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Research Article

Association between pelvic lymph node dissection and survival among patients with prostate cancer treated with radical prostatectomy

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ABSTRACT

Introduction: Although the clinical benefits of pelvic lymph node dissection (PLND) at the time of radical prostatectomy for prostate cancer remain uncertain, major guidelines recommend PLND based on risk profile. Thus, the objective of this study was to examine the association between PLND and survival among patients undergoing RP stratified by Gleason grade group (GG) with the aim of allowing patients and physicians to make more informed care decisions about the potential risks and benefits of PLND.

Materials and methods: From the SEER-17 database, we examined overall (OS) and prostate cancer-specific (PCSS) survival of prostate cancer patients who underwent RP from 2010 to 2015 stratified by GG. We applied propensity score matching to balance pre-operative characteristics including race, age, PSA, household income, and housing status (urban/rural) between patients who did and did not undergo PLND for each GG. Statistical analyses included log-rank test and Kaplan-Meier curves.

Results: We extracted a matched cohort from 80,287 patients with GG1-5 who underwent RP. The median PSA value was 6.0 ng/mL, and the median age was 62-years-old. 49,453 patients underwent PLND (61.60%), while 30,834 (38.40%) did not. There was no difference in OS and PCSS between patients who received PLND and those who did not for all Gleason GG (OS—GG1: $P = 0.20$, GG2: $P = 0.34$, GG3: $P > 0.05$, GG4: $P = 0.55$, GG5: $P = 0.47$; PCSS—GG1: $P = 0.11$, GG2: $P = 0.96$, GG3: $P = 0.81$, GG4: $P = 0.22$, GG5: $P = 0.14$).

Conclusions: In this observational study, PLND at the time of RP was not associated with improved OS or PCSS among patients with cGS of 3 + 3, 3 + 4, 4 + 3, 4 + 4, 4 + 5, and 5 + 4. These findings suggest that until definitive clinical trials are completed, prostate cancer patients who have elected RP should be appropriately counseled on the potential risks and lack of proven survival benefit of PLND.

1. Introduction

Prostate cancer (PCa) is the most common solid malignancy in men and the fifth leading cause of cancer death globally; it comprises 1.6 million cases and accounts for over 300,000 deaths annually.[1-3] Pelvic lymph node dissection (PLND), commonly performed simultaneously during radical prostatectomy (RP), is considered the gold standard for PCa nodal staging.[4] While PLND was historically viewed as imperative due to the incidence of nodal involvement exceeding 20%, the advent of modern screening approaches including PSA has drastically diminished the proportion of patients who present with nodal metastases.[5] Moreover, contemporary imaging modalities including next-generation molecular imaging substantially improve the identification of occult

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nodal metastases.[6] In some patients with nodal involvement, PLND has been suggested to be therapeutic.[7] However, the oncologic benefits of PLND remain uncertain.[4,7-15]

Current guidelines by the National Comprehensive Cancer Network (NCCN) and European Association of Urology (EAU) recommend PLND as an acceptable standard of care in PCa patients undergoing RP, setting the threshold for PLND based on nomogram-based risk of pelvic lymph node metastasis between 2% and 5% risk of lymph node invasion.[13,16,17] In this framework, a study of North American patients with lymph node invasion risk greater than 5% determined that neither PLND nor its extent was significantly associated with survival.[11] In addition, a study of post-RP patients with lymph node invasion also concluded that no association exists between removal of a greater number of lymph nodes and patient survival and instead that prognosis depends exclusively on tumor biology.[14]

Notwithstanding, there is a body of literature that suggests that there may be a subgroup of men with PCa who may benefit from PLND. Specifically, it has been reported that higher lymph node yield is associated with improved cancer-specific survival.[8] Similarly, it has been suggested that a more extensive PLND involving more than three regional lymph nodes primarily benefits patients with Gleason scores $\geq$8, whereas cancer-specific survival is unchanged in patients with lower stage PCa regardless of the number of lymph nodes removed.[4]

While the oncologic benefit of PLND is debatable, there are real potential complications associated with the procedure. These include lymphocele, lower extremity edema, increased blood loss, iliac vessel injury, longer operative time, and longer hospital stay.[18] Furthermore, PLND may also adversely impact healthcare costs both through procedural costs and management of downstream complications. Therefore, the purpose of this study is to evaluate the overall survival (OS) and PCa-specific survival (PCSS) benefit of PLND among patients categorized by clinical Gleason score (cGS). Furthermore, to determine whether clinically relevant subsets could be identified for whom PLND was associated with a survival benefit, we stratified these analyses by Gleason grade group (GG).

2. Methods

2.1. Data sources

The study examined patients at least 25 years old diagnosed with PCa from 2010–2015 from the Surveillance, Epidemiology, and End Results (SEER) 17 registries database submitted in November 2021 using the SEER*Stat program. Registries include the Alaska Native Tumor Registry, Connecticut, Atlanta, Greater Georgia, Rural Georgia, San Francisco-Oakland, San Jose-Monterey, Greater California, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Mexico, New Jersey, Seattle-Puget Sound, and Utah. The cohort was limited to patients diagnosed from 2010 to 2015 due to the availability of study variables. Information on radiotherapy was obtained from SEER's Research Plus supplementary database.

2.2. Study variables

We compiled patient clinical and demographic characteristics related to age, prostate-specific antigen (PSA), race, area-level median household income, housing status (rural vs. urban), Gleason score at biopsy or cGS, lymph node invasion status, PLND status based on the number of lymph nodes identified, the number of positive regional lymph nodes, and radiotherapy status. cGS was categorized into five Gleason GGs (GG1: 3 + 3; GG2: 3 + 4; GG3: 4 + 3; GG4: 3 + 5, 4 + 4, 5 + 3; GG5: 4 + 5, 5 + 4, 5 + 5). Radiation treatment was defined as “beam radiation,” “combination of beam with implants or isotopes,” “radiation, not otherwise specified method or source no specified,” “radioactive implants (includes brachytherapy) (1988+),” or “radioisotopes (1988+).”

2.3. Statistical analysis

The primary outcomes included OS and prostate cancer-specific survival (PCSS). We prespecified our analysis to stratify these outcomes by PLND status, Gleason GG, and the number of lymph nodes removed. Both OS and PCSS were estimated using the Kaplan-Meier method. For each cGS category, all analyses were performed both on the overall cohort between those who did and did not undergo PLND as well as a 1:1 nearest neighbor propensity score-matched (PSM) cohort matched by age, race, PSA, area-level income, and rural-urban housing status. Additionally, we applied PSM by the same variables mentioned above for each cGS category further stratified by PSA category as well. PSM was used to create groups of patients who did and did not undergo PLND balanced on measured potential confounders. The statistical significance of the changes in the distribution of patient characteristics between patients with and without PLND in the unmatched cohort was measured with Pearson's chi-squared test and the standardized mean difference (SMD), while that of the matched cohort was measured with the SMD only. All statistical analyses were conducted using Stata/SE 15.0.

3. Results

3.1. There are no significant differences in patient characteristics between patients who did and did not have PLND in the propensity score-matched cohort

The unmatched cohort consisted of 80,287 patients who were diagnosed with PCa from January 2010 to December 2015 (30,834 PLND and 49,453 non-PLND), while the matched cohort was composed of 44,160 patients (22,080 PLND and 22,080 non-PLND). The median follow-up was 86 months (IQR: 40) and 4,985 died during the follow-up period including 1,265 patients from PCa. In the unmatched cohort, statistically significant differences regarding age, race, PSA, area-level income, rural-urban status, Gleason GG at biopsy, lymph node invasion, number of lymph nodes removed, number of positive regional nodes, and radiotherapy status were present between patients who did and did not undergo PLND ($p < 0.001$) (Table 1). Prior to matching and using a standard cutoff of 0.100, SMD between the PLND and non-PLND groups were balanced for race, area-level income, and rural-urban status ($|SMD| < 0.100$ for all categories, Table 1) but not balanced for age and PSA ($|SMD| = 0.157$ and $|SMD| = 0.302$, respectively, Table 1). After propensity score matching by age, race, PSA, area-level income, and rural-urban status for each GG, there were no statistically significant standardized differences in age, PSA, race, area-level income, and rural-urban status ($|SMD|<0.100$ for all categories, Table 1).

Overall, the incidence of lymph node invasion as well as the proportion of patients who underwent PLND generally increased with higher GG (Supplementary Table 1). Additionally, the use of radiotherapy was higher among patients who received PLND in both the unmatched and matched cohorts ($P < 0.001$) (Table 1). A breakdown by GG for the unmatched cohort indicated that use of radiotherapy was significantly different between PLND and non-PLND patients across all GG (GG1: 2.9 vs. 1.8%, $P < 0.01$; GG2: 5.2% vs. 3.5%, $P < 0.01$; GG3: 9.7% vs. 7.2%, $P < 0.01$; GG4: 14.5% vs. 9.9%, $P < 0.01$) except for those in GG5 (23.1 vs. 22.4%, $P = 0.76$) (Supplementary Table 2). In contrast, in the matched cohort, only GG1 had significantly higher use of radiotherapy in the PLND group

Table 1
Patient characteristics

	Overall sample				Propensity-score matched sample		
	No PLND No. (n =) (% or IQR)	PLND No. (n =) (% or IQR)	P	Standardized mean difference	No PLND No. (n =) (% or IQR)	PLND No. (n =) (% or IQR)	Standardized mean difference
Age Range							
<40	40 (0.13)	30 (0.06)	<0.001	0.157	18 (0.08)	16 (0.07)	−0.010
40–49	1,839 (5.96)	2,230 (4.51)			1,119 (5.07)	1,157 (5.24)	
50–59	11,393 (36.95)	15,897 (32.15)			7,600 (34.42)	7,637 (34.59)	
60–69	14,583 (47.30)	24,783 (50.11)			10,948 (49.58)	10,856 (49.17)	
>70	2,979 (9.66)	6,513 (13.17)			2,395 (10.85)	2,414 (10.93)	
PSA							
≤4	5,057 (17.68)	5,901 (12.77)	<0.001	0.302	3,397 (15.38)	3,532 (16.00)	0.037
4 < PSA ≤10	20,619 (72.09)	29,210 (63.20)			15,822 (71.66)	15,016 (68.01)	
10 < PSA ≤20	2,389 (8.35)	7,774 (16.82)			2,328 (10.54)	2,763 (12.51)	
20 < PSA ≤50	384 (1.34)	2,681 (5.80)			382 (1.73)	618 (2.80)	
>50	152 (0.53)	655 (1.42)			151 (0.68)	151 (0.68)	
Race							
Non-Hispanic White	22,001 (71.77)	35,187 (71.71)	<0.001		16,046 (72.67)	16,056 (72.72)	
Non-Hispanic Black	3,900 (12.72)	6,198 (12.63)		−0.005	2,748 (12.45)	2,734 (12.38)	−0.001
Hispanic	3,295 (10.75)	4,765 (9.71)		−0.036	2,219 (10.05)	2,205 (9.99)	<0.001
Asian/Pacific Islander	1,355 (4.42)	2,754 (5.61)		0.051	1,009 (4.57)	1,025 (4.64)	0.004
American Indian/Alaska Native	104 (0.34)	167 (0.34)		−0.003	58 (0.26)	60 (0.27)	0.002
Area-Level Median Household Income							
$0–$54,999	7,640 (24.78)	10,988 (22.22)	<0.001	0.051	5,403 (24.47)	5,490 (24.86)	−0.015
$55,000–$64,999	8,786 (28.50)	15,332 (31.01)			6,315 (28.60)	6,847 (31.01)	
$65,000–74,999	6,152 (19.95)	8,052 (16.28)			4,326 (19.59)	3,281 (14.86)	
> $75,000	8,254 (26.77)	15,078 (30.49)			6,036 (27.34)	6,462 (29.27)	
Housing Status (Urban vs. Rural)							
Urban	27,407 (88.92)	44,319 (89.65)	0.001	−0.020	19,865 (89.97)	19,741 (89.41)	0.021
Rural	3,415 (11.08)	5,116 (10.35)			2,215 (10.03)	2,339 (10.59)	
Gleason grade group at biopsy (Gleason scores)							
1 (3 + 3)	18,650 (60.49)	11,927 (24.12)	<0.001		10,821 (49.01)	10,821 (49.01)	
2 (3 + 4)	8,504 (27.58)	17,694 (35.78)			7,891 (35.74)	7,891 (35.74)	
3 (4 + 3)	2,434 (7.89)	9,016 (18.23)			2,228 (10.09)	2,228 (10.09)	
4 (3 + 5, 4 + 4, 5 + 3)	911 (2.95)	6,814 (13.78)			827 (3.75)	827 (3.75)	
5 (4 + 5, 5 + 4, 5 + 5)	335 (1.09)	4,002 (8.09)			313 (1.42)	313 (1.42)	
Lymph node invasion	20 (0.07)	2,916 (5.90)	<0.001		16 (0.07)	604 (2.74)	
Number of removed nodes			<0.001				
0	30,549 (100.00)	0 (0.00)			21,849	0 (0.00)	
1–3	0	15,215 (31.40)			0 (0.00)	7,501 (34.66)	
>3	0	33,243 (68.60)			0 (0.00)	14,140 (65.34)	
Number of Positive Regional Lymph Nodes							
0/Unknown	30,817 (99.94)	46,574 (94.18)	0.001		22,067 (99.94)	21,086 (97.27)	
1–2	14 (0.05)	2,270 (4.59)			11 (0.05)	500 (2.31)	
≥3	3 (0.01)	609 (1.23)			2 (0.01)	92 (0.42)	
Radiotherapy							
No/Unknown	29,851 (96.81)	45,409 (91.82)	<0.001		21,230 (96.15)	21,047 (95.32)	
Yes	983 (3.19)	4,044 (8.18)			850 (3.85)	1,033 (4.68)	

when compared to non-PLND group (3.1 vs. 2.2%, $P < 0.001$) (Supplementary Table 3).

OS of patients with and without PLND in the unmatched cohort was not significantly different across all GGs (GG1: $P = 0.21$, GG2: $P = 0.93$, GG3: $P = 0.80$, GG4: $P = 0.84$, GG5: $P = 0.94$) (Fig. 1a). For PCSS of the unmatched cohort, there were no statistically significant differences between PLND and non-PLND patients across all GGs except for GG1, for whom those with PLND experienced worse survival than those without PLND. (GG1: $P = 0.01$, GG2: $P = 0.30$, GG3: $P = 0.35$, GG4: $P = 0.76$, GG5: $P = 0.57$) (Fig. 1b). After propensity score matching, PLND status was not significantly associated with either OS or PCSS across all GGs (OS—GG1: $P = 0.20$, GG2: $P = 0.34$, GG3: $P > 0.05$, GG4: $P = 0.55$, GG5: $P = 0.47$; PCSS—GG1: $P = 0.11$, GG2: $P = 0.96$, GG3: $P = 0.81$, GG4: $P = 0.22$, GG5: $P = 0.14$) (Fig. 2a and b, respectively). Propensity score matching on each cGS category further stratified by PSA category also showed no significant differences in OS or PCSS between PLND and non-PLND patients (Supplementary Figures 1–10).

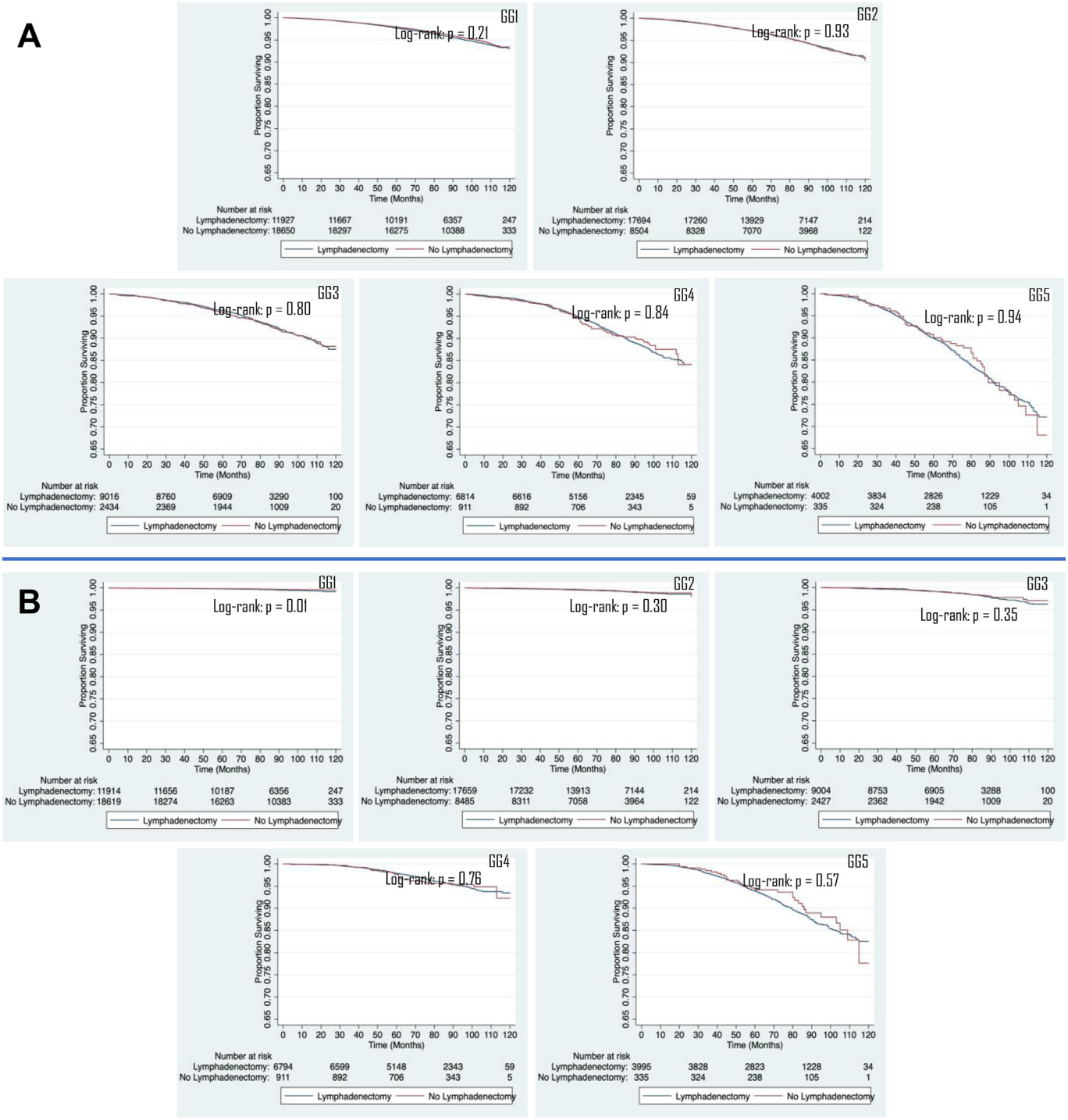

Figure 1. A) Overall survival of patients with and without PLND by Gleason GG in overall sample. B) Prostate cancer-specific survival of patients with and without PLND by Gleason GG in overall sample. GG1 patients with PLND experienced worse survival than non-PLND patients. No significant survival difference was observed in other subgroups.

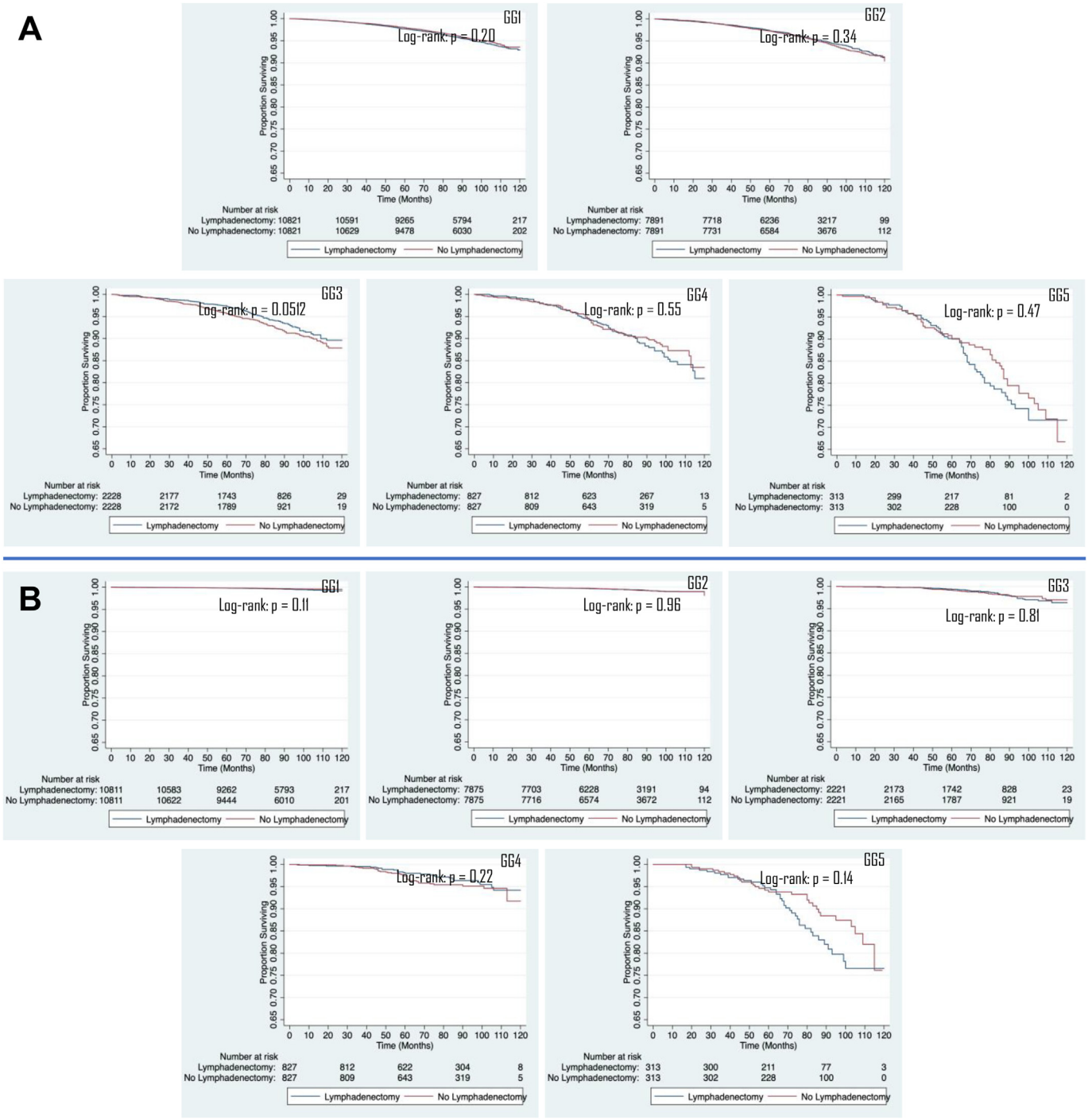

Figure 2. A) Overall survival of patients with and without PLND by Gleason GG in propensity-score matched sample. B) Prostate cancer-specific survival of patients with and without PLND by Gleason GG in propensity-score matched sample. No significant survival difference was observed in all subgroups.

Both OS and PCSS were not significantly different between patients undergoing PLND with 4 or more lymph nodes removed and those who did not undergo PLND in both the unmatched and matched cohorts across all GGs (OS—GG1: $P = 0.22$, GG2: $P = 0.14$, GG3: $P = 0.12$, GG4: $P = 0.96$, GG5: $P = 0.78$; PCSS—GG1: $P > 0.05$, GG2: $P = 0.99$, GG3: $P = 0.61$, GG4: $P = 0.24$, GG5: $P = 0.06$) (Fig. 3a and b, respectively).

In the unmatched cohort, while only 0.46% of patients who did not undergo PLND were staged as pathologic N1 (pN1), 5.79% of PLND patients were designated pN1 (Supplementary Table 4). Similarly, in the matched cohort, 0.05% of non-PLND patients were staged pN1 compared to 2.69% of PLND patients (Supplementary Table 5).

4. Discussion

To better inform clinical decision-making, we evaluated the association between PLND and survival outcomes among patients with PCa undergoing RP using the SEER database. We found no significant OS and PCSS differences between patients who did and

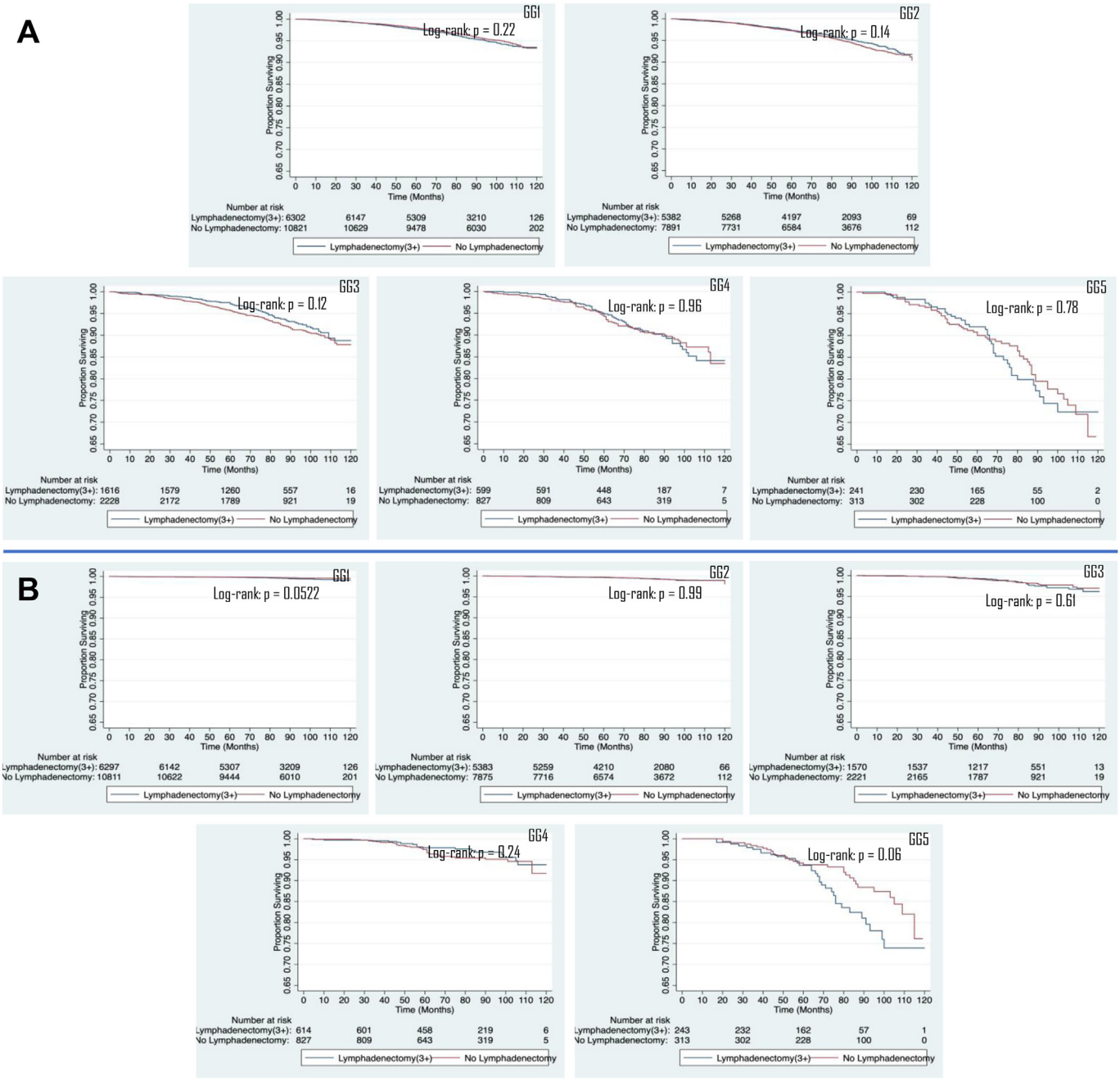

Figure 3. A) Overall survival of patients with PLND who had 4 or more lymph nodes removed vs. without PLND by Gleason GG in propensity-score matched sample. B) Prostate cancer-specific survival of patients with PLND who had 4 or more lymph nodes removed vs. without PLND by Gleason GG in propensity-score matched sample. No significant survival difference was observed in all subgroups.

did not have PLND in both the unmatched and PSM cohorts across all Gleason GGs and PSA categories except for the unmatched GG1 group wherein PLND patients experienced worse PCSS outcomes. Patients who had undergone more adequate PLND defined as 4 or more lymph nodes removed similarly lacked significant differences in OS and PCSS outcomes when compared to patients who did not undergo PLND. Taken together, these findings question the clinical benefit of routine PLND based on guidelines and underscore the need for a higher level of therapeutic evidence.

PCa clinical practice guidelines suggest a risk-adapted approach to the selection of PLND during RP. For example, NCCN and EAU advise PLND if the risk of lymph node invasion is greater than 2% and 5%, respectively.[16,17] When MRI-targeted biopsy is used, EAU recommends 7% cut-off for risk of lymph node invasion in performing PLND.[19] The American Urological Association guidelines for management of PCa recommend PLND for intermediate-risk (PSA >10, cGS $\geq 3 + 4$) and high-risk patients (PSA >20, cGS $\geq 4 + 4$).[20] Widespread adoption of these guidelines likely resulted in the significant PSA and cGS differences between the PLND and non-PLND groups in the unmatched cohort.[20,21] As for age, older men are more likely to present with higher PSA levels and cGS and therefore have increased likelihood of receiving PLND as was seen in the unmatched cohort.[22,23] Racial differences between the unmatched PLND and non-PLND groups were most pronounced with respect to patients of Asian and Pacific Islander descent, who were significantly more likely to undergo PLND. It has previously been

reported that Asian men are more likely to be diagnosed after age 70 and more frequently present with poorly differentiated PCa as compared with other racial and ethnic groups.[24,25] The risk of lymph node invasion increased directly with higher cGS, as lymph node invasion is indicative of poor prognosis and advanced stage in PCa.[17] In addition, because PLND is commonly recommended for nodal staging of patients with high risk of lymph node invasion, rates of lymph node invasion were higher among PLND patients. Our observation that patients who had undergone PLND in the unmatched cohort had higher rates of radiotherapy can be explained, in part, by the frequent use of radiotherapy as an adjuvant treatment for lymph node–positive disease.[7] The presence of positive nodes in 16 patients who did not receive PLND was likely diagnosed via biopsy of regional lymph nodes.

Overall, our matched and unmatched samples revealed no significant increase in OS and PCSS for patients with PLND compared to without PLND, suggesting that PLND does not offer a survival benefit. In fact, among GG1 patients in the unmatched cohort, those who received PLND had lower PCSS than those who did not. This outcome may be explained by the low likelihood for GG1 patients, who have a cumulative 10-year PCSS of >99%, to experience metastasis or clinically significant symptoms; thus, undergoing PLND merely increases mortality risk in this subset by way of exposure to intra-operative and postoperative complications.[26,27] There are two major proposed oncologic benefits of simultaneous PLND at the time of RP. First, a small proportion of men with lymph node-positive PCa may be cured by PLND. A previous study reported that up to 19% of patients with pathological N1 PCa have a 5-year biochemical recurrence-free survival following RP alongside PLND without adjuvant therapies.[28] Second, PLND is by consensus the most accurate nodal staging technique. By identifying patients with lymph node–positive disease early, PLND may result in the implementation of adjuvant therapies such as radiotherapy. In this regard, radiotherapy use in the current matched cohort is higher in the PLND group. When stratified by Gleason GG, such differences in the utilization of radiation was significant only in GG1 patients in the matched cohort. Although the precise reason for such difference is not clear, the observed differences of approximately 1% in radiotherapy use may not be clinically meaningful. Regardless, we propose that the higher rate of postoperative radiation use in GG1 following PLND is likely due to the detection of pN1 disease following RP for the following two reasons. First, lower cGS patients likely do not receive adjuvant radiotherapy postoperatively due to low risk of recurrence. Second, the overall rate of recurrence in cGS 3 + 3 group between the PLND and non-PLND groups is likely similar. Therefore, salvage radiotherapy use between the two groups may be similar. It should also be noted that the overall rate of radiotherapy among higher cGS groups remained the same between the non-PLND and PLND groups. Since observation followed by salvage radiotherapy is the preferred management approach following RP, the similar utilization rates of radiotherapy between the non-PLND and PLND groups suggest no real benefit of PLND in higher cGS patients. Further analysis of the outcomes based on early vs. later use of radiotherapy in pN1 PCa patients is necessary to verify this concept.

Consistent with the body of accumulating data, we found no improvement in survival with increased lymph node yield. On the other hand, Abdollah et al. and Preisser et al. reported that the number of nodes removed during PLND was inversely related with cancer-specific mortality in PCa patients either with or without the presence of lymph node invasion.[8,9] It should be noted that more extensive PLND enables greater accuracy when staging PCa, ensuring sufficient lymph node yield during PLND to properly diagnose node-positive patients.[29] Thus, subsequent treatment of these patients with adjuvant or salvage therapies such as radiotherapy and androgen deprivation therapy (ADT) may lead to the observed survival outcomes, rather than any intrinsic therapeutic benefit of PLND. Nevertheless, the results of the present study contrasted with these findings, demonstrating that higher lymph node yield (<4 vs. 4 or more) did not invoke a superior survival response compared to foregoing PLND. Our results are supported by the work of Mandel et al. and Washington et al., which found no association between the number of lymph nodes dissected and oncological outcomes as measured by biochemical recurrence-free survival, OS, and PCSS.[12,13] Furthermore, a 66-study meta-analysis carried out by Fossati et al. revealed that both limited and extensive PLND may in fact precipitate higher mortality, due to protracted surgical duration predisposing to a higher rate of complications.[18] Indeed, PLND is associated with significant surgical morbidity. Known intra- and postoperative complications resulting from PLND include thromboembolism, lymphoceles, and regional neurovascular damage.[30] Finally, Chen et al. found no significant differences in OS and PCSS between patients with and without PLND in a cohort that had been matched based on 8 baseline characteristics including D'Amico risk stratification, cT stage, and pT stage.[11]

Current guidelines on pN1 PCa patients include observation, radiotherapy with or without chemohormonal therapy, and ADT. Since these options essentially provide no guidance to physicians in treating their patients, well-designed and carefully executed clinical trials are necessary. Clinical trials NCT01407263 and NCT05109910 are currently investigating the oncologic difference between PLND and non-PLND in men undergoing RP. These studies will determine the direct therapeutic effect of PLND.

As previously stated, one of the theoretical benefits of early diagnosis of lymph node–positive disease is the implementation of effective adjuvant therapy. In this regard, permanent ADT is the only adjuvant treatment with level 1 evidence showing improved survival in pN1 patients, as a 2021 study found that whole pelvic nodal radiotherapy did not demonstrate an OS benefit compared to prostate-only radiotherapy in patients with high-risk, locally advanced PCa.[31,32] However, adjuvant ADT in pN1 PCa remains controversial due to the flawed execution of the study as well as long-term adverse effects of ADT. Accordingly, in pN1 PCa patients, adjuvant radiotherapy combined with a limited duration of ADT has been advocated by many experts.[31,33] Indeed, NCT04134260 (NRG-GU008) is currently recruiting patients to determine the optimal ADT combination in men with pN1 PCa. Unfortunately, this study's impact is undermined by the lack of solid supporting data on the use of adjuvant radiotherapy. Therefore, a more urgent study in pN1 PCa patients is the comparison of adjuvant vs. observation followed by salvage radiotherapy after failure. Until such a study is completed, clinical decisions regarding PLND in the absence of clear survival data should involve a thorough risk assessment and be made via shared decision-making with patients.

A key strength of our study was stratifying the data by Gleason GG and the implementation of 1:1 propensity score matching by age, race, PSA, area-level income, and rural-urban status in each GG category, which facilitated the creation of groups with similar baseline characteristics. Such an approach provides a more reliable study sample to evaluate the link between PLND and survival in lieu of a randomized controlled trial.[34] In addition, the use of the population-based SEER database contributed to the strength of our study by illuminating patterns and trends based on real-world practice in a large sample size drawn from various geographical regions, which would not be feasible in randomized controlled trials. Nevertheless, our study was limited by several factors inherent to the SEER database. First, SEER does not include data on biochemical-recurrence-free survival, rendering OS and PCSS the only viable options to track survival outcomes. Second, treatment with ADT or other systemic therapies is not cataloged in SEER,

precluding our ability to evaluate their effect on survival.[10] Third, the use of SEER effectively requires the study design to be retrospective in nature. Fourth, limiting lymph node dissection stratification to '4 or more' does not adequately characterize the impact of a more extended PLND. Lastly, clinical staging is not uniformly available in SEER due to the use of "best" staging. Accordingly, propensity score matching for clinical and pathologic staging could not be conducted. Nevertheless, such a limitation does not undermine the conclusion of this study because of the equivalent survival between the non-PLND and PLND groups. Indeed, the relatively low percentage of non-PLND patients with pathologic N1 disease compared to PLND patients in both the matched and unmatched cohorts suggests that a significant portion of non-PLND patients have been staged as clinical N0, but in reality, have pathologic N1 disease. If PLND has any survival benefit, then the survival of non-PLND patients should be worse due to the residual disease. Thus, the observed lack of survival difference between PLND and non-PLND patients continues to support the hypothesis that PLND may not be clinically beneficial. Regardless, the current study should be treated as a hypothesis-generating study that may be bolstered through further investigation using different population-based databases.

5. Conclusion

When PCa patients with cGS ranging from 3 + 3 to 5 + 4 were matched by age, race, PSA, area-level income, and rural-urban status, PLND was not associated with OS and PCSS benefit compared to those who did not undergo a PLND. The risk of PLND remains real and significant, while there is no contemporary level 1 evidence supporting the procedure in PCa patients who have elected RP. Therefore, we advocate that PLND during RP should be performed preferably under clinical trials and via shared decision between the patient and provider and not be carried out simply based on arbitrary risk thresholds of guidelines.

Data availability statement

This study used publicly available data from the Surveillance, Epidemiology, and End Results Program (SEER) database at https://seer.cancer.gov/data/.

Ethical approval statement

Since data from the Surveillance, Epidemiology, and End Results Program (SEER) database is publicly available and de-identified, this study did not require approval by an Institutional Review Board (IRB).

Conflicts of interest

No significant conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prnil.2024.01.002.

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