Liss et al.[18]	2013	ePLND vs. lPLND vs. no PLND	492	54	231	207	All	11.6	29.6 % @0.8 yrs	14.7% @ 1.1 yrs	3.4 % @0.9 yrs	<0.001*
Mitsuzuka et al.[13]	2013	lPLND vs. no PLND	222	-	147	75	Low	26-60	-	87.6% @5 yrs	87.1% @5 yrs	0.65
Daimon et al.[12]	2012	lPLND vs. no PLND	139	-	85	54	Low	69.4	-	88.3% @7 yrs	82.4% @7 yrs	0.278
Jung et al.[14]	2012	ePLND vs. lPLND	200	45	155	-	High	24	-	-	-	-
Ku et al.[11]	2011	lPLND vs. no PLND	199	-	111	88	High	37.0	-	-	-	0.355
Schiavina et al.[22]	2011	>9 nodes vs. 0-9 nodes	470	211	259		Int & High		58.5% @10 yrs	46.4% @10 yrs		0.023*
Schiavina et al.[21]	2010	>9 nodes vs 1-9 nodes	614	319	295	-	All	62.5	Not reported	Not reported	-	0.019*
Berglund et al.[10]	2007	lPLND vs. no PLND	4693	-	3961	732	All	-	-	74% @5 yrs	70% @5 yrs	0.11
Weight et al.[9]	2007	lPLND vs. no PLND	336	-	140	196	Low	-	-	84% @10 yrs	88% @10 yrs	0.33
Joslyn and Konety[19]	2006	Lymph nodes removed vs. none	9182	-	-	-	All	+120	-	-	-	*
DiMarco et al.[20]	2005	<5 nodes vs. 5-9 vs. 10-14 vs. 15-19 vs. >19	7036	-	-	-	All	69.6	-	-	-	-
Bhatta-Dhar et al.[8]	2004	lPLND vs. no PLND	336	-	140	196	Low	60		86% @6 yrs	88% @6 yrs	0.28
Allaf et al.[15]	2004	ePLND vs. lPLND	4000	2135	1865	-	All	-	34.4% @5 yrs	16.5% @5 yrs		0.07
Fergany et al.[7]	2000	lPLND vs. no PLND	575	-	372	203	Low	38		91% @4 yrs	97% @4 yrs	0.16

Key: Pts: patients, FU: Average (median/mean) Follow up, BCRFS: Biochemical recurrence free survival Int: Intermediate Risk Group

of variance in the methodology used, including patient groups, length of follow up and outcome measures, which made direct comparison between the papers (with the exception of the updates) very challenging. Comparable data taken from the direct comparison studies are presented in Table 1.

lPLND vs. no PLND

Of the 7 studies studies that compared lPLND with no PLND in exclusively low risk patients, PLND showed no benefit in terms of BCR. Fergany et al.[7], Bhatta-Dhar et al.[8] and Weight et al.[9] were a series of papers following the same group of patients

over 4, 6 and 10 years respectively. At no stage did they find any significant difference in BCR free survival rates (BCRFS) between lPLND and none, finding 4, 6 and 10-year BCRFS rates of 91% vs. 97% (p=0.16), 86% vs. 88% (p=0.28), and 84% and 88% (p=0.33) respectively. Daimon et al.[12] looked at the same risk group but in 139 men who had received laparoscopic procedures and also saw no statistically significant difference, this time at 7 years (88.3% vs. 82.4%, p=0.278). Mitsuzuka et al.[13] looked at 222 Japanese men with low risk PCa and found the 5 year BCRFS rates to be nearly identical between the two groups (p=0.65).

When comparing lPLND with none in 4693 patients across all risk groups, Berglund et al.[10] also found no significant difference in BCRFS at 5 years (74% vs. 70%, p=0.11). Ku et al.[11] looked at lPLND compared with no PLND in 199 Korean men with high risk PCa and found no significant difference in BCRFS rates (p=0.355).

lPLND vs. ePLND

When comparing ePLND with lPLND, Allaf et al.[15] looked at 5 year BCRFS in 4000 patients across all risk groups. They failed to find any significant difference between the two techniques though they reported a trend towards increased survival in those who received ePLND (34.4% vs. 16.5, p=0.07). Further analysis showed that there was a significant difference in BCRFS at 5 years (42.9% vs. 10.0%, p=0.01) in a subgroup of men found to have positive lymph nodes in less than 15% of the nodes removed. In a later paper, Bivalacqua et al.[17] reported these results with a follow up of 10.5 years. They showed a significant finding for 5-year BCRFS rates at 30.1% vs. 7.1% (p=0.018) and a trend towards improved CSS at 10 years for the ePLND group (83.6% vs. 52.6%, p=0.199). In subsequent analysis with Cox proportional hazard models, the proposed benefit to BCRFS lost its significance though they still reported a trend, (hazard ratio (HR): 0.596; 95% confidence interval (CI) 0.313-1.034; p=0.064) and there was no difference seen for CSS (HR: 0.495; CI 0.163-1.504;p=0.215). Again, in the subset of patients with node positive disease and less than 15% involvement in sampled nodes, they reported significant differences in BCRFS at 5 years, with the ePLND subgroup rate at 39.4% and the lPLND rate at 0.0% (p=0.003). This gave a HR of 0.350 (CI: 0.150-0.819; p=0.016).

Liss et al.[18] looked at ePLND compared with lPLND during robot assisted radical prostatectomy and also compared this to those who received no PLND. With 492 patients across all risk groups they found that ePLND was significantly associated with an increased risk of BCR (p=0.001, depicted in a Kaplan-Meier graph). However after multivariate analysis adjusting for the fact that high-risk patients were more likely to receive an ePLND this association disappeared (p=0.294).

Kim et al.[16] looked at ePLND versus lPLND in 464 intermediate and high-risk patients that received robot assisted surgery. They propensity score matched the groups to try and eliminate some of the bias associated with retrospective analysis. They found that in the whole cohort the 3 year BCRFS in the ePLND group was lower than the lPLND group (72.7% vs. 79.8%, HR: 1.48, CI 1.00-2.18, p=0.048), however, in the matched cohort they reported that this reversed and suggested a trend towards favouring ePLND (77.8% vs. 73.5%, HR: 0.85, CI0.52-1.36, p=0.497) although this wasn't statistically significant.

When exclusively looking at 200 patients from the high-risk group, Jung et al.[14] showed greater rates of diagnosis of lymph node metastasis with ePLND but failed to show improved BCRFS compared to lPLND. The study was limited by the median follow up was just 24 months (interquartile range (IQR): 15-34) and 13 months (IQR: 10-17) respectively.

In the papers that used the number of nodes removed as a surrogate for the extent of dissection, Joslyn and Konety[19] identified 9,182 patients in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program who had undergone radical prostatectomy with a recorded number of lymph nodes removed and a minimum 10 years follow up. They found that CSS was improved in all patients that received PLND and had more than 4 nodes removed compared to 3 or less (HR: 0.77, CI 0.64-0.93, p=0.0069), and that CSS in patients found to have negative nodes after PLND improved if 10 or greater nodes were removed (HR: 0.85 CI, 0.72-0.99, p=0.03282).

Similarly, Schiavina et al.[21] found that in node negative patients, those with 10 or greater nodes removed had improved BCRFS than those with less taken (HR 0.564, CI 0.390-0.814, p=0.002). Another paper from the same author and institution[22] looking at intermediate and high-risk groups found that 10 or greater nodes removed was associated with a benefit to BCRFS rates at 10 years here too (58.5% vs. 46.4%, p=0.023). They also reported significance when looking at 33 patients found to have less than 2 positive nodes, with 10-year BCRFS rates of 43.3% for those with greater than 10 nodes removed compared to 0.0% for those with 1-9 nodes removed (p=0.014). Conversely, DiMarco et al.[20] found that when looking at 7036 patients with negative lymph nodes over a median follow up of 69 months, there was no association between increased lymph node dissection and improved BCRFS across all risk groups (Risk ratio: 0.99, CI 0.98-1.02, p=0.062).

Discussion

With PCa being the highest incidence cancer in men it is vital that treatment is effective. It is important to assess if PLND is part of the therapy, and not just in the staging the disease. Bader

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et al.[3] found PCa patients treated with surgery alone had disease free rates at ten years that compared favourably with those who received adjuvant treatment. They theorised that PLND may remove occult metastases from patients and prevent progression or recurrence. The aim of this review has been to assess the available data that directly compares the extents of PLND performed.

From the papers reviewed here, Fergany et al.[7], Bhatta-Dhar et al.[8], Weight et al.[9], Daimon et al.[12] and Mitsuzuka et al.[13] all conclude that there is no need to perform lPLND in low risk PCa patients. There are a number of issues with all these papers beyond the selection bias that comes with their retrospective approach. All were performed in single centres and have fairly low number of patients included. Despite this, their results were consistent and there are no studies that disagree with their findings. Similarly, Berglund et al.[10] and Ku et al.[11] found no benefit to lPLND across other risk groups so it would seem sound to conclude that there is no need to perform lPLND in any patient with PCa. This is supported further by other studies that show the use of just lPLND removes significantly less lymph nodes than ePLND and is not as accurate a staging tool.[24] Concerns that ePLND may cause more complications appear to be unfounded as recent studies show a similar incidence of complications between the two extents.[24,25] Whether ePLND can be of benefit to low risk PCa patients cannot be assessed as no studies have looked into this area, however, current European guidance states that if PLND is to be performed at all it should be extended[26] but there is no need to perform PLND in men from the low risk group as they are at very low risk of metastasis[27] and potential complications outweigh any benefits.

In the case of ePLND, evidence is inconclusive. Jung et al.[14] stated that there was no extra benefit in performing an extended dissection, however, the follow up time used was too short and while a supporting paper by DiMarco et al.[20] had an appropriate length of follow up time at 5.8 years and a suitable study size, its use of number of nodes as a surrogate for the extent of PLND and variability in the PLNDs performed by the 5 surgeons make firm conclusions difficult to draw. Its findings are also at odds with the other papers using similar methods. Joslyn and Konety[19] and the two papers from Schiavina et al.[21,22] also used the surrogate measure for dissection extent but did find an improvement in outcomes. They also both found particular improvement in patients who had minimal positive nodal involvement, which was echoed in Allaf et al.[15] and the follow up to this paper.[17] It is possible that in these patients with minimal disease, the removal of more nodes from more sites can remove micrometastases undetectable at biopsy and therefore completely remove the disease. This still however needs to be approached cautiously due to a statistical phenomenon called the Will Rogers effect, in which the moving of data from one group to another has the effect of raising the average in both. In relation to these studies, patients who received only lPLND may have been incorrectly classified as having node negative disease that would have been diagnosed with a more extensive dissection. As the patients in these studies did not receive any adjuvant hormonal or radiotherapy, the perception could be one of an improved outcome due to the ePLND when it is actually down to stage migration.

The studies as a whole have many issues. The most striking being that they are all retrospective analyses. This makes all of them open to various biases, particularly selection bias and information bias that could confound results. Another issue is that no power calculations are given in any of the papers, with only two[19,20] mentioning that they believed their study to be suitably powered. The number of patients included in the majority was below 500 patients, and of the five that had in excess of 4000 patients, 3 looked at data across a range of surgeons without clarifying what the exact techniques of the surgeons were. The largest study[19] used a database that lacked information on whether patients had also been treated with adjuvant hormonal therapy, which the other studies had all used as an exclusion criterion when selecting patients, which could again confound results.

Furthermore, the outcome measure for the vast majority of studies was BCR, with only Bivalacqua et al.[17] and Joslyn and Konety[19] looking at CSS. Whilst BCR is a helpful endpoint and can be used clinically to find PCa recurrence well before metastatic disease, many men who have BCR may not experience any symptoms associated with a recurrence of PCa and likewise many will not die from it.[28] How clinically relevant BCR therefore is in terms of measuring the therapeutic benefit of PLND is questionable. The far more meaningful endpoint would be CSS, but as the course of PCa can be in excess of 15 years[29] this was well beyond the design of the studies featured here and any future study would require a lot of long term planning.

It is worth noting that a review in 2005 on the role PLND in PCa[30] acknowledged the potential therapeutic benefit but stated that randomised controlled studies would be required to properly assess this, and yet a decade later none have been done. To date, the only randomised study in the area was performed by Clark et al.[31] in 2003 where they performed both ePLND and lPLND in the same patients, but did not look at BCR rates. With this lack of robust studies, it is interesting to note that two trials are listed on ClinicalTrials.gov that will randomise patients to either ePLND or lPLND and the results from these will be awaited with interest.

In conclusion, from this limited data set, it is possible to conclude that lPLND is of no therapeutic benefit during radical prostatectomy for prostate cancer. An ePLND may have a therapeutic benefit in terms of BCR, particularly in a subset of patients with minimal nodal disease, and in keeping with current guidelines

when PLND is performed in intermediate and high risk patients it should be extended. However, the evidence for any potential benefit is not strong and may be down to stage migration from more accurate staging of the cancer and whether any benefit in BCR reduction translates into increased cancer specific survival remains to be seen. Randomised controlled studies are needed to establish answers to these questions but as these are awaited, ePLND can continue to be used in intermediate and high-risk patients as the most accurate staging method for prostate cancer.

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References

1. Burkhard FC, Studer UE. The role of lymphadenectomy in high risk prostate cancer. World J Urol 2008;26:231-6. [CrossRef]
2. Wagner M, Sokoloff M, Daneshmand S. The role of pelvic lymphadenectomy for prostate cancer--therapeutic? J Urol 2008;179:408-13.
3. Bader P, Burkhard FC, Markwalder R, Studer UE. Disease progression and survival of patients with positive lymph nodes after radical prostatectomy: is there a chance of cure? J Urol 2003;169:849-54.
4. Briganti A, Blute ML, Eastham JH, Graefen M, Heidenreich A, Karnes JR, et al. Pelvic lymph node dissection in prostate cancer. Eur Urol 2009;55:1251-65. [CrossRef]
5. D'Amico AV. Combined-modality staging for localized adenocarcinoma of the prostate. Oncology (Williston Park). 2001;15:1049-75.
6. Gil-Vernet JM. Prostate cancer: Anatomical and surgical considerations. Br J Urol 1996;78:161-8. [CrossRef]
7. Fergany A, Kupelian PA, Levin HS, Zippe CD, Reddy C, Klein EA. No difference in biochemical failure rates with or without pelvic lymph node dissection during radical prostatectomy in low-risk patients. Urology 2000;56:92-5. [CrossRef]
8. Bhatta-Dhar N, Reuther AM, Zippe C, Klein EA. No difference in six-year biochemical failure rates with or without pelvic lymph node dissection during radical prostatectomy in low-risk patients with localized prostate cancer. Urology 2004;63:528-31. [CrossRef]
9. Weight CJ, Reuther AM, Gunn PW, Zippe CR, Dhar NB, Klein EA. Limited pelvic lymph node dissection does not improve biochemical relapse-free survival at 10 years after radical prostatectomy in patients with low-risk prostate cancer. Urology 2008;71:141-5. [CrossRef]
10. Berglund RK, Sadetsky N, DuChane J, Carroll PR, Klein EA. Limited pelvic lymph node dissection at the time of radical prostatectomy does not affect 5-year failure rates for low, intermediate and high risk prostate cancer: Results from CaPSURE. J Urol 2007;177:526-30. [CrossRef]
11. Ku JH, Jeong CW, Park YH, Cho MC, Kwak C, Kim HH. Biochemical recurrence after radical prostatectomy with or without pelvic lymphadenectomy in korean men with high-risk prostate cancer. Jpn J Clin Oncol 2011;41:656-62. [CrossRef]
12. Daimon T, Miyajima A, Maeda T, Hattori S, Yasumizu Y, Hasegawa M, et al. Does pelvic lymph node dissection improve the biochemical relapse-free survival in low-risk prostate cancer patients treated by laparoscopic radical prostatectomy? J Endourol 2012;26:1199-202.
13. Mitsuzuka K, Koie T, Narita S, Kaiho Y, Yoneyama T, Kawamura S, et al. Is pelvic lymph node dissection required at radical prostatectomy for low-risk prostate cancer? Int J Urol 2013;20:1092-6.
14. Jung JH, Seo JW, Lim MS, Lee JW, Chung BH, Hong SJ, et al. Extended pelvic lymph node dissection including internal iliac packet should be performed during robot-assisted laparoscopic radical prostatectomy for high-risk prostate cancer. J Laparoendosc Adv Surg Tech A 2012;22:785-90. [CrossRef]
15. Allaf ME, Palapattu GS, Trock BJ, Carter HB, Walsh PC. Anatomical extent of lymph node dissection: Impact on men with clinically localized prostate cancer. J Urol 2004;172:1840-4. [CrossRef]
16. Kim KH, Lim SK, Kim HY, Shin TY, Lee JY, Choi YD, et al. Extended vs standard lymph node dissection in robot-assisted radical prostatectomy for intermediate- or high-risk prostate cancer: A propensity-score-matching analysis. BJU Int 2013;112:216-23. [CrossRef]
17. Bivalacqua TJ, Pierorazio PM, Gorin MA, Allaf ME, Carter HB, Walsh PC. Anatomic extent of pelvic lymph node dissection: Impact on long-term cancer-specific outcomes in men with positive lymph nodes at time of radical prostatectomy. Urology 2013;82:653-8. [CrossRef]
18. Liss MA, Palazzi K, Stroup SP, Jabaji R, Raheem OA, Kane CJ. Outcomes and complications of pelvic lymph node dissection during robotic-assisted radical prostatectomy. World J Urol 2013;31:481-8. [CrossRef]

Turk J Urol 2016; 42(4): 240–6
DOI:10.5152/tud.2016.52893

19. Joslyn SA, Konety BR. Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. Urology 2006;68:121-5. [CrossRef]
20. DiMarco DS, Zincke H, Sebo TJ, Slezak J, Bergstralh EJ, Blute ML. The extent of lymphadenectomy for pTXNO prostate cancer does not affect prostate cancer outcome in the prostate specific antigen era. J Urol 2005;173:1121-5. [CrossRef]
21. Schiavina R, Bertaccini A, Franceschelli A, Manferrari F, Vagnoni V, Borghesi M, et al. The impact of the extent of lymph-node dissection on biochemical relapse after radical prostatectomy in node-negative patients. Anticancer Res 2010;30:2297-302.
22. Schiavina R, Manferrari F, Garofalo M, Bertaccini A, Vagnoni V, Guidi M, et al. The extent of pelvic lymph node dissection correlates with the biochemical recurrence rate in patients with intermediate- and high-risk prostate cancer. BJU Int 2011;108:1262-8. [CrossRef]
23. Ji J, Yuan H, Wang L, Hou J. Is the impact of the extent of lymphadenectomy in radical prostatectomy related to the disease risk? A single center prospective study. J Surg Res 2012;178:779-84. [CrossRef]
24. Heidenreich A, Ohlmann CH, Polyakov S. Anatomical extent of pelvic lymphadenectomy in patients undergoing radical prostatectomy. Eur Urol 2007;52:29-37. [CrossRef]
25. Heidenreich A, Varga Z, Von Knobloch R. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: High incidence of lymph node metastasis. J Urol 2002;167:1681-6. [CrossRef]
26. Mottet N, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, et al. EAU guidelines on prostate cancer. part II: Treatment of advanced, relapsing, and castration-resistant prostate cancer. Eur Urol 2011;59:572-83. [CrossRef]
27. Abdollah F, Suardi N, Gallina A, Bianchi M, Tutolo M, Passoni N, et al. Extended pelvic lymph node dissection in prostate cancer: A 20-year audit in a single center. Ann Oncol 2013;24:1459-66. [CrossRef]
28. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA 1999;281:1591-7. [CrossRef]
29. Bill-Axelson A, Holmberg L, Garmo H, Rider JR, Taari K, Busch C, et al. Radical prostatectomy or watchful waiting in early prostate cancer. N Engl J Med 2014;370:932-42. [CrossRef]
30. Burkhard FC, Schumacher M, Studer UE. The role of lymphadenectomy in prostate cancer. Nat Clin Pract Urol 2005;2:336-42. [CrossRef]
31. Clark T, Parekh DJ, Cookson MS, Chang SS, Smith ER Jr, Wells N, et al. Randomized prospective evaluation of extended versus limited lymph node dissection in patients with clinically localized prostate cancer. J Urol 2003;169:145-8. [CrossRef]