

Clinical value of extended pelvic lymph node dissection in patients subjected to radical prostatectomy

Jakub Dobruch, Sebastian Piotrowicz, Michał Skrzypczyk, Tomasz Gołąbek, Piotr Chłosta, Andrzej Borówka

Center of Postgraduate Medical Education, Otwock, Poland

Videosurgery Miniinv 2014; 9 (1): 64–70

DOI: 10.5114/wiitm.2014.40986

Abstract

Introduction: Extended pelvic lymph node dissection (ePLND) is advised to complement radical prostatectomy (RP) in intermediate and high risk prostate cancer patients.

Aim: To assess the risk of nodal involvement in patients subjected to laparoscopic radical prostatectomy and to characterize the group of patients with lymph node (LN) metastases.

Material and methods: Data of patients subjected to laparoscopic radical prostatectomy with ePLND between February 2011 and June 2013 were analyzed. The LN that were removed included presacral nodes, common, external and internal iliac nodes and obturator ones.

Results: Mean number of removed LNs was 19. Metastases within LN were found in 13 (16.6%) patients. In comparison to those without LN involvement, patients who were found to have LN metastases had a greater number of positive biopsy cores (3.7 vs. 5.3, $p < 0.01$), maximum percentage of cancer in biopsy core (47.0 vs. 67.6, $p < 0.01$), greater biopsy and specimen Gleason scores (7.0 vs. 7.7 and 7.0 vs. 7.8) and more frequently advanced clinical and pathological stage. The most frequent landing sites of prostate cancer were obturator and presacral nodes (100% and 38%). Eleven patients (85%) among those with positive LN had locally advanced disease.

Conclusions: The risk of LN metastases in intermediate and high risk prostate cancer patients is significant. Therefore, if radical prostatectomy is chosen, ePLND should be performed. The majority of patients with involvement of pelvic LN have locally advanced disease which would refer them to adjuvant radiation if managed without nodal dissection.

Key words: extended pelvic lymph node dissection, laparoscopic radical prostatectomy, prostate cancer.

Introduction

Prostate cancer (PCa) is one of the most common malignancies found in men. In 2012, 241,740 new PCa cases were registered in the USA [1]. Organ confined at the beginning, the cancer gradually infiltrates periprostatic tissues and metastasizes through blood and lymphatic vessels [2]. Lymph nodes (LN) are found to be one of the most frequent landing sites of PCa.

Radical prostatectomy (RP) is the mainstay therapy of patients with localized PCa. Although many efforts have been undertaken to identify sentinel LN

during RP, wide pelvic lymphadenectomy remains the most accurate way of regional LN status assessment. Therefore, in intermediate and high risk prostate cancer, RP is recommended to be complemented with extended pelvic lymph node dissection (ePLND) [3]. If done so, positive LN are identified in up to 46% of men [4]. One out of five of them does not experience prostate-specific antigen (PSA) below 0.2 ng/ml [5]. The phenomenon would be explained by the presence of clinically unidentified distant metastases rather than improper surgery.

Address for correspondence

Jakub Dobruch MD, PhD, Centre of Postgraduate Medical Education, European Health Centre Otwock, 14/18 Borowa St, 05-400 Otwock, Poland, phone: +48503072230, e-mail: kubadobr@wp.pl

In recent years, dynamic improvement of minimally invasive techniques involved in the management of patients with cancers has been observed [6, 7]. Currently, the majority of radical prostatectomies in western countries are performed with the endoscopic approach. However, there is controversy that technical difficulty and extraperitoneal access to RP may compromise surgical radicality with respect to ePLND. New surgical techniques must allow the surgeon to adhere to all established surgical principles and facilitate the necessary steps to complete the planned procedure. To our knowledge, the role of laparoscopic extended pelvic LN dissection in PCa remains to be clarified.

It is reasonable that those who were found to have LN involved after radical prostatectomy would benefit from systemic therapy as the disease is already disseminated [8]. In contrast, those who were found after RP to have locally advanced disease, especially those with positive surgical margins, yet no LN infiltration, would benefit from local radiation [9]. The role of locoregional adjuvant therapy in patients with positive LN requires further investigation.

Aim

In our study, we present the technique of extended laparoscopic pelvic LN dissection in patients subjected to radical prostatectomy. Its perioperative morbidity and early results with clinical value are also described.

Material and methods

The data of all 165 consecutive men subjected to radical prostatectomy between February 2011 and June 2013 were prospectively collected and evaluated. Seventy-eight patients (47.3%) had extended, endoscopic pelvic LN dissection in complement to radical prostatectomy. Extended pelvic LN dissection was done only in subjects with intermediate or high risk, localized prostate cancer, specifically in those with PSA above 10 ng/ml, Gleason score (Gls.) ≥ 7 , or clinical stage of prostate cancer \geq cT2b. All patients gave their informed consent to be included in the database.

Surgical technique

In supine, tilted position an umbilical incision was made and 12 mm Hg pneumoperitoneum was created with a Veress needle. Five trocars were

placed: two 10 mm and three 5 mm. Extended pelvic LN dissection preceded radical excision of the prostate. The anatomic boundaries of LN removal were: the aortic bifurcation proximally, the node of Cloquet distally, the genito-femoral nerve laterally and the bladder medially. At the beginning the peritoneum was incised along umbilical ligaments and the ureter was identified and transposed medially to expose the presacral space (Photo 1). The LN in the area below the aortic bifurcation were then removed and named "presacral" (Photo 1). When possible, proximal and distal lymphatic extents were clipped. After common iliac artery dissection lymphatic tissue located laterally and superiorly to iliac vessels' bifurcation were removed and named "common iliac". The next lymphatic package was isolated from the area above external iliac vessels and medially to the genito-femoral nerve and named "external iliac" (Photo 2). The "obturator" LN were removed last, frequently together with "internal iliac" as they coalesce commonly after dissection performed laterally to the external iliac vessels and medially to pelvic floor muscles (Photo 3).

All specimens were removed separately through a 10 mm trocar incision and sent for histological evaluation within containers named appropriately. In cases of large LN packages EndoCatch bags were used to retrieve the specimens.

After ePLND, resection of the prostate was performed. The bladder was mobilized to allow free excess into the Retzius space but it was not detached from the abdominal wall completely. After prostate removal and filling the bladder with 200 ml of saline solution tightness of the anastomosis was con-



Photo 1. Presacral area after lymph node dissection

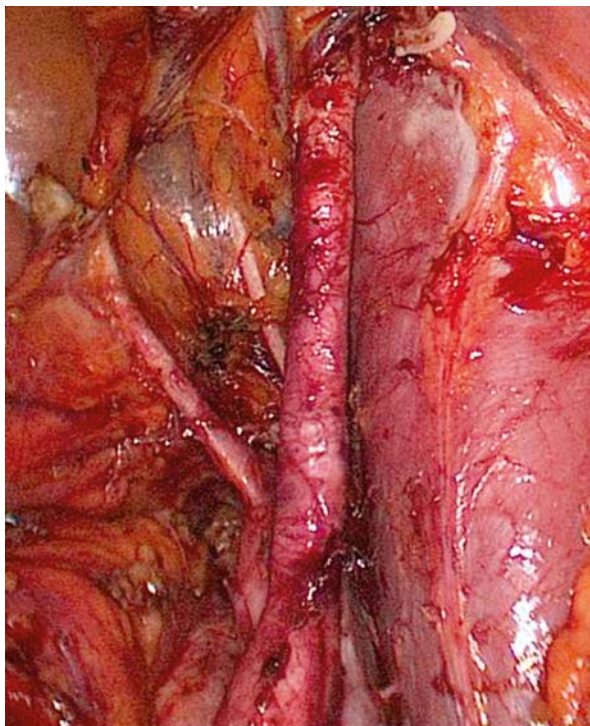


Photo 2. Template after removal of common and external iliac nodes

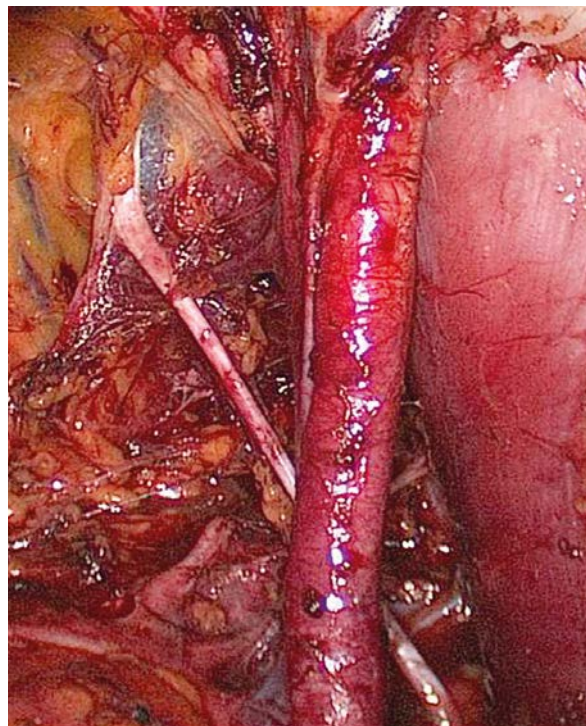


Photo 3. Obturator fossa after lymphatic tissue removal

firmed. The drain was left in the pelvis and removed on the second postoperative day. Before removal, when the output exceeded 150 ml/day in order to exclude urine leakage creatinine concentration was checked.

Statistical analysis

Comparison among different clinicopathological features was performed with χ^2 and Student *t*-tests. A test with $p \leq 0.05$ was considered significant.

Results

Mean (median) number of LN removed was 19 [19]. Lymph nodes metastases were found in 13 (16.6%) patients. In comparison to those without LN involvement, patients who were found to have LN metastases had a greater number of positive biopsy cores (3.7 vs. 5.3, $p < 0.01$), maximum percentage of cancer in biopsy core (47.0 vs. 67.6, $p < 0.01$), greater biopsy and specimen Gleason scores (7.0 vs. 7.7 and 7.0 vs. 7.8) and more frequently advanced clinical and pathological stage (Table I). The most common locations of metastases were obturator and presacral nodes (Table II). There was no patient who had nodal

infiltration without involvement of obturator nodes. Conversely there was no patient who had invasion of internal iliac nodes when assessed separately. In 12 (92%) cases of LN positivity, the primary tumor was present in both lobes of the prostate specimen. Only 1 patient (Gls. 8, pT2b sin) had metastases within presacral nodes located contralateral to the primary tumor within the prostate. The majority (69%) of patients had positive nodes on both sides.

Eleven patients (85%) among those with positive LN had locally advanced disease. This would potentially suggest referral for adjuvant radiation if no LN would be removed during surgery. Prostate-specific antigen assessed after 6 weeks did not reach values below 0.2 in 7 (54%) cases with LN metastases and in only 1 patient (1%) without nodal involvement.

The mean hospitalization time was 4 days. There was no major complication which would result from extended pelvic LN dissection. The most frequent one was lymphocele which required percutaneous drainage in only 1 case. The patient had the drain left after surgery kept in place until the output was lower than 50 ml. The policy of the drainage has changed. It is removed on the second postoperative day regardless of the amount of lymphatic collec-

Table I. Descriptive data of entire cohort

Parameter	Lymph node status		Entire cohort	Value of <i>p</i>
	Lymph node positive	Lymph node negative		
Number of patients (rate)	13	65	78	NA
Age, mean	62	62.4	62.3	NS
PSA, mean	15.2	12.2	12.7	NS
PSAD, mean	0.34	0.33	0.33	NS
Prostate volume, mean	48.6	43	42.1	NS
Abnormal DRE	13 (100%)	63 (96%)	76 (97%)	NS
Abnormal TRUS	13 (100%)	53 (81%)	66 (84%)	NS
Number of positive biopsy cores	5.29	3.75	3.5	< 0.01
Maximum percentage of cancer in biopsy core	67.6	47	50.4	< 0.01
Biopsy Gleason score	7.7	7.0	7.2	0.01
Clinical stage:				
Organ confined	6 (46%)	49 (75%)	55 (70%)	0.04
Locally advanced	7 (54%)	16 (25%)	23 (30%)	
Pathological stage:				
T2a	0	4 (6%)	4 (5%)	0.04
T2b	1 (8%)	4 (6%)	5 (6%)	
T2c	0	33 (51%)	33 (42%)	
Organ confined	1 (8%)	41 (63%)	42 (54%)	
T3a	2 (15%)	13 (20%)	15 (19%)	
T3b	10 (77%)	10 (15%)	20 (26%)	
T4	0	1 (1.5%)	1 (1%)	
Locally advanced	12 (92%)	24 (37%)	36 (46%)	
Surgical margins:				
Positive	3 (23%)	9 (14%)	12 (15%)	NS
Negative	10 (77%)	56 (86%)	66 (85%)	
Specimen Gleason score	7.8	7.0	7.1	< 0.01

PSAD – prostate specific antigen density, DRE – digital rectal examination, TRUS – transrectal ultrasound

tion. There has been no lymphocele since then. Seven patients were found to have mild edema of the lower extremities.

Discussion

Our study presents the technique of laparoscopic, pelvic LN dissection that completes radical

prostatectomy. The endoscopic approach completely facilitates all surgical steps necessary to remove entire lymphatic tissue from the pelvis that might be infiltrated by prostate cancer. It allowed us to detect the presence of LN invasion in 13 (16.6%) of our patients. According to published results the rate of LN metastases ranges from a few to more than 40% of radical prostatectomy cases

Table II. Characteristics of removed lymph nodes

Removed lymph nodes	Mean number of removed nodes	Percentage positive among removed lymph nodes	Percentage positive among entire cohort of infiltrated lymph nodes
Presacral	2.8	28	38
Common iliac	5.0	10	8
External iliac	7.5	23	15
Obturator	7.0	26	100
Internal iliac	2.0	0	0

Table III. Series of extended pelvic lymph node dissections during radical prostatectomy

Author	Type of surgery	Number of patients	LNI rate (%)
Abdollah [10]	RRP	3115	10.8
Daneshmand [11]	RRP	1936	12.1
Palapattu [12]	RRP	3264	4.4
Joniau [13]	RRP	74	46
Jung [14]	RARP	45	22.2
Feicke [15]	RARP	99	16
Lattouf [16]	LRP	35	31.4
Wyler [17]	LRP	123	17
Meinhardt [18]	LRP	121	40

RRP – retropubic radical prostatectomy, RARP – robot-assisted radical prostatectomy, LRP – laparoscopic radical prostatectomy, LNI – lymph node infiltration

(Table III). We and others have shown that it is associated with several clinical and pathological features that characterize the cancer including high PSA, periprostatic infiltration and Gleason score. It is apparent that all mirror unfavorable biological cancer behavior. Although the differences among the studies might reflect different populations of patients and their cancers qualified for surgery the rate of LN involvement may also depend on several facts not related to cancer itself. The most important one is the surgical template that is used to remove the tissue with LN. There is a limited number of studies that include entire pelvic lymphatic tissue in the pathologic analysis in patients subjected to radical prostatectomy [19]. Among several open, robotic and laparoscopic techniques there are only a few that truly incorporate an extended template during ePLND in patients with prostate cancer [16, 17, 19, 20]. Even though the authors describe extended pelvic LN dissection, it is uncommon to

remove presacral nodes as their location makes surgery more demanding during endoscopic procedures [16, 17]. We have found metastases in presacral nodes in 18% of cases. The majority of studies define ePLND as the removal of obturator, hypogastric and external iliac nodes [16], which is described as standard LN dissection by others [21]. We are among the few who include in the dissection the presacral and common iliac areas which together with previously mentioned lymphatic tissue form the template named extended pelvic LN dissection.

The wider the template, the greater the number of LNs removed. According to EAU Guidelines [3], the number of LN dissected in patients subjected to radical prostatectomy should exceed 20. In our cohort the mean number of removed LN is 19. However, having the same template in different patients we have noticed its wide range (6–34). It was shown that quality of pathological assessment and the usage of immu-

nohistochemical and other sophisticated techniques influence the number of LN found and assessed in the specimen [22]. We have also noticed that separate removal of specified pelvic LN packages is associated with a greater number of localized and assessed nodes in comparison to en-bloc removal of lymphatic tissue. To summarize, the template reflects the quality of surgery, and the number of removed LN remains the ubiquitous method of evaluation of LN dissection status by clinicians.

The most common location of LN metastases is the obturator fossa. This is in agreement with several authors who have used the extended template [13]. However, in as many as 38% of cases PCa invasion is found within presacral nodes. None of the patients had metastases without obturator LN involvement. Unfortunately, despite advanced imaging tools, nomograms and tracing techniques, it is not possible to predict with certainty the presence of LN invasion and its localization in patients subjected to radical prostatectomy. What would have happened if the infiltrated nodes were left after surgery? Would it influence the outcome? There are no answers to the questions but we may speculate that this would change further management. Extended dissection remains the best method of pelvic LN assessment.

To our knowledge there are only retrospective series published so far that focus on the impact of ePLND on survival. It was shown that long-term biochemical-free survival, clinical progression-free survival and overall survival of patients with positive LN

were 20%, 35–75%, and 78%, respectively [11, 19, 23]. The greater the number of LN removed, the better is survival [24]. Conversely, the greater the number of LN invaded by cancer, the worse the outcome [11]. Fifteen years cancer specific survival of patients in whom a single LN was infiltrated equaled 84%, while survival of those who had more than two nodes involved was 62% [19]. Irrespectively of the influence of ePLND on overall survival of prostate cancer patients, currently the staging retains its precious value.

High risk prostate cancer requires a multidisciplinary approach. We have learned that those with locally advanced disease, especially those with positive surgical margins yet negative nodes, benefit from early, adjuvant radiation that follows surgery [9, 25]. In contrast, those who are found to have gross invasion of pelvic LN after radical prostatectomy require early hormonal manipulation as the disease is most likely to be disseminated at the time of surgery [8]. However, there is a small percentage of patients who have invasion limited only to one or two regional LN that might benefit from additional, local therapy as the disease might still be localized [26]. Only 7 (54%) of our patients who were found to have LN invasion had undetectable PSA 6 weeks after radical prostatectomy. Those will probably benefit from adjuvant local therapy if indicated by the status of the specimen (Figure 1).

Several limitations of the study are acknowledged. Its retrospective nature is one of them. We continue to collect the data of patients subjected to

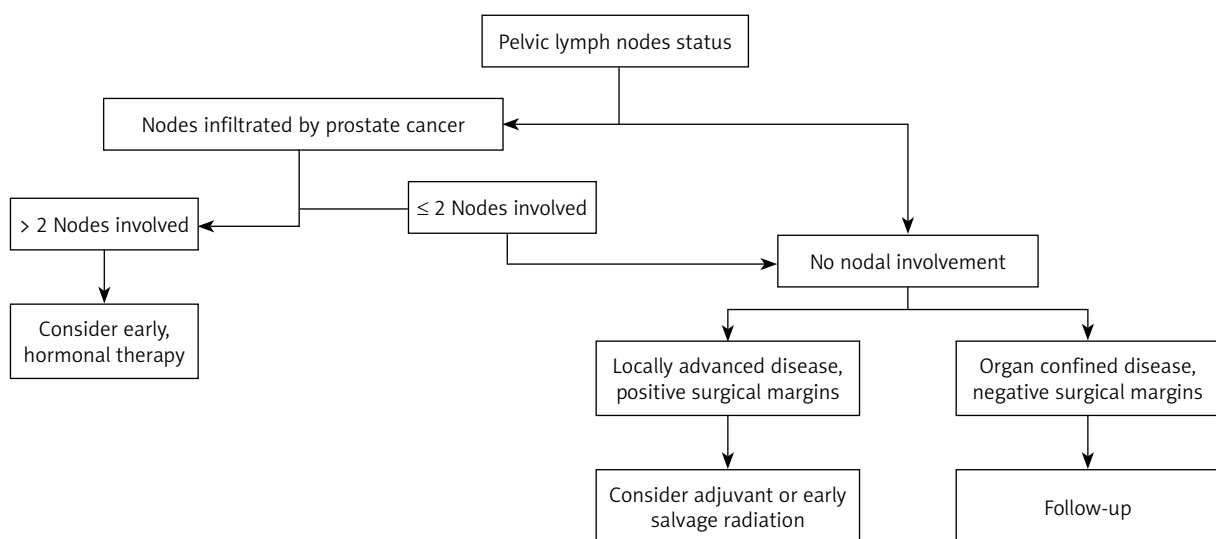


Figure 1. Management chart of patients subjected to radical prostatectomy with extended lymphadenectomy in correlation with the status of lymph nodes

laparoscopic ePLND prospectively. More mature analysis with a greater number of patients will be presented in the following years. Determining the value of lymphadenectomy in prostate cancer requires a randomized, controlled trial that would compare extended with no LN dissection in high risk patients. However, we doubt it will ever be conducted.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics 2012. *CA Cancer J Clin* 2012; 62: 10-29.
2. Bednarsz N, Eltze E, Semjonow A, et al. BRCA1 loss preexisting in small subpopulations of prostate cancer is associated with advanced disease and metastatic spread to lymph nodes and peripheral blood. *Clin Cancer Res* 2010; 16: 3340-8.
3. Heidenreich A, Bastian PJ, Bellmunt J, et al. Guidelines on Prostate Cancer. *Uroweb* 2013; available at http://www.uroweb.org/gls/pdf/09_Prostate_Cancer_LR.pdf
4. Joniau S, Van den Bergh L, Lerut E, et al. Mapping of pelvic lymph node metastases in prostate cancer. *Eur Urol* 2013; 63: 450-8.
5. Messing EM, Manola J, Sarosdy M, et al. Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer. *N Engl J Med* 1999; 341: 1781-8.
6. Chłosta P, Drewa T, Siekiera J, et al. Lymph node dissection during laparoscopic (LRC) and open (ORC) radical cystectomy due to muscle invasive bladder urothelial cancer (pT2-3, TCC). *Videosurgery Miniinv* 2011; 6: 127-31.
7. Chłosta PL, Drewa T, Jaskulski J, et al. Bladder neck preservation during classic laparoscopic radical prostatectomy – point of technique and preliminary results. *Videosurgery Miniinv* 2012; 7: 89-95.
8. Messing EM, Manola J, Yao J, et al. Immediate versus deferred androgen deprivation treatment in patients with node-positive prostate cancer after radical prostatectomy and pelvic lymphadenectomy. *Lancet Oncol* 2006; 7: 472-9.
9. Thompson IM, Tangen CM, Paradelo J, et al. Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term follow-up of a randomized clinical trial. *J Urol* 2009; 181: 956-62.
10. Abdollah F, Cozzarini C, Sun M, et al. Assessing the most accurate formula to predict the risk of lymph node metastases from prostate cancer in contemporary patients treated with radical prostatectomy and extended pelvic lymph node dissection. *Radiother Oncol* 2013; 109: 211-6.
11. Daneshmand S, Quek ML, Stein JR, et al. Prognosis of patients with lymph node positive prostate cancer following radical prostatectomy: long-term results. *J Urol* 2004; 172: 2252-5.
12. Palapattu GS, Allaf ME, Trock BJ, et al. Prostate specific antigen progression in men with lymph node metastases following radical prostatectomy: results of long-term follow-up. *J Urol* 2004; 172: 1860-4.
13. Joniau S, Van den Bergh L, Lerut E, et al. Mapping of pelvic lymph node metastases in prostate cancer. *Eur Urol* 2013; 63: 450-8.
14. Jung JH, Seo JW, Lim MS, 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.
15. Feicke A, Baumgartner M, Talimi S, et al. Robotic-assisted laparoscopic extended pelvic lymph node dissection for prostate cancer: surgical technique and experience with the first 99 cases. *Eur Urol* 2009; 55: 876-83.
16. Lattouf JB, Beri A, Jeschke S, et al. Laparoscopic extended pelvic lymph node dissection for prostate cancer: description of the surgical technique and initial results. *Eur Urol* 2007; 52: 1347-55.
17. Wyler SF, Sulser T, Seifert HH, et al. Laparoscopic extended pelvic lymph node dissection for high-risk prostate cancer. *Urology* 2006; 68: 883-7.
18. Meinhardt W, van der Poel HG, Valdés Olmos RA, et al. Laparoscopic sentinel lymph node biopsy for prostate cancer: the relevance of locations outside the extended dissection area. *Prostate Cancer* 2012; 2012: 751-3.
19. Briganti A, Blute ML, Eastham JH, et al. Pelvic lymph node dissection in prostate cancer. *Eur Urol* 2009; 55: 1251-65.
20. Yuh B, Artibani W, Heidenreich A, et al. the role of robot-assisted radical prostatectomy and pelvic lymph node dissection in the management of high-risk prostate cancer: a systematic review. *Eur Urol* 2013; in press; doi:pil: S0302-2838(13)00492-2.
21. Touijer KA, Ahallal Y, Guillonneau BD. Indications for and anatomical extent of pelvic lymph node dissection for prostate cancer: Practice patterns of uro-oncologists in North America. *Urol Oncol* 2013; 31: 1517-21.
22. Wawroschek F, Wagner T, Hamm M, et al. The influence of serial sections, immunohistochemistry and extension of pelvic lymph node dissection on the lymph node status in clinically localized prostate cancer. *Eur Urol* 2003; 43: 132-7.
23. Paul A, Ploussard G, Nicolaiew N, et al. Oncologic outcome after extraperitoneal laparoscopic radical prostatectomy: midterm follow-up of 1115 procedures. *Eur Urol* 2010; 57: 267-72.
24. Joslyn SA, Konety BR. Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. *Urology* 2006; 68: 121-5.
25. Wiegel T, Bottke D, Steiner U, et al. Phase III postoperative adjuvant radiotherapy after radical prostatectomy compared with radical prostatectomy alone in pT3 prostate cancer with postoperative undetectable prostate-specific antigen: ARO 96-02/AUO AP 09/95. *J Clin Oncol* 2009; 27: 2924-30.
26. Briganti A, Karnes RJ, Da Pozzo LF, et al. Combination of adjuvant hormonal and radiation therapy significantly prolongs survival of patients with pT2-4 pN+ prostate cancer: results of a matched analysis. *Eur Urol* 2011; 59: 832-40.

Received: 12.09.2013, accepted: 11.10.2013.