Effect of Extended Pelvic Lymph Node Dissection on Oncologic Outcomes in Patients with D'Amico Intermediate and High Risk Prostate Cancer Treated with Radical Prostatectomy: A Multi-Institutional Study

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Abbreviations and Acronyms

BCR = biochemical recurrence
CSM = cancer specific mortality
ePLND = extended PLND
LNI = lymph node invasion
PCa = prostate cancer
PLND = pelvic lymph node dissection
PSA = prostate specific antigen
RP = radical prostatectomy

Purpose: Pelvic lymph node dissection represents the gold standard of lymph node staging in patients with prostate cancer. We sought to assess the effect of extended pelvic lymph node dissection on oncologic outcomes in patients with characteristics of D'Amico intermediate or high risk prostate cancer treated with radical prostatectomy.

Materials and Methods: In a multi-institutional database of 4 centers we identified 9,742 patients who underwent radical prostatectomy from 2000 to 2017 with or without pelvic lymph node dissection. Only patients with a greater than 5% probability of lymph node invasion according to the Briganti nomogram were included in study. We performed 2:1 propensity score matching to account for potential differences between the 2 cohorts. Cox regression models were used to test the effect of pelvic lymph node dissection on biochemical recurrence, metastasis and cancer specific mortality.

Results: Overall 707 patients (7.3%) did not undergo pelvic lymph node dissection, of whom 520 and 187 harbored D'Amico intermediate and high risk characteristics, respectively. A median of 14 lymph nodes (IQR 8–21) were removed in the pelvic lymph node dissection cohort and 1,714 of these cases (19.0%) harbored lymph node metastasis. After propensity score matching the biochemical recurrence-free, metastasis-free and cancer specific mortality-free survival rates were 60.4% vs 65.6% (p=0.07), 87.0% vs 90.0% (p=0.06) and 95.2% vs 96.4% (p=0.2) for pelvic lymph node dissection vs no pelvic lymph node dissection 120 months after radical prostatectomy. Multivariable Cox regression models adjusted for postoperative and preoperative tumor characteristics revealed that pelvic lymph node dissection

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performed at radical prostatectomy was no independent predictor of biochemical recurrence, metastasis or cancer specific mortality (all p $\geq$0.1).

Conclusions: There was no significant difference in oncologic outcomes in patients with D'Amico high or intermediate risk prostate cancer in whom pelvic lymph node dissection was or was not performed at radical prostatectomy. The therapeutic value of pelvic lymph node dissection remains unclear.

Key Words: prostatic neoplasms, prostatectomy, neoplasm metastasis, lymph node excision, mortality

PELVIC lymph node dissection represents an integral part of RP in patients with intermediate or high risk PCa characteristics. Indeed, according to European guidelines for PCa ePLND is recommended in patients with a greater than 5% nomogram derived LNI probability.[1] However, previous studies have demonstrated that PLND can be avoided in some of those patients with an unneglectable risk of LNI.[2]

The role of PLND in PCa staging is undebatable since it can help identify patients who would benefit from adjuvant treatment or those in whom adjuvant treatment can be omitted.[3] Conversely the therapeutic value of PLND remains controversial.[3] Several previous studies have shown a decrease in CSM in patients treated with more extensive PLND at RP compared to that in patients with less extensive PLND.[4–7] However, others did not confirm this relationship.[8] Moreover, other previous studies compared outcomes according to pathological lymph node status instead of PLND performance, focused only on patients without LNI or compared limited vs extended PLND.[9–11] However, lymph node status is unknown at the time of PLND and when the decision is made to perform PLND.

The effect of PLND on BCR is also unclear.[12] Weight et al reported no effect of limited PLND on BCR.[13] Mandel et al also reported no effect of PLND on BCR in patients with D'Amico intermediate risk PCa and a Gleason score of 6 at RP.[8] Conversely Allaf et al found a BCR-free survival benefit in patients with ePLND compared to patients treated with limited PLND at RP.[14] However, PLND is associated with adverse side effects at RP, such as longer operative time or lymphoceles.[12]

Due to the lack of missing prospective, randomized trials and studies focusing on the effect of ePLND in contemporary patients, we aimed to clarify the potential therapeutic value of ePLND. Specifically, we compared oncologic outcomes in patients who did not undergo PLND vs those who underwent ePLND at RP. We also tested the relationship of PLND performance to BCR, metastasis development and CSM.

PATIENTS AND METHODS

Study Population

After receiving Institutional Review Board approval (IRB No. 2281/21.11.2018) we identified 32,865 patients who underwent RP between 2000 and 2017 at a total of 4 European tertiary referral institutions, including Henri Mondor Hospital, Antonius Hospital, Ospedale San Raffaele and Martini-Klinik Prostate Cancer Center. The study represents the work of members of the EAU-YAUWP (European Association of Urology Young Academic Urologists Working Party on Prostate Cancer).

Only patients with D'Amico intermediate disease and patients at high risk were included in analysis. All patients had available information on clinical tumor stage, biopsy Gleason score, PSA and the percent of positive cores. Of the patients we selected only those with a nomogram derived LNI probability greater than 5% according to the updated Briganti nomogram, which includes information on the percent of positive biopsy cores.[15] Patients with unknown PLND performance, pathological tumor stage or surgical margin status were excluded from study. These selection criteria yielded 9,742 patients for analysis, who represented the current study cohort. Adjuvant treatment was performed according to guideline recommendations.[1]

Surgical Approach

Surgery was done via an open retropubic or robot-assisted laparoscopic approach as previously described.[16–19] All patients in whom PLND was performed underwent extended PLND, as previously described in guidelines.[1]

End Points

BCR was defined as 2 consecutive PSA values of 0.2 ng/ml or greater, or rising PSA after surgery. Time to BCR was calculated as the time from RP to BCR or the last followup. Metastasis-free survival was defined as no radiological sign of metastasis on further imaging studies.[20] Imaging consisted of bone scan and/or computerized tomography, abdominal magnetic resonance imaging and/or ^{11}C-choline positron emission tomography/computerized tomography. Time to metastasis was calculated as the time from RP to metastasis or the last followup. CSM was defined as death attributable to the PCa diagnosis and time to CSM was defined as time from RP to death.

Statistical Analyses

Descriptive statistics include the frequency and proportion for categorical variables. The median and IQR are reported for continuously coded variables. We used the chi-square and Mann-Whitney U tests to examine differences in proportions and medians, respectively.

To account for potential important differences between RP cases with vs without PLND performed at RP we relied on 2:1 nearest neighbor propensity score matching.[21] A caliper of 0.04 was used for matching to achieve 2 homogenous cohorts (supplementary table 1, https://www.jurology.com). Thus, the propensity score matched

cohort was balanced by pathological tumor characteristics, namely the primary pathological Gleason pattern, pathological tumor stage, PSA level and surgical margin status. Kaplan-Meier analysis was done to graphically depict BCR-free, metastasis-free and CSM-free survival rates after propensity score matching.

Two sets of multivariable Cox regression models were fitted to test the relationship between PLND performance and each of the 3 oncologic outcomes. Specifically, the first Cox regression models focused on the relationship between PLND performance and BCR, the second Cox regression models focused on the relationship between PLND performance and metastasis, and the third model focused on the relationship between PLND performance and CSM. In the first set adjustment was made for postoperative covariates, including age at surgery, year of surgery, preoperative PSA, pathological tumor stage, surgical margin status and primary pathological Gleason pattern. In the second set adjustment was made for preoperative covariates, including age at surgery, year of surgery, preoperative PSA, clinical tumor stage and biopsy Gleason score.

R, version 3.4.0 (https://www.r-project.org/) was used for all statistical analyses. All tests were 2-sided with significance considered at $p < 0.05$.

RESULTS

Descriptive Statistics

Overall 707 of the 9,742 identified patients (7.3%) did not undergo PLND (supplementary table 2, https://www.jurology.com). Median followup was 33.5 months, including 30.5 and 60.7 months in patients who did and did not undergo PLND at RP, respectively. Of the patients without PLND at RP 520 and 187 harbored D'Amico intermediate and high risk characteristics, respectively. Men without PLND at RP had significantly lower median PSA (7.5 ng/ml, IQR 5.5–10.3 vs 8.7, IQR 5.8–14.0, $p < 0.001$) and more frequently harbored a biopsy Gleason score of 6 (53.6 vs 6.1%, $p < 0.001$) and pathological stage T2 (64.9% vs 43.7%, $p < 0.001$) than patients with PLND performed at RP. In the PLND cohort a median of 14 lymph nodes (IQR 8–21) were removed and 1,714 patients (19.0%) who underwent PLND harbored lymph node metastasis.

Pelvic Lymph Node Dissection Effects

Biochemical Recurrence and Biochemical Recurrence-Free Survival. After 2:1 propensity score matching the BCR-free survival rate 120 months after RP was 60.4% vs 65.6% for PLND vs no PLND at RP ($p = 0.07$, supplementary fig. 1, https://www.jurology.com). In multivariable Cox regression models after adjusting for pathological covariates PLND at RP did not achieve independent predictor status for BCR (HR 1.12, 95% CI 0.95–1.33, $p = 0.2$, see table). Similar results were recorded for PLND at RP in Cox regression models after adjusting for preoperative tumor characteristics (HR 1.18, 95% CI 0.98–1.41, $p = 0.1$, see table).

Metastasis and Metastasis-Free Survival. After 2:1 propensity score matching the metastasis-free survival rate 120 months after RP was 87.0% vs 90.0% for PLND vs no PLND at RP ($p = 0.06$, supplementary fig. 2, https://www.jurology.com). In multivariable Cox regression models after adjusting for pathological covariates PLND at RP did not achieve independent predictor status for metastasis (HR 1.17, 95% CI 0.79–1.72, $p = 0.4$, see table). Similar results were recorded after adjusting for preoperative tumor characteristics (HR 1.50, 95% CI 0.98–2.29, $p = 0.1$, see table).

Cancer Specific Mortality and Cancer Specific Mortality-Free Survival. After 2:1 propensity score matching the CSM-free survival rate 120 months after RP was 95.2% vs 96.4% for PLND vs no PLND at RP ($p = 0.2$, supplementary fig. 3, https://www.jurology.com). In multivariable Cox regression models after adjustment for pathological covariates PLND at RP did not achieve independent predictor status for CSM (HR 1.45, 95% CI 0.65–3.24, $p = 0.4$, see table). Similar results were recorded after adjusting for preoperative tumor characteristics (HR 2.26, 95% CI 0.98–5.18, $p = 0.1$, see table).

DISCUSSION

The role of ePLND in PCa staging is undebatable. However, its potential therapeutic value is still under debate and prospective trials addressing this void are missing. To shed further light on the therapeutic value of ePLND we compared oncologic outcomes, namely BCR, metastasis and CSM, in patients with a nomogram derived greater than 5% probability of LNI according to the updated Briganti nomogram[15] in patients who did vs did not undergo ePLND at RP. Our analyses revealed several noteworthy findings.

1) PLND was not performed at RP in only 707 of all included patients (7.3%). Of the patients who did not undergo PLND 520 harbored D'Amico intermediate risk characteristics. This result demonstrated that even when ePLND is recommended, it is sometimes not performed. These results are in accord with a previous study by Suardi et al, who reported a PLND rate of 64.9% and 91.2% in patients at D'Amico intermediate and high risk, respectively, in a multi-institutional European database.[2] However, the proportion of patients (7.3%) who did not undergo PLND in our cohort is lower than the proportion reported by Suardi et al. This difference could be related to the fact that many patients at D'Amico intermediate risk in the study by Suardi et al had a 5% or less nomogram

Multivariable Cox regression model predicting BCR, metastasis and CSM after RP adjusted for postoperative and preoperative tumor characteristics

	BCR Prediction		Metastasis Prediction		CSM Prediction	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Adjusted for postop tumor characteristics						
PLND:						
No	Referent		Referent		Referent	
Yes	1.12 (0.95–1.33)	0.2	1.17 (0.79–1.72)	0.4	1.45 (0.65–3.24)	0.4
Primary Gleason score:						
3	Referent		Referent		Referent	
4 or Greater	2.66 (2.42–2.93)	<0.001	4.70 (3.75–5.89)	<0.001	7.10 (4.00–12.58)	<0.001
Pathological tumor stage:						
T2	Referent		Referent		Referent	
T3 or greater	2.28 (2.06–2.54)	<0.001	2.94 (2.32–3.72)	<0.001	2.43 (1.33–4.43)	0.004
Surgical margin:						
Neg	Referent		Referent		Referent	
Pos	1.41 (1.29–1.54)	<0.001	1.37 (1.15–1.63)	<0.001	2.44 (1.60–3.71)	<0.001
Age at surgery	0.99 (0.99–1.00)	0.1	0.98 (0.97–1.00)	0.01	0.99 (0.96–1.02)	0.5
Surgery yr	0.97 (0.96–0.98)	<0.001	1.35 (1.31–1.40)	<0.001	0.91 (0.85–0.97)	0.003
PSA	1.02 (1.01–1.02)	<0.001	1.00 (1.00–1.01)	0.4	1.00 (0.97–1.02)	0.7
Adjusted for preop tumor characteristics						
PLND:						
No	Referent		Referent		Referent	
Yes	1.18 (0.98–1.41)	0.1	1.50 (0.98–2.29)	0.1	2.26 (0.98–5.18)	0.1
Biopsy Gleason score:						
6	Referent		Referent		Referent	
7	1.62 (1.37–1.93)	<0.001	1.65 (1.11–2.43)	<0.05	1.23 (0.60–2.53)	0.6
8 or Greater	2.84 (2.38–3.40)	<0.001	3.76 (2.52–5.60)	<0.001	3.48 (1.63–7.45)	<0.01
Clinical tumor stage:						
T1	Referent		Referent		Referent	
T2	1.42 (1.31–1.55)	<0.001	1.52 (1.27–1.82)	<0.001	1.99 (1.29–3.05)	<0.01
T3	1.93 (1.64–2.27)	<0.001	1.35 (1.01–1.81)	<0.05	4.72 (2.37–9.39)	<0.001
Age at surgery	1.00 (0.99–1.01)	0.9	0.99 (0.98–1.00)	0.1	0.99 (0.97–1.03)	0.9
Surgery yr	0.97 (0.96–0.98)	<0.001	1.33 (1.28–1.38)	<0.001	0.90 (0.85–0.96)	<0.01
PSA	1.04 (1.03–1.04)	<0.001	1.02 (1.02–1.03)	<0.001	1.02 (1.01–1.04)	<0.05

derived probability of LNI and so PLND was not indicated in these patients. Moreover, Suardi et al focused only on a cohort of robot-assisted laparoscopic RP cases between 2005 and 2012. It can be assumed that during this time some surgeons may still have been in the robot-assisted laparoscopic RP learning curve, which could have resulted in a higher rate of PLND avoidance to reduce operative time.

2) Our analyses demonstrated that omitting PLND did not adversely affect the BCR-free survival rate. At 120 months after RP the BCR-free survival rate was 60.4% vs 65.6% for PLND vs no PLND at RP ($p=0.07$). Moreover, in multivariable Cox regression models PLND achieved no independent predictor status for BCR after adjusting for postoperative and preoperative tumor characteristics (HR 1.12, $p=0.2$, and HR 1.18, $p=0.1$, respectively). Our results corroborate the findings by Weight et al, who reported no effect of limited PLND on BCR after 10 years in a historical cohort (1995 to 1999) of patients at D'Amico low risk.[13] Our findings are also in accord with the study by Mandel et al, who reported no effect of PLND on BCR-free survival in patients with intermediate risk PCa and a Gleason score of 6 at RP.[8]

3) Omitting PLND also did not adversely affect metastasis-free survival after RP. At 120 months after RP the metastasis-free survival rate was 87.0% vs 90.0% for PLND vs no PLND performed at RP ($p=0.06$). Moreover, in multivariable Cox regression models PLND was not an independent predictor of metastasis after adjusting for postoperative and preoperative tumor characteristics (HR 1.17, $p=0.4$, and HR 1.50, $p=0.1$, respectively). To our knowledge this is a novel finding and no previous study has focused on the relationship of PLND performance at RP and metastasis development after RP.

4) Omitting PLND also did not negatively affect CSM. At 120 months after RP the CSM-free survival rate was 95.2% vs 96.4% for PLND vs no PLND at RP ($p=0.2$). Moreover, in multivariable Cox regression models PLND was not an independent predictor of CSM after adjusting for postoperative or preoperative tumor characteristics (HR 1.45, $p=0.4$, and HR 2.26, $p=0.1$, respectively).

Taken together, our analyses demonstrated that performing ePLND has no impact on oncologic outcomes after RP. Thus, avoiding PLND might be considered in patients at high risk for complications due to PLND. However, surgeons should be careful when avoiding ePLND in patients at risk for LNI. In

these patients information on pathological lymph node status is required in the decision making process to select the right candidates for adjuvant treatment options. For example, Jegadeesh et al recently reported a survival benefit for adjuvant radiotherapy and hormone therapy in patients with PCa who harbored LNI at RP.[22] However, to our knowledge no study has shown a benefit of pelvic nodal radiotherapy in conjunction with local radiotherapy to the prostate, suggesting that local therapy of nodal metastasis may not improve survival. Hopefully ongoing trials such as the PIVOTAL (Prostate and Pelvis versus Prostate Alone Treatment for Locally Advanced Prostate Cancer) study (RTOG [Radiation Therapy Oncology Group] 0924) will clarify the role of local therapy of nodal metastasis. Moreover, our results may shed doubt on the oncologic value of salvage lymph node dissection.

Our study is not devoid of limitations. Foremost is that our results were derived from retrospective analyses with those inherent limitations. Ideally multi-institutional prospective, randomized trials should be performed to clarify the therapeutic value of PLND. However, to our knowledge no such trial is currently recruiting or ongoing.

Moreover, our database does not contain information on why PLND was omitted in some patients. Thus, there is a possible selection bias despite our reliance on multivariable adjustment and propensity score matching. For instance, surgeons may have decided to perform PLND in cases with unfavorable tumor characteristics, which might have affected our results and masked a benefit of PLND.

Finally, although all RP specimens were evaluated by dedicated uropathologists, no central pathological review was performed. Thus, the possibility of interobserver variability may have further confounded our results.

CONCLUSIONS

There was no significant difference in oncologic outcomes in patients with D'Amico high or intermediate risk PCa whether PLND was or was not performed at RP. While PLND is the most accurate staging procedure to determine pelvic lymph node status, its therapeutic value remains unclear. Prospective multi-institutional, randomized trials are necessary to determine whether PLND at RP has any therapeutic value.

REFERENCES

1. 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.
2. Suardi N, Larcher A, Haese A et al: Indication for and extension of pelvic lymph node dissection during robot-assisted radical prostatectomy: an analysis of five European institutions. Eur Urol 2014; **66:** 635.
3. Withrow DR, DeGroot JM, Siemens DR et al: Therapeutic value of lymph node dissection at radical prostatectomy: a population-based case-cohort study. BJU Int 2011; **108:** 209.
4. Moschini M, Fossati N, Abdollah F et al: Determinants of long-term survival of patients with locally advanced prostate cancer: the role of extensive pelvic lymph node dissection. Prostate Cancer prostatic Dis 2016; **19:** 63.
5. Abdollah F, Gandaglia G, Suardi N et al: More extensive pelvic lymph node dissection improves survival in patients with node-positive prostate cancer. Eur Urol 2015; **67:** 212.
6. Preisser F, Bandini M, Marchioni M et al: Extent of lymph node dissection improves survival in prostate cancer patients treated with radical prostatectomy without lymph node invasion. Prostate 2018; **78:** 469.
7. Joslyn SA and Konety BR: Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. Urology 2006; **68:** 121.
8. Mandel P, Kriegmair MC, Bogdan K et al: Association between lymph node counts and oncological outcomes in lymph node positive prostate cancer. Eur Urol Focus 2017; **3:** 248.
9. Abdollah F, Schmitges J, Sun M et al: A critical assessment of the value of lymph node dissection at radical prostatectomy: a population-based study. Prostate 2011; **71:** 1587.
10. Murphy AM, Berkman DS, Desai M et al: The number of negative pelvic lymph nodes removed does not affect the risk of biochemical failure after radical prostatectomy. BJU Int 2010; **105:** 176.
11. DiMarco DS, Zincke H, Sebo TJ et al: 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.
12. 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.
13. Weight CJ, Reuther AM, Gunn PW et al: 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.
14. Allaf ME, Palapattu GS, Trock BJ et al: Anatomical extent of lymph node dissection: impact on men with clinically localized prostate cancer. J Urol 2004; **172:** 1840.
15. 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.
16. Michl U, Tennstedt P, Feldmeier L et al: Nerve-sparing surgery technique, not the preservation of the neurovascular bundles, leads to improved long-term continence rates after radical prostatectomy. Eur Urol 2016; **69:** 584.
17. Gandaglia G, De Lorenzis E, Novara G et al: Robot-assisted radical prostatectomy and extended pelvic lymph node dissection in patients with locally-advanced prostate cancer. Eur Urol 2017; **71:** 249.
18. Budaus L, Isbarn H, Schlomm T et al: Current technique of open intrafascial nerve-sparing

retropubic prostatectomy. Eur Urol 2009; **56:** 317.

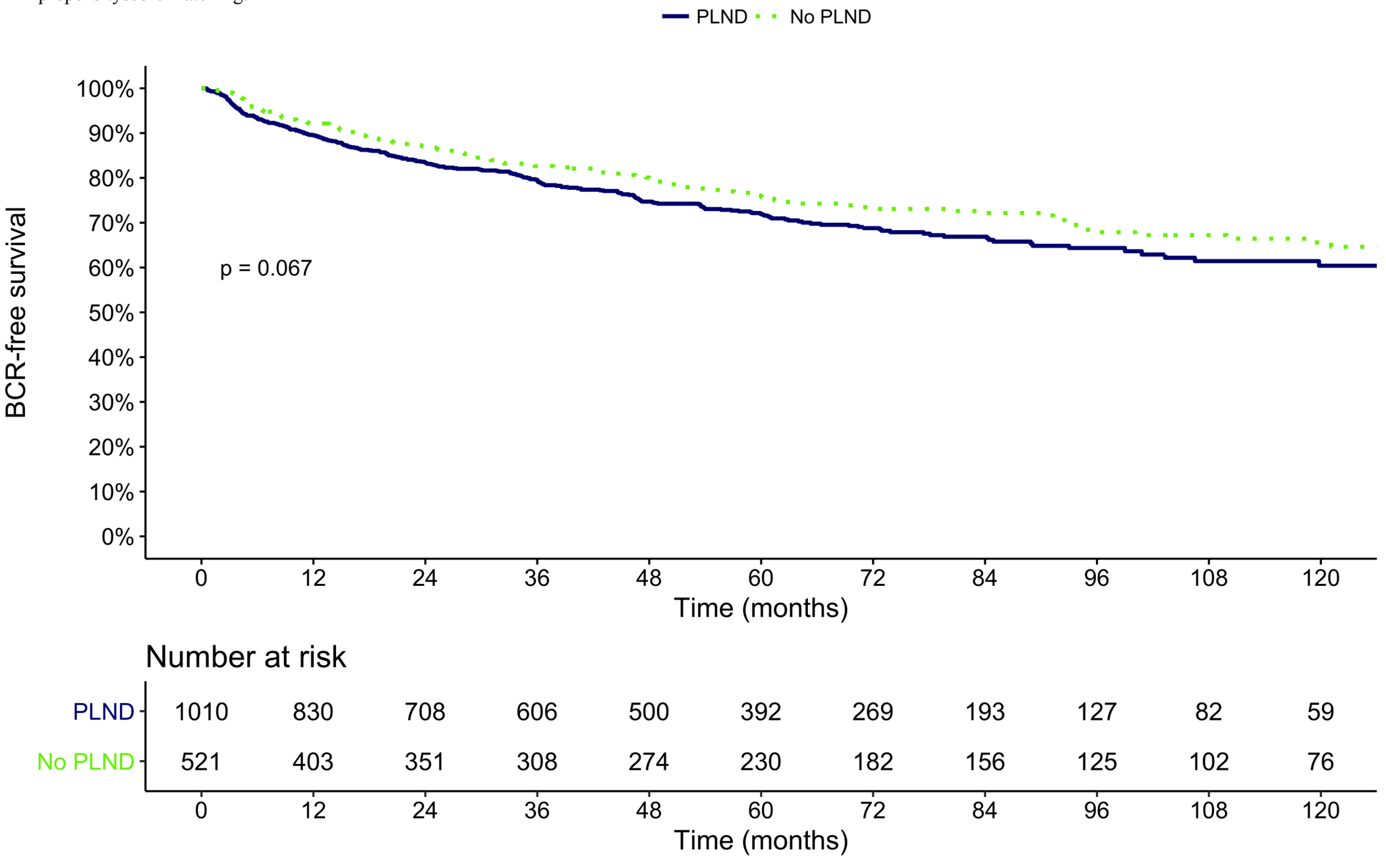
19. Schlomm T, Tennstedt P, Huxhold C et al: Neurovascular structure-adjacent frozen-section examination (NeuroSAFE) increases nerve-sparing frequency and reduces positive surgical margins in open and robot-assisted laparoscopic radical prostatectomy: experience after 11 069 consecutive patients. Eur Urol 2012; **62:** 333.

20. Tilki D, Preisser F, Tennstedt P et al: Adjuvant radiation therapy is associated with better oncological outcome compared with salvage radiation therapy in patients with pN1 prostate cancer treated with radical prostatectomy. BJU Int 2017; **119:** 717.

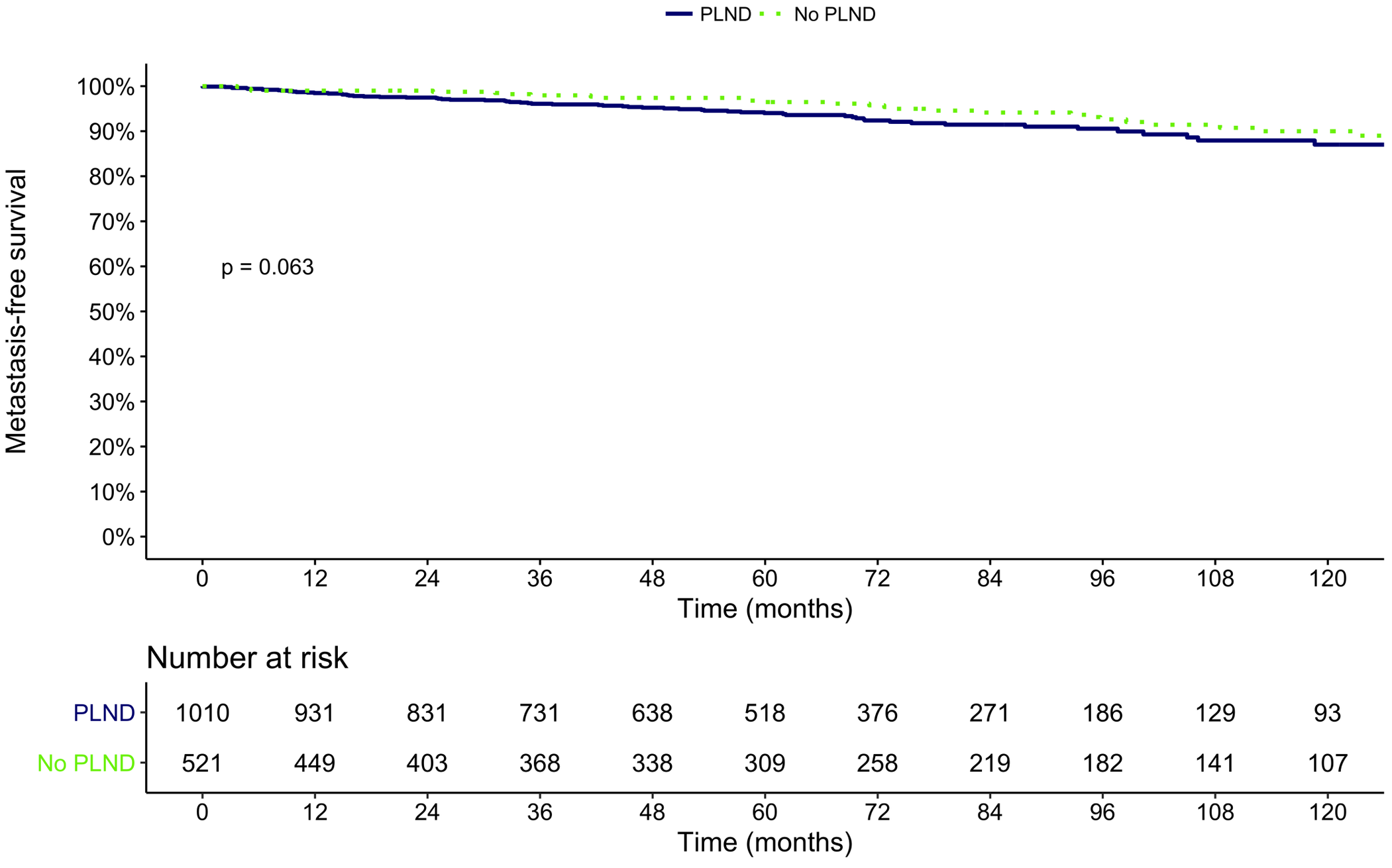
21. Bandini M, Pompe RS, Marchioni M et al: Improved cancer-specific free survival and overall free survival in contemporary metastatic prostate cancer patients: a population-based study. Int Urol Nephrol 2018; **50:** 71.

22. Jegadeesh N, Liu Y, Zhang C et al: The role of adjuvant radiotherapy in pathologically lymph node-positive prostate cancer. Cancer 2017; **123:** 512.

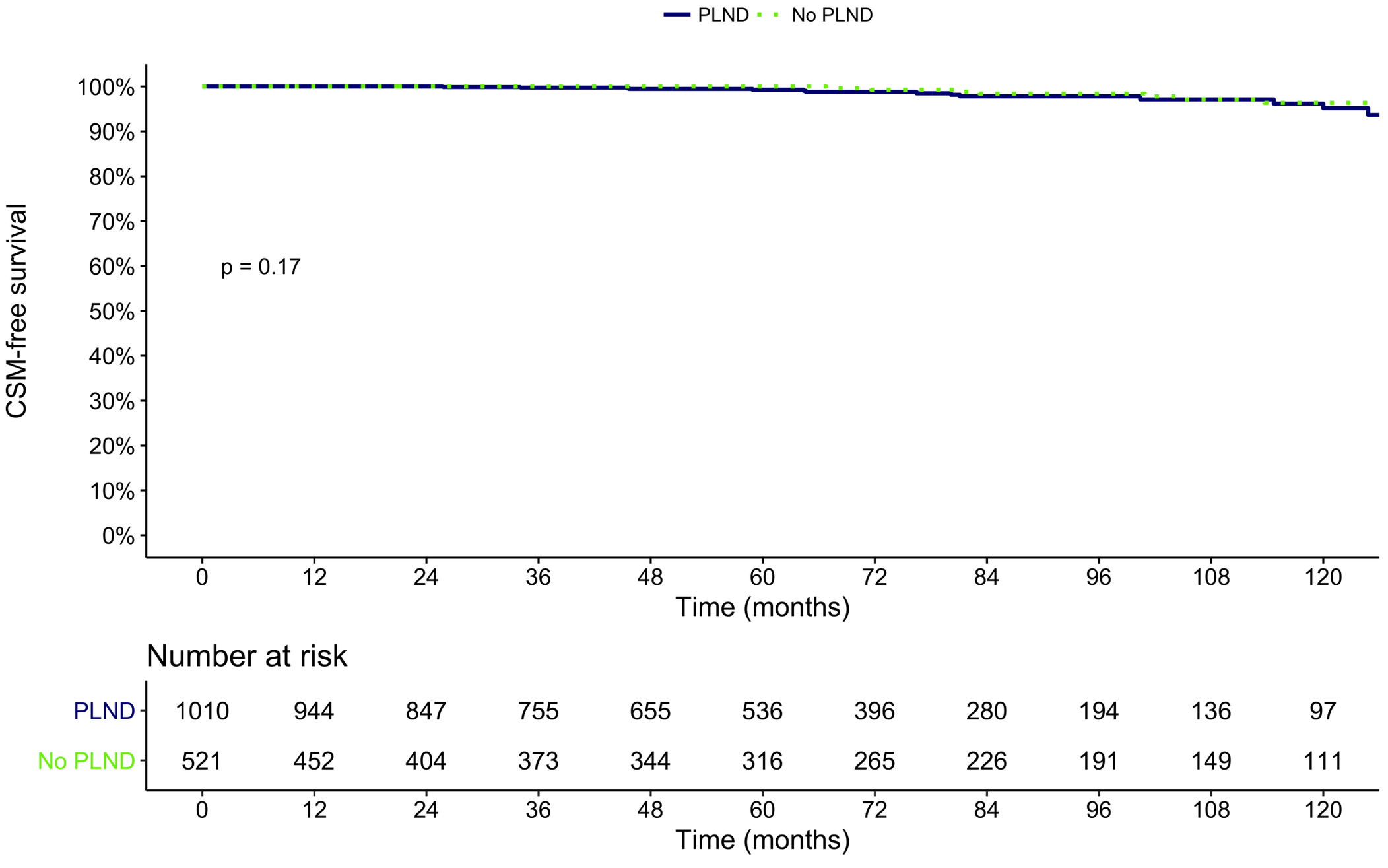
Supplementary figure 1: Kaplan-Meier analysis depicting biochemical recurrence freesurvival for patients who undergo PLND or do not undergo PLND at RP, after 2:1 propensityscore matching.



Supplementary figure 2: Kaplan-Meier analysis depicting metastasis free survival for patientswho undergo PLND or do not undergo PLND at RP, after 2:1 propensity score matching.



Supplementary figure 3: Kaplan-Meier analysis depicting cancer-specific free survival forpatients who undergo PLND or do not undergo PLND at RP, after 2:1 propensity scorematching.



Supplementary table 1. Descriptive characteristics of radical prostatectomy patients with or without pelvic lymph node dissection (PLND), before and after 2:1 propensity score matching, balanced for PSA, pathologic tumor stage, primary pathologic Gleason and surgical margin status.

	Before 2:1 propensity score matching			After 2:1 propensity score matching		
	PLND performed (n=9,035, 92.7%)	**No PLND performed (n=707, 7.3%)**	**smd**	**PLND performed (n=1,010)**	**No PLND performed (n=521)**	**smd**
Year of surgery, mean (sd)	2012.05 (3.50)	2008.29 (4.71)	0.907	2009.33 (3.56)	2007.72 (4.72)	0.386
Age at surgery, yrs, mean (sd)	64.68 (6.71)	63.32 (6.59)	0.204	64.02 (6.30)	62.99 (6.27)	0.163
PSA, ng/ml, mean (sd)	11.27 (8.43)	8.80 (5.82)	0.340	9.06 (5.97)	8.88 (5.88)	0.031
Pathologic tumor stage, n (%)			0.435			0.042
pT2	3951 (43.7)	459 (64.9)		678 (67.1)	360 (69.1)	
≥pT3	2727 (56.3)	162 (35.1)		332 (32.9)	161 (30.9)	
Primary pathologic Gleason, n (%)			0.623			0.024
3	4538 (50.7)	543 (78.5)		854 (84.6)	443 (85.0)	
4	4021 (44.9)	145 (21.0)		153 (15.1)	77 (14.8)	
5	399 (4.5)	4 (0.6)		3 (0.3)	1 (0.2)	
Surgical margin status, n (%)			0.045			0.023
Negative	6523 (72.2)	496 (70.2)		701 (69.4)	356 (68.3)	
Positive	2512 (27.8)	211 (29.8)		309 (30.6)	165 (31.7)	

Abbreviations: PLND – pelvic lymph node dissection; PSA – prostatic specific antigen; sd – standard deviation; smd – standardized mean difference.

Supplementary Table 2. Descriptive characteristics of 9,742 radical prostatectomy patients, stratified according to no pelvic lymph node dissection (PLND) performed vs. PLND performed.

	No PLND performed (n=707, 7.3%)	PLND performed (n=9,035, 92.7%)	P-value
Year of surgery, median (IQR)	2008 (2004-2012)	2013 (2010-2015)	<0.001
Age at surgery, yrs, median (IQR)	63.6 (59.1-68.2)	65.5 (60.2-69.8)	<0.001
Median PSA, ng/ml (IQR)	7.5 (5.5-10.3)	8.7 (5.8-14.0)	<0.001
D'Amico risk, n (%)			
Intermediate-risk	520 (73.6)	4723 (52.3)	<0.001
High-risk	187 (26.4)	4312 (47.7)	
Clinical tumor stage, n (%)			
cT1	298 (42.1)	4854 (53.7)	<0.001
cT2	371 (52.5)	3736 (41.4)	
cT3	38 (5.4)	445 (4.9)	
Biopsy Gleason Score, n (%)			
6	379 (53.6)	551 (6.1)	<0.001
7	289 (40.9)	5317 (58.8)	
≥8	39 (5.5)	3167 (35.1)	
Pathologic tumor stage, n (%)			
pT2	459 (64.9)	3951 (43.7)	<0.001
pT3a	162 (22.9)	2727 (30.2)	
≥pT3b	86 (12.2)	2357 (26.1)	
Primary pathologic Gleason, n (%)			
3	543 (76.8)	4538 (50.2)	<0.001
≥4	149 (21.1)	4420 (48.9)	
NA	15 (2.1)	77 (0.9)	
Surgical margin status, n (%)			
Negative	496 (70.2)	6523 (72.2)	0.3
Positive	211 (29.8)	2512 (27.8)	
Lymph node status, n (%)			
pN0	0 (0)	7321 (81.0)	
pN1	0 (0)	1714 (19.0)	
pNX	707 (100)	0 (0)	

Abbreviations: IQR – interquartile range; PLND – pelvic lymph node dissection; PSA – prostatic specific antigen