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Original Article: Clinical Investigation

Utilization and impact of surgical technique on the performance of pelvic lymph node dissection at radical prostatectomy: Results from the Shared Equal Access Regional Cancer Hospital database

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Abbreviations & Acronyms
AUA = American Urological Association
BMI = body mass index
ORP = open radical prostatectomy
PC = prostate cancer
PLND = pelvic lymph node dissection
PSA = prostate-specific antigen
RARP = robotic-assisted radical prostatectomy
RP = radical prostatectomy
SEARCH = Shared Equal Access Regional Cancer Hospital
SEER = Surveillance, Epidemiology and End Results
VA = Veterans Administration

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Objective: To evaluate performance of pelvic lymph node dissection during radical prostatectomy within an equal access care setting over a period of time, and stratified by prostate cancer risk group and surgical technique.
Methods: We identified men in the Shared Equal Access Regional Cancer Hospital database who had open or robotic-assisted radical prostatectomy from 2006 to 2013. Univariable logistic regression was used to test the association between age, race, body mass index, total biopsy cores, number of positive biopsy cores, risk group, year, center, surgical volume and surgical technique on pelvic lymph node dissection use. Multivariable logistic analysis was used to examine surgical technique and pelvic lymph node dissection performance. Spearman's correlation examined temporal changes in pelvic lymph node dissection utilization stratified by risk group and surgical technique.
Results: A total of 1425 men met inclusion criteria; 67% of them underwent pelvic lymph node dissection. On multivariable analysis, robotic-assisted radical prostatectomy was associated with an 92% decreased use of pelvic lymph node dissection in low-risk, 84% decreased in intermediate-risk and 91% decreased in high-risk men (all $P < 0.001$). In robotic-assisted radical prostatectomy, there was a trend for increased pelvic lymph node dissection utilization over time in high-risk men (Spearman; $P = 0.077$) reaching ~85% in 2012–2013, which was accompanied by increased use in low-risk men ($P = 0.016$). For open radical prostatectomy, fewer pelvic lymph node dissections were carried out in low-risk men over time, decreasing to ~35% ($P = 0.047$) in 2012–2013, whereas rates remained high for high-risk men throughout (~95%; $P = 0.621$).
Conclusion: Regardless of risk group, pelvic lymph node dissection is carried out significantly less during robotic-assisted radical prostatectomy. For robotic-assisted radical prostatectomy, pelvic lymph node dissection utilization increased over time for high-risk men, but rates also increased for low-risk men. Further attention to the discrepancy between provided and guideline recommended pelvic lymph node dissection performance is required to improve prostate cancer care.

Key words: lymph node excision, prostatectomy, prostatic neoplasms, quality of health care, robotic surgical procedures.

Introduction

A greater understanding of the utility and morbidity of PLND at the time of RP has evolved over the past 15 years. This work, coupled with improved preoperative staging and nomogram development, resulted in current guideline recommendations defining patients who should undergo a PLND. Since 2010, the National Comprehensive Cancer Center Guidelines

have recommended PLND for men with ≥2% probability of nodal metastases,[1,2] based on the nomogram by Briganti.[3] Since 2013, the European Association of Urology Guidelines have advised an extended PLND for all men with intermediate- and high-risk PC at the time of RP.[4] The rationale is that PLND improves staging and might have therapeutic benefit, though this latter point remains debated.[5–7] For men with low-risk PC,[8] PLND likely provides no benefit, with similar oncological outcomes achieved.[9,10] However, PLND might not be as benign as traditionally thought, with overall complications directly related to PLND ranging between 4.1% and 19.8%.[11]

Recent USA and European studies highlight the continued discrepancy between guideline recommendations and clinical practice. Using the National Cancer Data Base, Wang *et al.* evaluated 50 671 men undergoing RP with pretreatment intermediate- or high-risk PC, and found 29.2% of patients did not receive guideline recommended treatment with PLND. Men who underwent an ORP and were treated at high-volume or academic centers were more likely to undergo a PLND.[12] Further evaluating previous work highlighting the underutilization of PLND in RARP,[13–15] Suardi *et al.* completed a retrospective analysis of prospectively collected data on 2985 patients undergoing RARP at five European institutions. Overall, 34.5% of low-risk, 64.9% of intermediate-risk and 91.2% of high-risk patients received a PLND.[16]

One unanswered question is how the rate of PLND is evolving over time, especially in more recent years, as RARP has become the predominant modality for RP. To address this, we evaluated PLND performance over time, stratified by PC risk group and surgical technique, within an equal access care setting.

Methods

Study population

After obtaining institutional review board approval, data from patients at VA Medical Centers (Palo Alto, CA; West Los Angeles, CA; San Diego, CA; Durham, NC; Augusta, GA) were combined into the SEARCH database. SEARCH is a national PC registry including retrospective clinical and pathological data from consecutive patients undergoing RP at select VA medical centers in the USA. In comparison with other national PC databases, SEARCH includes a large percentage of minority men, and is more inclusive of men with low socioeconomic status.[17] SEARCH does not include patients treated with preoperative androgen deprivation or radiation therapy. As RARP began in 2006 in the VA centers captured by SEARCH, we limited analyses to men treated in 2006 or later (n = 1828). Patients who underwent a perineal (n = 28), pure laparoscopic (n = 57) or unknown type of prostatectomy (n = 18), and patients with cancer diagnosed by transurethral resection of the prostate rather than prostate biopsy (n = 5), were excluded. Surgical center volume was calculated as the number of each type of surgical approach carried out at that center in any given year. We excluded patients with missing data on race (n = 3), PSA (n = 12), biopsy Gleason score (n = 9), clinical stage (n = 78), BMI (n = 48), total number of cores (n = 115) and total number of positive biopsy cores (n = 30). This resulted in a final study population of 1425 men.

Statistical analysis

Differences in demographic characteristics, clinicopathological features and surgical technique between men who had a PLND at the time of RP versus those who did not were examined using t-tests for normally distributed continuous variables, Wilcoxon rank–sum tests for non-normally distributed continuous variables and χ^2-tests for categorical variables.

The association between PLND performance and age, year of surgery, race, BMI, AUA risk group,[8] number of positive prostate biopsy cores, surgical center and surgical center volume was tested using univariable logistic regression models with stratification by surgical technique.

The association between surgical technique and PLND performance stratified by AUA risk group was examined using multivariable logistic regression. Models were adjusted for age (continuous), race (white *vs* black *vs* other), BMI (<25 kg/m^2 *vs* 25–29.9 kg/m^2 *vs* ≥30 kg/m^2), number of positive cores (continuous), surgery year (continuous), surgical center volume (continuous) and surgery center. To ensure the reliability of our data, sensitivity analyses were carried out excluding centers that performed exclusively one surgical technique for >3 years within our study period.

Spearman's correlation was used to examine temporal changes in disease burden, as well as temporal changes in PLND utilization stratified by risk group and surgical technique. Locally weighted scatterplot smoothing was used to show the relationship between year of surgery and performance of PLND stratified by AUA risk group.

Statistical analyses were carried out using Stata 13.1 (StataCorp, College Station, TX, USA). Statistical significance was two-sided, with $P < 0.05$.

Results

Among the 1425 men who met study inclusion criteria, 477 (33%) did not have a PLND and 948 (67%) did have a PLND (Table 1). Compared with those who did not have a PLND, men who did were older (61.5 *vs* 60.8 years; $P = 0.030$), had a more remote median surgery year (2010 *vs* 2011; $P = 0.007$), had a greater number of cores taken (12 [IQR = 11, 12] *vs* 12 [IQR = 10, 12]; $P = 0.022$) and median positive cores on preoperative prostate biopsy (4 *vs* 3; $P < 0.001$), were more likely to have higher-risk disease (31% of AUA low-risk, 73% of AUA intermediate-risk, and 91% of AUA high-risk underwent PLND; $P < 0.001$) and were more likely to have an ORP (77 *vs* 54%; $P < 0.001$). Patients were more likely to receive a PLND at some surgical centers than others ($P < 0.001$); higher volume centers were less likely to carry out a PLND at the time of an ORP ($P = 0.016$). Surgical center volume of RARP did not affect PLND performance. There were no significant differences in race or BMI between groups.

Table 1 Characteristics of study population undergoing radical prostatectomy from 2006 to 2013

	No PLND n = 477 (33%)	PLND completed n = 948 (67%)	P-value
Mean age (years)	60.8 ± 5.7	61.5 ± 5.9	0.030*
Median year of surgery (Q1, Q3)	2011 (2009, 2012)	2010 (2008, 2012)	0.007**
Race, n (%)			0.186***
White	217 (32)	459 (68)	
Black	230 (36)	413 (64)	
Other	30 (28)	76 (72)	
BMI, n (%)			0.934***
Normal (≤24.9 kg/m^2)	94 (34)	186 (66)	
Overweight (25.0–29.9 kg/m^2)	217 (34)	423 (66)	
Obese (≥30.0 kg/m^2)	166 (33)	339 (67)	
AUA risk category, n (%)			<0.001***
Low risk†	255 (69)	114 (31)	
Intermediate risk‡	191 (27)	527 (73)	
High risk§	31 (9)	307 (91)	
Median total cores (Q1, Q3)	12 (10, 12)	12 (11, 12)	0.022*
Median positive cores (Q1, Q3)	3 (2, 5)	4 (3, 7)	<0.001**
Surgical center			<0.001***
Center A	10 (4)	221 (96)	
Center B	103 (47)	117 (53)	
Center C	187 (43)	246 (57)	
Center D	140 (42)	197 (58)	
Center E	37 (18)	167 (82)	
Median surgical center volume (Q1, Q3)¶			
ORP	40 (35, 55)	37 (30, 52)	0.016**
RARP	44 (30, 72)	44 (32, 59)	0.887**
Surgical technique, n (%)			<0.001***
ORP	173 (23)	585 (77)	
RARP	304 (46)	363 (54)	

P-value calculated using *t-test, **rank-sum test or ***χ^2-test. †AUA low-risk patients had PSA ≤10, clinical stage T1c–T2a and biopsy Gleason ≤6. ‡AUA intermediate-risk patients had PSA >10 and ≤20, clinical stage T2b, and biopsy Gleason 7. §AUA high-risk patients had PSA >20, clinical stage T2c and biopsy Gleason ≥8. ¶As many centers carried out solely ORP or RARP in a given year, the volume of cases per type and year is not cumulative.

Among the five VA centers, the greatest number of patients underwent RP at center C (30%; Table 2). RARP was introduced at the various centers between 2006 and 2011. By 2012, all centers were carrying out more RARP than ORP.

For men undergoing an ORP, performance of a PLND on univariable analysis was associated with more remote surgery year (P = 0.040), higher AUA risk category (all P < 0.001), higher number of total biopsy cores (P = 0.025) and positive biopsy cores (P < 0.001), surgical center (all P ≤ 0.003 relative to center A), and surgical center volume (P = 0.007; Table 3). For men undergoing a RARP, performance of a PLND on univariable analysis was associated with older age (P = 0.002), more recent surgery year (P < 0.001), race (black men, P = 0.003), higher AUA risk category (all P < 0.001), higher number of positive biopsy cores (P < 0.001) and surgical center (center C *vs* A, P = 0.008).

On multivariable analysis, when adjusted for age, race, BMI, total number of biopsy cores, number of positive cores, surgery year, center and center volume, RARP was associated with a 92% decreased use of PLND in the low-risk group (P < 0.001), 84% decreased use in intermediate-risk (P < 0.001) and 91% decreased use in high-risk men (P < 0.001; Table 4). On sensitivity analyses, PLND remained markedly less likely with RARP compared with ORP in all AUA risk groups (79–98% decreased use, all P ≤ 0.003).

Figure 1 shows the relationship between year of surgery and performance of PLND stratified by AUA risk category as shown using locally weighted scatterplot smoothing plots. Over time, PLND was increasingly used with RARP in low-risk patients (P = 0.016); a trend of increased PLND performance with RARP in high-risk men was noted (P = 0.077), reaching ~85% in 2012–2013 versus ~95% in ORP. For ORP, PLND decreased over time in low-risk men (P = 0.047) to ~35% in 2012–2013. There were no changes in PLND rates in intermediate- or high-risk men undergoing ORP between 2006 and 2013.

Because of the statistically significant changes in PLND performance in low-risk patients over time, evaluation of changes in disease burden within the AUA low-risk category was completed. Between 2006 and 2013, there were no changes in PSA or the number of positive biopsy cores among men with low-risk disease undergoing ORP (PSA Spearman ρ = −0.034; P = 0.637; positive cores Spearman ρ = 0.083; P = 0.242) or RARP (PSA Spearman ρ = −0.048; P = 0.541; positive cores Spearman ρ = 0.066; P = 0.393).

Discussion

For men with intermediate- and high-risk PC, PLND improves staging and might have a therapeutic benefit.[5–7] These advantages appear to supersede the associated morbidity of PLND, leading most guidelines to recommend PLND for higher-risk patients. However, for men with low-risk PC, the risk of morbidity likely outweighs the potential staging benefit and no oncological benefit has been identified.[9,10] We evaluated trends over time in PLND performance among men with low-, intermediate- and high-risk PC undergoing both ORP and RARP within an equal access setting. Using the SEARCH database, including men undergoing RP between 2006 and 2013, we compared men receiving a PLND versus those who did not. We stratified our findings by AUA risk group and surgical technique and found that, regardless of risk group, PLND was markedly less likely to be carried out when a RARP was carried out. However, over time, although PLND increased with RARP in high-risk men, this was accompanied by a significant increase in PLND use in low-risk men. Among men undergoing ORP, fewer PLND among low-risk men were carried out over time, whereas PLND rates remained fairly steady in men with intermediate- and high-risk disease. In general, PLND remains overutilized in low-risk men, and under-utilized in high-risk men regardless of surgical technique relative to current guidelines. The fact that the reduction in underuse in high-risk men undergoing RARP was accompanied by increased overuse in low-risk men is concerning and clinically important.

Table 2 Center-level data reviewing RP performance over time

Center	Total *n* (%)	Year 2006	2007	2008	2009	2010	2011	2012	2013
Total RP center A	231 (16)	31	34	28	38	36	28	11	25
ORP	207	97%	100%	100%	100%	100%	100%	36%	36%
RARP	24	3%	0%	0%	0%	0%	0%	64%	64%
Total RP center B	220 (15)	12	21	31	29	37	40	30	20
ORP	53	83%	33%	52%	31%	22%	5%	3%	0%
RARP	167	17%	67%	48%	69%	78%	95%	96%	100%
Total RP center C	433 (30)	39	51	46	51	48	43	79	76
ORP	287	100%	100%	100%	100%	100%	91%	14%	3%
RARP	146	0%	0%	0%	0%	0%	9%	86%	97%
Total RP center D	337 (24)	35	28	26	36	43	55	69	45
ORP	190	100%	100%	100%	97%	47%	24%	25%	36%
RARP	147	0%	0%	0%	3%	53%	76%	75%	64%
Total RP center E	204 (14)	9	3	11	13	24	43	57	44
ORP	21	100%	100%	73%	0%	4%	0%	0%	0%
RARP	183	0%	0%	27%	100%	96%	100%	100%	100%

Table 3 Univariable model examining characteristics associated with performance of a lymph node dissection at the time of RP from 2006 to 2013, stratified by surgical technique

Variable	ORP Odds ratio	ORP 95% CI	ORP *P*-value	RARP Odds ratio	RARP 95% CI	RARP *P*-value
Age	1.01	0.99–1.04	0.315	1.04	1.02–1.07	0.002
Year of surgery	1.10	1.00–1.20	0.040	1.22	1.10–1.36	<0.001
Race						
White	1 (Ref)	–	–	1 (Ref)	–	–
Black	0.97	0.69–1.37	0.863	0.61	0.44–0.84	0.003
Other	2.04	0.77–5.39	0.151	1.17	0.68–2.01	0.562
BMI						
Normal	1 (Ref)	–	–	1 (Ref)	–	–
Overweight	1.14	0.73–1.77	0.573	0.96	0.63–1.47	0.857
Obese	1.07	0.67–1.69	0.787	1.13	0.73–1.75	0.595
AUA risk category						
Low risk†	1 (Ref)	–	–	1 (Ref)	–	–
Intermediate risk‡	6.55	4.39–9.76	<0.001	10.88	6.62–17.88	<0.001
High risk§	24.88	12.06–51.32	<0.001	35.60	18.79–67.43	<0.001
Total cores	1.08	1.01–1.15	0.025	0.99	0.95–1.04	0.762
Positive cores	1.38	1.27–1.51	<0.001	1.26	1.18–1.35	<0.001
Surgical center						
Center A	1 (Ref)	–	–	1 (Ref)	–	–
Center B	0.03	0.01–0.15	<0.001	0.42	0.17–1.03	0.058
Center C	0.02	0.00–0.08	<0.001	0.29	0.12–0.73	0.008
Center D	0.02	0.00–0.09	<0.001	0.43	0.17–1.07	0.069
Center E	0.06	0.01–0.37	0.003	2.19	0.87–5.54	0.097
Surgical center volume	0.98	0.97–1.00	0.007	1.00	0.99–1.01	0.465

†AUA low-risk patients had PSA ≤10, clinical stage T1c–T2a and biopsy Gleason ≤6. ‡AUA intermediate-risk patients had PSA >10 and ≤20, clinical stage T2b and biopsy Gleason 7. §AUA high-risk patients had PSA >20, clinical stage T2c and biopsy Gleason ≥8.

A discrepancy in PLND performance by surgical technique was first identified in a national dataset by Feifer *et al.* In their study of 6608 men captured in the SEER database from 2003 to 2007, men undergoing an ORP were over fivefold more likely to receive a PLND than men undergoing a minimally invasive RP.[14] Similarly, in a single institution series of men undergoing RP from 2003 to 2008 at the University of California, San Francisco, Cooperberg *et al.* found that while the likelihood of a PLND increased over time regardless of surgical technique, RARP patients were markedly less likely to undergo a PLND compared with ORP patients (OR 0.18, 95% CI 0.11–0.32).[18] The learning curve for robotics

Table 4 Multivariable model examining the association between surgical technique (RARP *vs* ORP) and performance of a pelvic lymph node dissection from 2006 to 2013

Performance of a lymph node dissection during RARP (*vs* ORP)			
Multivariable model	Odds ratio	95% CI	*P*-value
AUA low-risk patients†	0.08	0.03–0.23	<0.001
AUA intermediate-risk patients†	0.16	0.08–0.33	<0.001
AUA high-risk patients†	0.09	0.03–0.32	<0.001

†Adjusted for age, race, BMI, total number of cores, positive cores, year of surgery, surgery center and surgery center volume.

was postulated to account for some of this discrepancy.[14] Following up on this idea, Gandaglia *et al.* evaluated 5804 men undergoing RP in the SEER database from 2008 to 2009. With increased utilization of RARP, surgical approach remained an independent predictor of PLND, but the odds of a PLND decreased to 2.7-fold higher in the ORP versus RARP group.[13]

Most recently, Wang *et al.* used the National Cancer Data Base to identify 50 671 men with pretreatment intermediate- or high-risk PC undergoing RP in 2010–2011 in the USA. In total, 81.8% of men with intermediate- or high-risk disease undergoing an ORP received a PLND, compared with 67.5% of men undergoing a RARP. Surgical approach (ORP *vs* RARP), hospital surgical volume (≥200 radical prostatectomies in 2010–2011 *vs* <200) and hospital type (academic *vs* non-academic) were associated with higher rates of PLND performance among men with intermediate- and high-risk PC.[12]

The present study continued to find that men undergoing RARP receive fewer PLND. Importantly, for high-risk men undergoing RARP in our cohort, rates of PLND performance improved over time, from just over 50% in 2006 to ~85% in 2013. Among men with high-risk PC undergoing ORP over the same time-period, PLND rates remained >90%. Although both reflect current practice of carrying out PLND for the vast majority of high-risk patients, there remains opportunities for improvement.

Unfortunately, over the same time-period, an increase in PLND among men with low-risk PC undergoing RARP occurred in our cohort, reaching nearly 20% in 2013. It is uncertain if this increase occurred to facilitate surgeon familiarity with PLND or reflects a transition in individual surgeon or center preference for PLND, regardless of risk group. The percentage of low-risk men in our cohort receiving a PLND compares favorably with the 34.5% of low-risk men receiving a PLND in Suardi's study of 3058 men undergoing RARP at five European institutions from 2005 to 2012.[16] This rate of PLND carried out with RARP in the European series matches the rate of PLND carried out with ORP in our cohort, which trended down to ~35% by 2013. Nevertheless, the increase in PLND in low-risk men undergoing RARP, while a decrease in PLND among low-risk men undergoing ORP, is a novel finding and cause for concern. Further efforts are required to educate providers about risk-adapted approaches for PC care.

One possibility for the changing rates of PLND performance in low-risk men is shifting disease burden characteristics among men undergoing RP. Specifically, we were concerned that low-risk patients in more recent years would be "higher"-risk than in the past, though still low-risk (i.e. higher PSA and more positive cores). To test this, we evaluated changes in PSA and the number of positive biopsy cores among men undergoing ORP and RARP between 2006 and 2013, and found no significant change in these indicators of disease burden to account for changes in PLND performance. Though our statistical power with 369 low-risk men undergoing surgery is limited, our results suggest other factors account for the observed temporal changes in PLND performance.

One factor previously associated with PLND performance is hospital RP volume. Although Wang's study of 50 671 men undergoing RP in 2010–2011 captured in the National Cancer Data Base found higher hospital volume was associated with an increased likelihood of PLND performance among men with intermediate and high-risk disease, we found an inverse volume association for men undergoing ORP, in that high-volume centers carried out fewer PLND.[12] As the VA hospitals in the present study serve as resident training facilities, potentially lower-volume open centers, which also correlated with high-volume RARP centers, might be more apt to use ORP as a teaching opportunity for instruction in the technique of PLND.

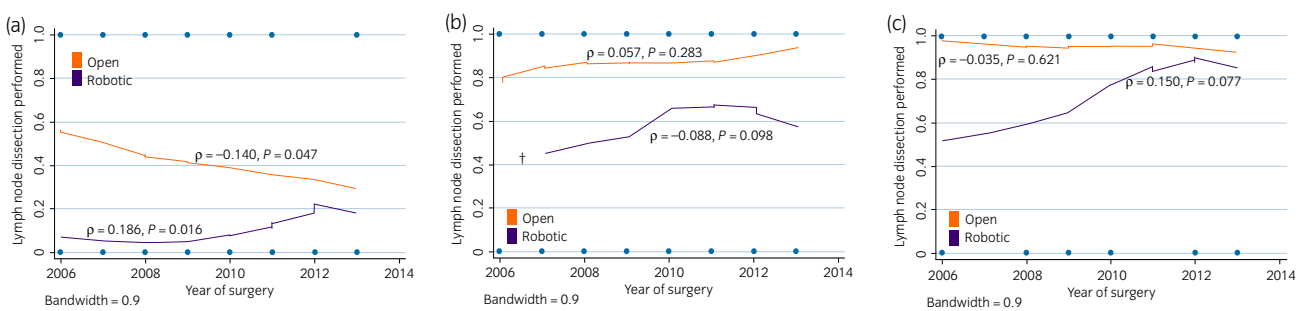

Fig. 1 (a) Proportion of AUA low-risk men undergoing a lymph node dissection from 2006 to 2013. (b) Proportion of AUA intermediate-risk men undergoing a lymph node dissection from 2006 to 2013. †No AUA intermediate-risk men underwent a RARP in 2006. (c) Proportion of AUA high-risk men undergoing a lymph node dissection from 2006 to 2013.

Differences in PLND by surgery center were evident. Among the five centers in SEARCH offering both ORP and RARP, 96% of patients at center A received a PLND, compared with just 53% at center B. On sensitivity analyses excluding centers that carried out exclusively one surgical technique for >3 years within our study period, we continued to find that men undergoing ORP were more likely to receive a PLND than men undergoing RARP. Although previous publications associated PLND performance in RARP with academic affiliation[12] and surgeon experience,[14] all centers in our database were academically affiliated, and individual surgeon-level data were not available. The influence of individual surgeon preference and learning curve on PLND performance is uncertain.

Complication data and information on the extent of PLND carried out were not available in the present retrospective study. Because of variations in reporting and no central pathology review, we were unable to determine with confidence the extent of PLND or number of nodes obtained during PLND. Thus, we cannot comment on the thoroughness of PLND carried out. All men in the present study received care in equal access settings with academic affiliations and participated in resident training. As surgery at an academically affiliated hospital has been identified as a predictor of PLND performance, the overall rate of PLND might be higher than non-academic affiliated centers.[12] In contrast to most payer systems, no remuneration for PLND performance exists in the VA system, removing any possible financial motivation associated with the procedure. Despite the homogeneity of our equal access environment, there might be other hospital, physician or patient characteristics beyond those we evaluated that affect PLND performance and limit the external validity of our findings.

Our findings highlight the continued discrepancy between guideline directed care for the surgical management of PC and PLND performance. Similar to larger studies from SEER and the National Cancer Data Base, we found PLND is markedly less likely to be carried out when a RARP is carried out, even in an equal access setting. Independent of surgical approach, rates of PLND in men with high-risk PC are high, but remain suboptimal and require action. In contrast, among men with low-risk PC, PLND is likely overutilized and exposes these men to possible morbidity without proven oncological benefit. The increasing rate of PLND among men with low-risk disease undergoing RARP, occurring over the same time-period as a decrease in PLND performance among low-risk men undergoing ORP, is concerning and clinically significant. Further attention to the discrepancy between provided and guideline recommended PLND performance is required to improve the quality of PC care, and is imperative as we transition to value-based care.

Conflict of interest

None declared.

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