Whether extended pelvic lymph node dissection should be performed in prostate cancer: The present evidence from a systematic review and meta-analysis

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Abstract

Purpose: To compare non-extended pelvic lymph node dissection (nePLND) with extended pelvic lymph node dissection (ePLND) in outcomes and complications of patients with prostate cancer (PCa).

Methods: A comprehensive search of the PubMed, EMBASE, and Web of Science was performed. We extracted the first author, year of publication, basic characteristics of patients, method of radical prostatectomy (RP), extent of PLND, number of lymph node yields (LNY), and percentage of LN metastasis. Besides, information about inpatients outcomes and complications were also collected. The modified Newcastle-Ottawa scale was compiled to assess the level of evidence of all controlled studies. Next, we used odds ratio (OR) with corresponding 95% confidence interval (CI) to evaluate the difference between nePLND and ePLND in meta-analysis, and a P value of <.05 was considered statistically significant.

Results: A total of 11 studies including 7489 patients were included in our study. Compared with nePLND, more LNY and metastasized LNs (OR = 3.104, 95% CI: 2.407-4.001, z = 8.74, P < .001) could be dissected by ePLND. Besides, more complications from ePLND group compared with nePLND group (ePLND vs nePLND: OR = 2.118, 95% CI: 1.107-4.051, z = 2.27, P = .023). Furthermore, the results of subgroup analysis revealed that ePLND group led to more complications from all three RP approaches. In addition, our results showed that extender PLND led to more blood loss and longer operating room time in PCa patients with open radical prostatectomy (ORP). No statistics discrepancy in postoperative length of stay and operating room time was observed except one single study. Finally, there were no significant difference observed in transfusion and prostate weight.

Conclusions: The results of our study indicated that extender PLND led to more LNY and more metastasized LNs. More harm would be brought by ePLND in ORP, whereas not in LRP and RALP. In addition, ePLND may lead to more overall complications than nePLND.

Keywords
meta-analysis, PLND, prostate cancer
Prostate cancer (PCa) disseminates initially to regional lymph nodes (LNs). Pelvic lymph node dissection (PLND) is the most accurate procedure to identify the histological status of LNs. Besides, PLND contributes improved therapeutic benefit by the removal of possible micrometastatic disease.

For intermediate and high risk PCa, the European Association of Urology (EAU), European Society for Radiotherapy & Oncology (ESTRO), International Society of Geriatric Oncology (SIOG), and the National Comprehensive Cancer Network (NCCN) clinical guidelines recommend a risk of nodal metastases >5% was an indication to perform an extended pelvic lymph node dissection (ePLND). In addition, the individual risk of lymph node invasion (LNI) can be estimated using models based on preoperative characteristics such as the Briganti and Memorial Sloan Kettering Cancer Center nomograms.

Historically, the lack of standardized definitions and terminologies of PLND has led to the difficulty of comparing various PLND approaches. It was reported that a wider extent of PLND led to longer operative duration and more hospitalization days. Conversely, some researchers held opposite opinions. The incidences of perioperative and postoperative complications are emphatically considered factors of urologists to decide the extent of PLND. Numerous studies revealed that ePLND had significantly more overall complications than non-extended PLND (nePLND). What is more, a randomized prospective self-control study demonstrated that an increased risk of complications attributable to the lymphadenectomy occurred to an extended dissection. However, the assertion that expending of extensive dissection leads to more overall complications has not always been confirmed. Yuh reported that there was no significant difference in overall complications in patients from nePLND group and ePLND group. Furthermore, it is difficult to draw a definite conclusion of specific complications due to no relatively consistent records on the type of specific complications to existing researches.

In this study, we sought to obtain more definitive results of the comparison between nePLND and ePLND, and explore the association with varying extent of PLND and complications by performing meta-analysis.

2 | MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-analyses guideline was conformed when our study was conducted and reported. Comparative studies between radical prostatectomy (RP) with any extent PLND in PCa patients were enrolled in our present study.

2.1 | Definitions

In order to standardize the terminologies of various PLND methods, five types of PLND approaches were categorized based on a reference expert panel (EAU Prostate Cancer Guideline Panel): (1) limited PLND: dissects obturator nodes; (2) standard PLND: dissects obturator and external iliac nodes; (3) extended PLND: dissects obturator, external iliac, and internal iliac nodes; (4) super-extended PLND: dissects obturator, external iliac, internal iliac common iliac nodes, and/or other nodes; (5) PLND extent undefined or unclassified. In our study, we defined ePLND as types 3 and 4; whereas defined nePLND as types 1 and 2.

2.2 | Search strategy

A systematic literature searched on PubMed, EMBASE, and Web of Science was performed to identify all published potentially appropriate studies (till 20 April 2017). The key words were "extended pelvic lymph node dissection," "pelvic lymph node dissection," "PLND," "prostate cancer," "PCa," "radical prostatectomy," or "RP." Additional publications were identified when we searched the reference list of original articles manually. A flow diagram of the selection process is presented in Figure 1.

2.3 | Inclusion and exclusion criteria

Articles met the following criteria were included: (a) randomized controlled trials (RCTs) and controlled studies (prospective or retrospective); (b) studies compared extended PLND or super-extended PLND with standard PLND or limited PLND; (c) patients were diagnosed as clinically localized PCa. On the other hand, articles enrolled patients with organ metastasis or patients had undergone reoperation,
## TABLE 1  
Basic clinical characteristics of the studies included in the systematic review and meta-analysis

| Study          | Year | Risk     | No. of patients | Mean age ± SD (range) | Mean PSA (ng/mL) | Extent | Method | NOS |
|----------------|------|----------|-----------------|-----------------------|-----------------|--------|--------|-----|
| Allaf19        | 2004 | NA       | 1875 2135       | 57.9 (35-74) 56.7 (33-74) | 7.2 7.1 | ORP 2 4 7 |
| Lindberg12     | 2009 | NA       | 64 108          | NA NA                  | 10 (2.3-26) 10 (2.7-64) | ORP 1 3 6 |
| Eden7          | 2009 | IR, HR   | 311 121         | 63.0 (43-76) 63.0 (43-74) | 11.0 (2-20) 8.0 (1-15) | LRP 2 3 7 |
| Jung9          | 2012 | HR       | 155 45          | 66 67                  | 8.7 15.5 | RALP 2 4 8 |
| Kim20          | 2013 | IR, HR   | 294 170         | 64.3 ± 7.4 65.2 ± 6.3 | 11.6 ± 12.4 13.7 ± 12.1 | RALP 2 4 7 |
| Liss8          | 2013 | LR, IR, HR| 231 54         | 63 61                  | 6.1 8.5 | RALP 2 4 8 |
| Hatzichristodoulou21 | 2016 | LR, IR, HR | 198 262 | 64.6 ± 7.8 64.9 ± 7.5 | 6.1 ± 1.9 9.9 ± 7.8 | ORP 1 4 7 |
| Stone11        | 1997 | LR, IR, HR | 150 39      | NA NA                  | NA NA | LRP 1 4 7 |
| Heidenreich22  | 2002 | LR, HR   | 100 103         | 63.5 (49-72) 61.8 (51-71) | 14.9 (1.6-109) 15.9 (12-129) | ORP 2 4 7 |
| Klevecka23     | 2008 | LR, HR   | 477 191         | 64.8 ± 6 (40-78) 65.1 ± 5.9 (42-81) | 10.7 ± 11.5 (0.5-135) 15.1 ± 20.9 (0.11-254.0) | ORP 2 4 6 |
| Yuh14          | 2013 | IR, HR   | 204 202         | 64 (58-70) 64 (58-69) | 5.9 (4.4-9.1) 5.5 (4.2-8.3) | RALP 1 4 7 |

Abbreviations: ePLND, extended pelvic lymph node dissection; HR, high risk; IR, intermediate risk; LR, low risk; LRP, laparoscopic radical prostatectomy; NA, not available; nePLND, non-extended pelvic lymph node dissection; NOS, Newcastle-Ottawa scale; ORP, open radical prostatectomy; RALP, robot assisted radical prostatectomy; SD, standard deviation.

## TABLE 2  
Inpatient results of the studies included in the meta-analysis

| Study          | Blood loss (mL) | Operating room time (min) | Postoperative length of stay (d) | Transfusion (no. of patients) | Prostate weighting |
|----------------|-----------------|---------------------------|---------------------------------|-----------------------------|-------------------|
|                | nePLND ePLND    | nePLND ePLND P value      | nePLND ePLND P value            | nePLND ePLND P value        | nePLND ePLND P value |
| Eden7          | 200 (10-1300)a  | 200 (10-800)b .13         | 180 (117-537) 206.5 (99-331)d   | <.001 3.0 (2-5)d 3.0 (2-4)d/.77 | 2 3 .27 56.5 (20-214) .09 |
| Jung9          | 250 (150-400)a  | 200 (100-300) .088        | 190 (165-211) 196 (180-224)d .027 | .027 4(3-7) 4(3-7) .998      | NA NA NA NA NA |
| Liss8          | 100 (100-200)a  | 150 (100-200) .322        | 182 ± 34 186 ± 29c .211          | .211 1.3 ± 0.8c 1.6 ± 1.6c .02 | 2 1 .436 48 (38.0-57.0).<.001 |
| Heidenreich22  | 590 (150-2100)b | 650 (200-1950) NA         | 125 (85-150) 179 (140-235)b .03 | .03 NA NA NA NA NA |
| Yuh14          | 200 (125-250)a  | 200 (150-250) .7          | 168 (156-180) 180 (174-198)b .001 | .001 NA NA NA NA NA |

Abbreviations: ePLND, extended pelvic lymph node dissection; HR, high risk; IR, intermediate risk; LR, low risk; LRP, laparoscopic radical prostatectomy; NA, not available; nePLND, non-extended pelvic lymph node dissection.

aMedian (IQR).
bMean (range).
cMean ± standard deviation (SD).
dMedian (range).
radiotherapy, adjuvant or neoadjuvant chemotherapy, or hormone therapy before PLND was excluded. In addition, references without available data were disregarded.

2.4 | Data extraction

Two reviewers (Y. G. and Y. Z.) independently extracted all available information involved in eligible articles according to the inclusion criteria performed above. The review of result was carried out by a third investigator (Y. C.). The following data was recorded for each selected study: name of first author, year of publication, basic characteristics of patients, method of RP, extent of PLND, number of LN yields (LNY), and percentage of LN metastasis. Besides, information on inpatients results and complications were also collected.

2.5 | Risk of bias assessment

Two investigators independently evaluated the quality of each reference using the Cochrane Risk of Bias Assessment Tool for Non-Randomized Study tool. Cochran’s Q test (chi square) and the I² method were performed to assess heterogeneity between articles.\(^1^7\) Begg’s funnel plots were compiled to estimate the presence of publication bias; \(P\) value <.05 and asymmetric plot suggest a potential publication bias.

2.6 | Statistical analysis

We used odds ratio (OR) with corresponding 95% confidence interval (CI) to evaluate the difference between nePLND and ePLND in meta-analysis. \(Z\) test was performed to determine the statistical significance of the OR, and a \(P\) value of <.05 was considered statistically significant. Statistical analyses were performed using STATA 12.0 software (Stata Corp, College Station, TX). All results were reported with 95% CIs. The modified Newcastle-Ottawa scale was applied to assess the level of evidence of all controlled studies.\(^1^8\) We did not analyze the blinding method since it was not applicable for surgery clinical trials.

3 | RESULTS

The flow diagram of studies enrolled in our study is performed in Figure 1. There were altogether 595 studies identified with the search strategy mentioned before. Next, we screened the full text in detail and eliminated 155 studies since they were reviews, duplicate reports, and conference articles. About 151 articles were excluded after titles and abstracts filtering. Finally, 11 references including a total 7489 patients with low, intermediate, or high-risk PCa were included in our study,\(^7^—^9,11,12,14,19—^2^3\) and the basic clinical characteristics are shown in Table 1. PLND performed in the open radical prostatectomy (ORP),
laparoscopic radical prostatectomy (LRP), and robot-assisted laparoscopic prostatectomy (RALP) were recorded in six,12,19,21-23 two,7,11 and four8,9,14,20 articles, respectively. Six studies8,9,19,20,22,23 compared standard PLND and super-extended PLND. Besides, three studies compared11,14,21 limited PLND and super-extended PLND. Lindberg's12 and Eden’s7 researches focused on the difference between limited PLND and extended PLND, super-extended PLND and extended PLND, respectively.

3.1 | Inpatient results

Inpatient results in five articles7-9,14,22 are demonstrated in Table 2. Extender PLND led to more blood loss (650 mL, range 200-1950 vs 590 mL, range 150-2100 mL) and longer operating room time (179 minutes, range 140-235 vs 125 minutes, range 85-150 minutes) in patients with ORP. However, no significant difference in blood loss was observed in patients with LRP (P = .13) or RALP (P = .088, P = .322, and P = .7). A longer operating room time was recorded in LRP and RALP patients (P < .001, P < .027, and P < .001) except in Liss’s study (P = .211). In addition, no statistics discrepancy between postoperative length of stay was shown in two individual articles (P = .77 and P = .998) apart from Liss’s study (P = .002). What is more, there were no significant difference was observed in transfusion (P = .27 and P = .436) and prostate weight (P = .09, P = .125, and P = .582).

3.2 | Complications

We extracted information on overall complications from seven references with 2051 patients, and the results are shown in Table 3.7,8,11,12,14,22 Besides, specific complication statistics were revealed in Table S1. Data demonstrated significantly more complications from ePLND group compared with nePLND group (Figure 2, ePLND vs nePLND: OR = 2.118, 95% CI: 1.107-4.051, z = 2.27, P = .023). Next, these seven studies were divided into three subgroups by surgery methods. The results of subgroup meta-analysis (Figure 3) revealed that ePLND group led to more complications from all three RP approaches (ORP: OR = 1.644, 95% CI: 0.522-5.176, z = 0.85, P = .396; LRP: OR = 7.559, 95% CI: 0.805-70.954, z = 1.77, P = .077; RALP: OR = 1.605, 95% CI: 0.582-4.427, z = 0.91, P = .361). Both overall analysis and subgroup analysis demonstrated the heterogeneity could not be ignored (overall analysis: I² = 79.1%; ORP: I² = 80.2%; LRP: I² = 74.8%; RALP: I² = 84.3%).

**TABLE 4** Number of LN yields and LN metastasis of the studies included in the meta-analysis

| Study         | NePLND yields | ePLND yields | P value | NePLND metastasis, no. of patients | ePLND metastasis, no. of patients |
|---------------|---------------|--------------|---------|-----------------------------------|----------------------------------|
| Stone         | 9.3 (1-31)    | 17.8 (2-51)  | <.05    | 11                                | 139                              |
| Eden          | 6.1 (2-8)     | 17.5 (2-23)  | .002    | NA                                | NA                               |
| Heidenreich   | 11 (6-19)     | 28 (21-42)   | <.01    | 12                                | 88                               |
| Kleveland     | 8 (1-27)      | 11 (1-34)    | <.01    | 30                                | 447                              |
| Jung          | 15 (11-19)    | 24 (18-28)   | <.01    | 12                                | 143                              |
| Liss          | 18 (12-25)    | 20 (16-28)   | .07     | 9                                 | 222                              |
| Yuh           | 7 (5-9)       | 21.5 (17-27) | <.0001  | 8                                 | 196                              |
| Hatzichristodoulou | 4.7 ± 4 | 20.4 ± 9.7 | <.001    | NA                                | NA                               |
| Kim           | 11.9 ± 4.6    | 21.3 ± 6.7   | <.001   | 10                                | 284                              |
| Allaf         | 8.9 (8)       | 11.6 (11)    | <.0001  | 21                                | 1854                             |

Abbreviations: ePLND, extended pelvic lymph node dissection; P, positive; N, negative; NePLND: non-extended pelvic lymph node dissection. 

*Median (IQR).*

*Mean (range).*

*Mean ± standard deviation (SD).*

*Median (range).*
the test result ($P < .001$). Meta-analysis result shown that extender PLND could discover more metastasized LN (OR = 3.104, 95% CI: 2.407-4.001, $P < .001$) except Liss's study ($P = .02$). The heterogeneity could be ignored according to the test result ($I^2 = 5.8\%$).

### 3.4 Evaluation of publication bias

Publication bias evaluated by Begg's test was found for all analyses ($P = .035$). The presence of publication bias is mainly due to the lack of enrolled studies. However, given the lack of current relevant researches and limited references, our study was still performed.

### 4 DISCUSSION

As the most common malignancy that affects the male genitourinary system, 
PCAs, the EAU, ESTRO, SIOG, and NCCN guidelines recommend a risk of nodal metastases $>5\%$ is an indication to perform an ePLND. 
However, a recent study had improved a nomogram predicting LNI in contemporary PCa patients with detailed biopsy reports. According to this updated model, a LN dissection exclusively in men with a risk of LNI $>7\%$, and the number of unnecessary pelvic nodal dissections were significantly reduced. 

Compared with nePLND, ePLND may have a therapeutic role in removing more micrometastases. 
An inverse correlation was reported on the number of normal LNs removed and the risk of biochemical recurrence. In addition, a retrospective study shown that a more extensive PLND might increase biochemical recurrence free survival in node-negative PCa patients. 
Although one study enrolled in our study revealed that ePLND might have the trend to improve overall survival in PCa patients, the difference was not statistically significant ($P = .07$). 
Our findings revealed that compared with nePLND, more LNY and metastasized LNs could be dissected by ePLND. However, the study of prostate lymph flow may change our existing view. 
It was reported that the lymphatic channel draining from the prostate was detected using a fluorescence navigation system after injecting indocyanine green, and the result shown that the major lymphatic pathway involved in the spreading of PCa is internal iliac LNs, which would mean that the dissection of external iliac LNs and obturator LNs covered in standard PLND might not keep the cancer from spreading.

To date, the strategy of ePLND application is still controversial because of the lack of solid evidence regarding its oncological benefit and the adverse events associated with it. 
Given to the improved LNs staging, it is advisable to replace nePLND with ePLND. However, the performance of ePLND was limited due to the consideration of long operating time, more blood loss and more complications. Actually, the assertion that more extensive PLND led to worse inpatient results had not always been confirmed. The difference between nePLND and ePLND in inpatients results might associate with surgical procedures. 
Our results shown that extender PLND led to more blood loss and longer operating room time in PCa patients with ORP. Apart from Liss's study, no statistics discrepancy of postoperative length of stay and operating room time was observed. Besides, no significant differences were observed in transfusion and prostate weight. 
What is more, our results demonstrated significantly more complications in ePLND group compared with nePLND group.

Significant and nonnegligible heterogeneity which could not been decreased by sensitivity analysis was identified from our results of meta-analysis. 
The following reasons may provide a reasonable explanation: first, the complex PCa clinical and pathological staging brought difficulty of patient grouping, which could lead to the difference in baseline characteristics between two groups. 
It is worth mentioning that urological surgeon and the pathologist may both influence the number of LNs removed and the number of positive LNs at final pathology. 
Second, RCTs and blinded studies were not applicable in surgical templates for PLND. 
Third, due to the discrepancy of medical conditions, surgical methods, technique level of urological surgeon, perioperative care, surgical equipment, and other factors which may
influence the effect of operation, the conclusions for most parameters may be easily changed. In addition, publication bias was identified might cause by only seven comparative reference enrolled in our meta-analysis. Indeed, not all relevant studies could be identified by computer-based literature searching. Additionally, grey literature and periodical achievement from undertaking prospective studies (eg. NCT01812902 and NCT01555086) could not be included in this study. Limitations also inevitably existed in our study. As mentioned before, significant heterogeneity which could not be adjusted by sensitivity analysis was identified among enrolled studies. What is more, limited original studies led to insufficient data available for further analysis.

5 | CONCLUSION

The results of this systematic review and meta-analysis indicated that extender PLND led to more LNY and more metastasized LNs. More harm would be brought by ePLND in ORP, whereas not in LRP and RALP. In addition, ePLND may lead to more overall complications than nePLND. Finally, RCTs and high-quality prospective comparative studies are needed to complete this study.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

(I) Conception and design: Feng Qi, Qing Zou; (II) Administrative support: Qing Zou; (III) Provision of study materials or patients: Yuxiao Zheng, Yang Gao; (IV) Collection and assembly of data: Yifei Cheng, Yuxiao Zheng, Feng Qi; (V) Data analysis and interpretation: Yuxiao Zheng, Yang Gao2, Yifei Cheng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

ETHICS STATEMENT

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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REFERENCES

1. Flocks RH, Culp D, Porto R. Lymphatic spread from prostatic cancer. J Urol. 1959;81:194-196.
2. Sundi D, Svatek RS, Nielsen ME, Schoenberg MP, Bivalacqua TJ. Extent of pelvic lymph node dissection during radical cystectomy: is bigger better? Rev Urol. 2014;16:159-166.
3. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol. 2017;71:618-629.
4. Briganti A, Larcher A, Abdollah F, et al. Updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection: the essential importance of percentage of positive cores. Eur Urol. 2012;61:480-487.
5. Godoy G, Chong KT, Cronin A, et al. Extent of pelvic lymph node dissection and the impact of standard template dissection on nomogram prediction of lymph node involvement. Eur Urol. 2011;60:195-201.
6. Roach M 3rd, Marquez C, Yuo HS, et al. Predicting the risk of lymph node involvement using the pre-treatment prostate specific antigen and Gleason score in men with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys. 1994;28:33-37.
7. Eden CG, Arora A, Rouse P. Extended vs standard pelvic lymphadenectomy during laparoscopic radical prostatectomy for intermediate- and high-risk prostate cancer. BJU Int. 2010;106:537-542.
8. 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;31:481-488.
9. Jung JH, Jeo 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;22:785-790.
10. Gao L, Yang L, Lv X, et al. A systematic review and meta-analysis of comparative studies on the efficacy of extended pelvic lymph node dissection in patients with clinically localized prostatic carcinoma. J Cancer Res Clin Oncol. 2014;140:243-256.
11. Stone NN, Stock RG, Unger P. Laparoscopic pelvic lymph node dissection for prostate cancer: comparison of the extended and modified techniques. J Urol. 1997;158:1891-1894.
12. Lindberg C, Davidsson T, Gudjonsson S, Hilmarsson R, Liedberg F, Bratt O. Extended pelvic lymphadenectomy for prostate cancer: will the previously reported benefits be reproduced in hospitals with lower surgical volumes? Scand J Urol Nephrol. 2009;43:437-441.
13. Clark T, Parekh DJ, Cookson MS, et al. Randomized prospective evaluation of extended versus limited lymph node dissection in patients with clinically localized prostate cancer. J Urol. 2003;169:145-147. Discussion 147-148.
14. Yuh BE, Ruel NH, Mejia R, Novara G, Wilson TG. Standardized comparison of robot-assisted limited and extended pelvic lymphadenectomy for prostate cancer. BJU Int. 2013;112:81-88.
15. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.
16. Fossati N, Willemse PM, Van den Broeck T, et al. The benefits and harms of different extents of lymph node dissection during radical prostatectomy for prostate cancer: a systematic review. Eur Urol. 2017;72:84-109.
17. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539-1558.
18. Phillips B. GRADE: levels of evidence and grades of recommendation. Arch Dis Child. 2004;89:489.
19. Alital 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;172:1840-1844.
20. Kim KH, Lim SK, Kim HY, 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;112:216-223.
21. Hatzichristodoulou G, Wagenpfel S, Wagenpfel G, et al. Extended versus limited pelvic lymph node dissection during bilateral nerve-sparing radical prostatectomy and its effect on continence and erectile function recovery: long-term results and trifecta rates of a comparative analysis. World J Urol. 2016;34:811-820.
22. Heidenreich A, Varga Z, Von Knobloch R. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastasis. *J Urol*. 2002;167:1681-1686.
23. Klevecka V, Musch M, Roggenbuck U, Stoerkel S, Kroepfl D, et al. The incidence of lymph node metastases in prostate carcinoma depends not only on tumor characteristics but also on surgical performance and extent of pelvic lymphadenectomy. *Medicina (Kaunas)*. 2008;44:601-608.
24. Siegel RL, Miller KD, Jemal A, et al. Cancer statistics, 2017. *CA Cancer J Clin*. 2017;67:7-30.
25. Gil-Vernet JM. Prostate cancer: anatomical and surgical considerations. *Br J Urol*. 1996;78:161-168.
26. Abdollah F, Karnes RJ, Suardi N, et al. Impact of adjuvant radiotherapy on survival of patients with node-positive prostate cancer. *J Clin Oncol*. 2014;32:3939-3947.
27. Touijer KA, Mazzola CR, Sjoberg DD, Scardino PT, Eastham JA, et al. Long-term outcomes of patients with lymph node metastasis treated with radical prostatectomy without adjuvant androgen-deprivation therapy. *Eur Urol*. 2014;65:20-25.
28. Riggs S, Burks RT. Extended pelvic lymph node dissection in prostate cancer: a 20-year audit in a single center. *Ann Oncol*. 2013;24:1423-1424.
29. Rincon Mayans A, Zudaire Bergera JJ, Rioja Zuazu J, et al. Pelvic lymph node dissection (extended vs standard) and prostate cancer. *Actas Urol Esp*. 2008;32:879-887.
30. Gandaglia G, Fossati N, Zaffuto E, et al. Development and internal validation of a novel model to identify the candidates for extended pelvic lymph node dissection in prostate cancer. *Eur Urol*. 2017;72:632-640.
31. Schiavina R, Bertaccini A, Franceschelli A, et al. The impact of the extent of lymph-node dissection on biochemical relapse after radical prostatectomy in node-negative patients. *Anticancer Res*. 2010;30:2297-2302.
32. Masterson TA, Bianco FJ Jr, Vickers AJ, et al. The association between total and positive lymph node counts, and disease progression in clinically localized prostate cancer. *J Urol*. 2006;175:1320-1324. discussion 1324-1325.
33. Inoue S, Shiina H, Arichi N, et al. Identification of lymphatic pathway involved in the spreading of prostate cancer by fluorescence navigation approach with intraoperatively injected indocyanine green. *Can Urol Assoc J*. 2011;5:254-259.
34. Briganti A, Blute ML, Eastham JH, et al. Pelvic lymph node dissection in prostate cancer. *Eur Urol*. 2009;55:1251-1265.
35. Budiharto T, Joniau S, Lerut E, et al. Prospective evaluation of 11C-choline positron emission tomography/computed tomography and diffusion-weighted magnetic resonance imaging for the nodal staging of prostate cancer with a high risk of lymph node metastases. *Eur Urol*. 2011;60:125-130.
36. Silberstein JL, Vickers AJ, Power NE, et al. Pelvic lymph node dissection for patients with elevated risk of lymph node invasion during radical prostatectomy: comparison of open, laparoscopic and robot-assisted procedures. *J Endourol*. 2012;26:748-753.
37. Lanowska M, Vasiljeva J, Chiantera V, et al. Implication of the examining pathologist to meet the oncologic standard of lymph node count after laparoscopic lymphadenectomy. *Oncology*. 2010;79:161-167.

**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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