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Comparative Effectiveness of Cancer Control and Survival After Robot Assisted versus Open Radical Prostatectomy

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Abstract

Introduction—Robot-assisted surgery has been rapidly adopted in the U.S. for prostate cancer (PCa). Its adoption has been driven by market forces and patient preference, and debate continues regarding whether it offers improved outcomes to justify higher cost relative to open surgery. We examined comparative effectiveness of robot assisted (RARP) versus open radical prostatectomy (ORP) in cancer control and survival in a nationally representative population.

Materials and Methods—Population based observational cohort study of PCa patients undergoing RARP and ORP during 2003–2012 captured in Surveillance, Epidemiology, and End

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Competing Interest

All authors declare they have no potential conflicts of interest.

Ethical Approval

The study was approved by the Weill Cornell Medical College institutional review board (protocol no 1409015491).

Author Contributions

Conceptualization, Design and conduct of the study: Hu, Chughtai, Sedrakyan

Collection, management, analysis of the data: Hu, O'Malley, Chughtai, Isaacs, Mao, Sedrakyan

Interpretation of the data: Hu, O'Malley, Chughtai, Mao, Hershman, Wright, Sedrakyan

Preparation, review, or approval of the manuscript: Hu, O'Malley, Chughtai, Mao, Isaacs, Hershman, Wright, Sedrakyan

Results (SEER)-Medicare linked database. Propensity score matching and time to event analysis was used to compare all-cause mortality, prostate cancer-specific mortality and use of additional treatment following surgery.

Results—6,430 RARP and 9,161 ORP performed during 2003–2012 were identified. RARP increased in use from 13.6% to 72.6% in 2003–2004 to 72.6% in 2011–2012. After median follow-up of 6.5 years (IQR 5.2–7.9), RARP was associated with equivalent risk of all-cause mortality (Hazard Ratio [HR] 0.85, [0.72–1.01]) and similar cancer-specific mortality (HR 0.85, [0.50–1.43]) versus ORP. RARP was also associated with less use of additional treatment (HR 0.78, [0.70–0.86]).

Conclusions—RARP has comparable intermediate cancer control, as evidenced by less use of additional postoperative cancer therapies and equivalent cancer-specific and overall survival. Longer-term follow-up is needed to assess for differences in PCa-specific survival, which was similar during intermediate follow-up. Our findings have significant quality and cost implications and provide reassurance regarding the adoption of more expensive technology in absence of randomized controlled trials.

Keywords

Radical Prostatectomy; Robotic-Assisted Surgery; Comparative Effectiveness; Cancer Control; Propensity Score Matching

INTRODUCTION

Prostate cancer (PCa) is the most common solid organ tumor in the U.S. and UK with an estimated incidence of 220,800 in the U.S. and 42,000 in the UK.^{1,2} More than 27,500 people in the U.S. die from PCa annually.¹ Radical prostatectomy remains the most common treatment for clinically localized PCa. In addition, robotic-assisted radical prostatectomy (RARP) has been rapidly adopted after it was introduced in 2000 and since 2008 comprises the majority of radical prostatectomies performed in the U.S.³ Similarly, the use of RARP is growing in the UK with 43% of all trusts conducting radical prostatectomy offering this procedure.⁴ Compared to open radical prostatectomy (ORP), RARP is associated with lower intra-operative blood loss, fewer transfusions, complications, anastomotic strictures, perioperative mortality and shorter length of hospital stay.³ However, it remains significantly more costly than ORP.⁵

The intermediate-term evidence for RARP is limited as no comparative effectiveness studies to date have accrued intermediate term follow-up. This is noteworthy in light of claims that that tactile feedback during ORP, which is lacking during robot assisted surgery, enables intraoperative decision-making that reduces positive surgical margins and thus improves long-term cancer control.⁶ Studies have been inconclusive in comparing cancer control and need for additional cancer therapy between surgical approaches.^{7–9} The objective of our study was to determine comparative effectiveness of RARP versus ORP in terms of primary outcomes of additional cancer therapy, all cause and prostate cancer-specific mortality in a nationally representative cohort.

METHODS

Population source

The observational cohort study is comprised of the recent release of Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database, covering SEER up to 2011, Medicare claims to 2012, and survival outcomes to 2013. SEER identifies 28% incident cancer cases in the U.S., and Medicare insures approximately 97% of Americans aged ≥ 65 years. Study was approved by the Weill Cornell Medical College Institutional Review Board.

Study population

Men who underwent ORP versus RARP between 2003–2012, whose procedures were performed within one year of primary diagnosis of PCa, were selected based on CPT procedure codes 55866 (RARP) versus 55840, 55842, and 55845 (ORP). To assure that patients' follow-up records were captured in the database, men who were not continuously enrolled in Medicare Part A and B, or were enrolled in a health maintenance organization during the year preceding the procedure and during the study interval were excluded. Additionally, those with prior cancers, underwent radiation or ADT prior to prostatectomy, those not linked to SEER, without hospitalization records or clinical or pathologic stage were excluded (Figure 1).

Covariates

Year of treatment, age at treatment, race, ethnicity, population density, marital status, region of the U.S., histology, combined T stage, N stage, and tumor grade, were assigned for each subject.¹⁰ Census tract socioeconomic status was determined using quartiles of median household income and percentage of individuals with high school diplomas. Patient comorbidity was assessed based on prior year encounters in an inpatient, outpatient, office, and home health settings. They were determined using ICD-9 coding algorithms created and validated for use with administrative data¹¹ with addition of acute myocardial infarction, coronary artery and cerebrovascular disease. Surgeon volume was determined based on quartiles. Unknown categories were created for race, ethnicity, marital status, T and N stage, cancer grade and SEER regions when patients have missing characteristics.

Outcomes

Overall survival was determined as time from procedure to all-cause mortality, with subjects censored at end of follow-up for survival data (Dec 31, 2013). For cancer-specific survival, subjects are further censored at time of non-cancer related death, determined by the cause of death provided in SEER. Freedom from additional treatment included time from surgery until ADT or radiation therapy; men are censored at time of death for any cause or end of follow-up for encounter data (Dec 31, 2012). The use of post-prostatectomy radiation and/or ADT was captured consistent with prior studies.³ Follow-up time was determined using the censoring distribution.¹²

Statistical analyses

Due to potential differences in men undergoing ORP and RARP, propensity score matching was performed. Propensity score matching is used in observational studies to select control subjects who are matched with treated subjects on controlled background covariates, which left uncontrolled for, may lead to biased estimates of treatment effects.¹³ Propensity scores were computed using logistic regression model for the probability of undergoing RARP, including all available demographic, hospital, and cancer related variables found to be associated with an outcome of interest. Then, one to one nearest neighbour matching¹⁴ was performed to pair observations with similar propensity for exposure within a specific limited range or caliper. In this case, the logit of the propensity score and a caliper of 0.25 times the standard deviation were used.¹⁵ Subsequently, covariate balance between matched groups was examined using post-match c-statistic and standardized difference.^{16,17} 6,430 RARP and 9,161 ORP were included in the entire cohort and 4,164 pairs of patients were included after applying propensity scores (Figure 1). The cohort was considered balanced regarding known confounding variables with post-match c-statistic of 0.527 and all standardized differences well below 10% (max 4.3%)(see Table 1 and Appendix Table 1 for propensity matching parameters).

Kaplan Meier charts illustrate survival outcomes in both full and paired cohorts and Cox-proportional hazard models are used to estimate hazard ratios. We also examined sensitivity to inclusion of additional therapies as time varying covariates in the survival models as well as inclusion of cancer Grade. Hospital level clustering and the propensity matched study design were accounted for with marginal model analysis and sandwich covariance matrix estimation.¹⁸ All analyses were performed using SAS version 9.3 (SAS Institute, Inc. Cary, NC).

RESULTS

We examined 15,591 men undergoing prostatectomy for PCa from 2003 to 2012. RARP accounted for 41.2% of radical prostatectomies during the study period, and increased in use from 13.6% (522 of 3829 cases) in 2003–2004 to 72.6% (489 of 674 cases) in 2011–2012 ($p<0.001$; Figure 2). Men undergoing ORP were more likely to be Black (8.5% of ORP vs. 6.3% of RARP, $p<0.001$), Spanish, Latino or Hispanic (7.7% of ORP vs. 5.1% of RARP, $p<0.001$), and were less likely to live in metropolitan areas (82.1% of ORP vs. 88.5% of RARP, $p<0.001$). Further, ORP subjects were more likely to reside in lower income areas with lower high school graduation rate ($p<0.001$, respectively). Men undergoing RARP vs. ORP were more likely to have at least one comorbidity (88.9% vs. 87.9%, $p<0.001$) and more likely to have multiple (≥ 4) comorbidities (26.8% vs. 24.1%, $p<0.001$). Full demographic and tumor characteristics are presented in Table 1.

Intermediate-term outcomes

Median follow-up for survival outcomes was 7.1 years (Interquartile Range (IQR) 5.4–9.0) in the full sample and 6.5 years (IQR 5.2–7.9) after matching. For the additional treatment endpoint, the follow-up was 5.9 years (IQR 4.2–7.8) in the full and 5.4 years (IQR 4.1–6.8) in the matched cohorts. In unadjusted analysis, RARP was associated with lower all cause

and prostate cancer-specific mortality, and freedom from additional treatment; however, only freedom from additional treatment remained significantly better with RARP in adjusted analyses (Figure 3). Specifically, the risk of undergoing additional treatment was 22% lower (HR 0.78, 95% CI 0.70–0.86, $p<0.001$). Prostate cancer-specific and all cause mortality were similar compared with ORP (PCM: HR 0.85, 95% CI 0.50–1.43, $p=0.54$; ACM: 0.85, 95% CI 0.72–1.01) (Table 2). These results were robust and did not change after inclusion of ADT and radiation therapies as time varying covariates in secondary analysis or in post-hoc sensitivity analysis stratified by grade (Appendix Table 2 & 3).

Additionally, we examined the association of additional ADT and radiation therapy with all cause, prostate cancer-specific, and non-cancer mortality in secondary analyses. We found that post-radical prostatectomy ADT was associated with worse all cause (HR 2.53, 95% CI 1.94–3.30; $p<0.001$), non-prostate cancer (HR 1.88, 95% CI 1.37–2.59; $p<0.001$) and prostate cancer-specific (HR 10.05, 95% CI 4.76–21.22; $p<0.001$) mortality. However, additional radiation therapy was associated with worse prostate cancer-specific (HR 5.84, 95% CI 2.56–13.30, $p<0.001$) and all cause mortality (HR 1.47, 95% CI 1.16–1.87; $p=0.002$) but not with non-prostate cancer mortality (HR 1.23, 95% CI 0.94–1.61; $p=0.14$) (Appendix Table 2).

DISCUSSION

Our study is the first study that demonstrates improved treatment-free survival associated with RARP versus ORP in the intermediate to long-term setting. We found that RARP all cause mortality and prostate cancer-specific mortality is similar compared to ORP. The advent of robot-assisted surgery has been criticized due to direct-to-consumer-advertising, higher costs, hidden risks and absence of level one evidence demonstrating significantly better outcomes.^{19–21} A number of single institution studies have reported similar, or improved outcomes with RARP versus ORP in the immediate peri-operative setting. Menon *et al.* demonstrated lower blood loss and shorter length of stay in patients undergoing RARP in an initial comparative study.²² Similarly, a number of studies consistently demonstrated similar findings in a variety of practice settings, from the United Kingdom, France, Canada, and Australia.^{23–26} However, in the presence of significantly higher costs,^{5,27} the clinical importance of lower blood loss, which does not necessitate transfusion²⁸, is questionable. Assurance of longer-term survival is critical in light of these controversies and there is only one study to date that demonstrates acceptable long term biochemical recurrence free-, metastasis-free-, and cancer specific-survival at 10 years with rates of 73.1, 97.5, and 98.8%, respectively.²⁹ However, there was no direct comparison with ORP and findings from this high-volume referral center may not be generalizable to other healthcare settings.

Our study fills a critical gap in evidence, as we observed similar prostate cancer-specific mortality with a median follow-up of 6.5 years (IQR 5.2–7.9). Given the high prevalence of PSA screening in Western countries with resultant lead-time bias, our study's prostate cancer-specific mortality is correspondingly low and should be reassuring for patients over 65 years of age. Longer term comparative effectiveness studies are needed to determine benefits in younger men. In two examples; the Scandinavian Prostate Cancer Group Study Number 4 (SPG4) and the Prostate Cancer Intervention Versus Observation Trial

(PIVOT),^{30,31} 12-year and 15-year follow-up was needed to reveal a relatively small absolute difference in prostate cancer-specific mortality between watchful waiting and radical prostatectomy.

We also found that RARP is associated with lower utilization of additional radiation and ADT. One prior study using a 5% sample of Medicare beneficiaries during the early adoption of RARP from 2003 through 2005 demonstrated greater use of additional cancer therapy within 6 months of RARP versus ORP.⁹ However, studies from tertiary referral centers have been inconclusive in determining superiority of any one approach for other oncologic outcomes. For instance, a study of the National Cancer Database demonstrated that more lymph nodes are removed during ORP versus RARP.³² Still, the role of lymph node dissection during radical prostatectomy remains controversial, with a recent study suggesting that the number of lymph node dissections needed to avoid one prostate cancer-specific death varies from 80 to 800, based on the current incidence of lymph node metastases.³³

More recently, Hu *et al.* demonstrated that RARP was associated with fewer positive surgical margins compared to ORP and less use of additional cancer therapy (ADT and/or radiation therapy) within two years of RARP.⁷ Our current study validates and extends these findings with up to median 6.5 years of follow-up, demonstrating more durable cancer control benefits for RARP compared to ORP. Moreover, additional post-prostatectomy radiation therapy is burdensome; it is associated with worse urinary and bowel function, poorer quality of life³⁴, and higher costs.³⁵ For instance, additional health care cost within a year of PCa diagnosis and radical prostatectomy was \$1,361 for ADT alone, \$12,040 for additional radiotherapy and \$23,487 for radiotherapy with ADT. Therefore, while RARP is more costly than ORP upfront, this is offset by less subsequent use of additional cancer therapy, and associated direct and indirect costs of treating complications of adjuvant radiation and/or ADT.

Finally, RARP was associated with non-inferior overall survival compared to ORP in men who were over 65 years old. This finding is noteworthy given that men undergoing RARP had more comorbidities prior to propensity matching and residual confounding related to observed factors might favor ORP. Additional residual confounding related to unobserved differences in our treatment groups might occur. For example, marketing and patient demand drove the early adoption of RARP and it was demonstrated that White and Asian men and those residing in areas of higher household income and education were more likely to elect RARP over ORP.³ Despite adjusting for race and socio-demographic differences in our study, men opting for RARP may be more likely to follow healthier lifestyles, such as exercising and the avoidance of smoking, which are not captured by SEER-Medicare.

Our study has limitations. First, we are unable to characterize post-radical prostatectomy PSA values, given the 5–18% error rate, and therefore compare biochemical recurrence-free survival. In addition, there is significant provider heterogeneity in administration of additional treatment post-prostatectomy³⁶, particularly across varied practice settings.³⁷ However, our use of additional ADT and radiation therapy as a surrogate for cancer control proves effective because both are independently associated with worse prostate cancer-

specific survival. Second, our study is limited to elderly Medicare beneficiaries, who may be less likely to receive additional therapy given the associated morbidity and competing mortality risks with advancing age. Third, there may exist an underestimation of the benefit of RARP on survival as some hospitals may incorrectly record the administrative code for designating robot-assisted surgery; consequently some RARP may be misclassified as ORP. In addition, inherent with observational study, there may be residual confounding that cannot be addressed by study design and analysis. However, sensitivity analysis showed little change to outcomes. Recent criticisms of SEER population data in regard to evaluating outcomes in PCa focus on a lack of granularity as prostate specific metrics, such as PSA and Gleason score, are not available or unreliable. However, the largest shift in stage, seen with the introduction of the AJCC 7th edition at the beginning of 2010³⁸, would lead to an underestimation of the effectiveness of RARP. There have been changes to Gleason score as well over time which has also impacted stage migration within this cohort.

Our study has several important implications from an oncological and global health perspective. While the adoption of RARP was not evidence based, the non-inferior intermediate-term survival in this population should be reassuring for critics. Reduction in additional cancer therapies associated with RARP is likely to offset the criticism of higher costs for robotic versus open surgery and stretch the benefits of RARP beyond perioperative advantages of lower blood loss, fewer transfusions and anastomotic strictures, shorter hospitalizations and lower 30-day mortality.³⁹

CONCLUSION

RARP is associated with less use post-operative ADT and radiation therapy, and equivalent prostate cancer-specific and all-cause mortality. This is reassuring and should lead to better health care decisions in the absence of robust comparative data for a procedure that has serious quality and costs implications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Appendix Table 1

Additional comorbidities, and refined year and registry breakdown used for propensity matching.

Variable	Full Sample			PS- Matched Cohort		
	RARP n=6430	ORP n=9161	Std. Diff	RARP n=4164	ORP n=4164	Std. Diff
Comorbidities:						
Pulm. Circulatory Disease	68 (1.1%)	123 (1.3%)	−2.6%	47 (1.1%)	47 (1.1%)	0.0%
Congestive Heart Failure	284 (4.4%)	384 (4.2%)	1.1%	192 (4.6%)	191 (4.6%)	0.1%
Coronary Artery Disease	1855 (28.8%)	2370 (25.9%)	6.7%	1146 (27.5%)	1130 (27.1%)	0.9%
Valvular Heart Disease	958 (14.9%)	1031 (11.3%)	10.9%	562 (13.5%)	550 (13.2%)	0.9%
COPD	1100 (17.2%)	1750 (19.1%)	−5.1%	723 (17.4%)	745 (17.9%)	−1.4%
Peripheral Vascular Disease	714 (11.1%)	1015 (11.1%)	0.1%	481 (11.6%)	473 (11.4%)	0.6%
Renal Failure	220 (3.4%)	203 (2.2%)	7.3%	127 (3.0%)	132 (3.2%)	−0.7%
Hypertension	4579 (71.4%)	6346 (69.4%)	4.5%	2931 (70.4%)	2951 (70.9%)	−1.1%
Cerebrovascular Disease ^a	589 (9.2%)	749 (8.2%)	3.5%	372 (8.9%)	375 (9.0%)	−0.3%
MI (past year) ^a	341 (5.3%)	475 (5.2%)	0.6%	217 (5.2%)	223 (5.4%)	−0.6%
Hypothyroidism	831 (13.0%)	988 (10.8%)	6.7%	485 (11.6%)	492 (11.8%)	−0.5%
Diabetes (uncomplicated)	1465 (22.9%)	2083 (22.8%)	0.2%	955 (22.9%)	968 (23.2%)	−0.7%
Diabetes (complicated)	297 (4.6%)	400 (4.4%)	1.3%	190 (4.6%)	195 (4.7%)	−0.6%
Paralysis	34 (0.5%)	49 (0.5%)	−0.1%	21 (0.5%)	21 (0.5%)	0.0%
Other Neurological Disorders	206 (3.2%)	280 (3.1%)	0.9%	140 (3.4%)	142 (3.4%)	−0.3%
HIV/AIDS	NR	NR	1.4%	NR	NR	0.0%
Coagulopathy	302 (4.7%)	331 (3.6%)	5.5%	176 (4.2%)	165 (4.0%)	1.3%
Weight Loss	136 (2.1%)	191 (2.1%)	0.2%	86 (2.1%)	83 (2.0%)	0.5%
Fluid/Electrolyte Disorders	518 (8.1%)	754 (8.2%)	−0.6%	316 (7.6%)	338 (8.1%)	2.0%
Deficiency Anemia	1092 (17.0%)	1548 (16.9%)	0.3%	673 (16.2%)	686 (16.5%)	−0.8%
Blood Loss Anemia	81 (1.3%)	244 (2.7%)	−10.1%	68 (1.6%)	72 (1.7%)	−0.8%
Ulcer with Bleeding	NR	23 (0.3%)	−2.9%	NR	NR	0.0%
Alcohol Abuse	77 (1.2%)	151 (1.7%)	−3.8%	61 (1.5%)	61 (1.5%)	0.0%
Drug Abuse	16 (0.2%)	26 (0.3%)	−0.7%	11 (0.3%)	12 (0.3%)	−0.5%
Depression	301 (4.7%)	443 (4.8%)	−0.7%	207 (5.0%)	201 (4.8%)	0.7%

Appendix Table 2

Hazard ratios from time varying covariate models.

Variable	Full Sample		PS- Matched Cohort	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
All-cause Mortality				
ADT	2.92 (2.48–3.42)	<0.001	2.53 (1.94–3.30)	<0.001
Radiation	1.27 (1.09–1.48)	0.003	1.47 (1.16–1.87)	0.002

Variable	Full Sample		PS- Matched Cohort	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
Cancer Specific Mortality				
ADT	12.92 (7.90–21.14)	<0.001	10.05 (4.76–21.22)	<0.001
Radiation	3.39 (2.10–5.47)	<0.001	5.84 (2.56–13.30)	<.0001
Non-Cancer Mortality				
ADT	2.11 (1.77–2.53)	<0.001	1.88 (1.37–2.59)	<0.001
Radiation	1.06 (0.88–1.27)	0.53	1.23 (0.94–1.61)	0.14

Appendix Table 3

Median follow-up times from censoring distribution.

Median (IQR) Follow-up Time in Years	Raw Cohort	PS- Matched Cohort
All-Cause Mortality	7.1 (5.4–9.0)	6.5 (5.1–7.9)
Cancer Mortality	6.8 (5.2–8.8)	6.4 (4.9–7.8)
Non-Cancer Mortality	7.0 (5.3–8.9)	6.5 (5.1–7.9)

Appendix Table 4

Hazard ratios of long term outcomes following RARP and ORP before and after matching stratified by cancer grade.

Outcome (RARP vs. ORP)	Full Sample		PS- Matched Cohort	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
Grade I and II				
All-cause Mortality	0.85 (0.67–1.06)	0.85	1.07 (0.79–1.46)	0.65
Cancer Specific Mortality	0.96 (0.55–1.66)	0.96	0.84 (0.26–2.74)	0.77
Additional Treatment	0.52 (0.43–0.64)	<0.001	0.68 (0.51–0.89)	0.005
Grade III and IV				
All-cause Mortality	0.68 (0.58–0.80)	<0.001	0.82 (0.66–1.00)	0.05
Cancer Specific Mortality	0.37 (0.24–0.56)	<0.001	0.74 (0.43–1.28)	0.28
Additional Treatment	0.73 (0.66–0.80)	<0.001	0.82 (0.74–0.92)	<0.001

Appendix Table 5

Predictors of all-cause mortality.

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
RARP vs. ORP	0.76(0.66–0.87)	<0.01	0.83(0.71–0.98)	0.02
Age Group (vs. 65–69)				
70–74	1.42(1.28–1.58)	<0.01	1.41(1.26–1.57)	<0.01
75–79	1.95(1.66–2.30)	<0.01	1.85(1.54–2.22)	<0.01

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
80	4.73(3.12–7.16)	<0.01	4.21(2.71–6.53)	<0.01
Hispanic vs. Non-Hispanic	0.97(0.76–1.23)	0.78	0.79(0.60–1.03)	0.08
Race (vs. Unknown)				
White	1.57(0.76–3.26)	0.23	1.14(0.55–2.38)	0.72
Black	2.56(1.21–5.41)	0.01	1.36(0.64–2.91)	0.42
Other	1.41(0.65–3.07)	0.39	0.90(0.41–1.99)	0.80
Non-Metro vs. Metro	1.34(1.15–1.56)	<0.01	1.08(0.92–1.28)	0.35
Unmarried vs. Married	1.37(1.20–1.57)	<0.01	1.26(1.10–1.44)	<0.01
Year of Procedure (vs. 2003–2004)				
2005–2006	1.10(0.95–1.27)	0.21	1.06(0.92–1.23)	0.44
2007–2008	1.25(1.06–1.48)	<0.01	1.17(0.98–1.41)	0.09
2009–2010	1.38(1.10–1.75)	<0.01	1.24(0.97–1.56)	0.08
2011–2012	1.04(0.51–2.11)	0.91	0.94(0.46–1.91)	0.86
Educated ≥12yr (vs. 75%)				
76%–85%	0.83(0.71–0.96)	0.01	0.93(0.77–1.12)	0.44
86%–90%	0.69(0.57–0.82)	<0.01	0.89(0.71–1.12)	0.33
91%–100%	0.55(0.47–0.64)	<0.01	0.86(0.69–1.09)	0.22
Median Income (vs. Q1)				
Q2	0.83(0.72–0.95)	<0.01	0.96(0.81–1.13)	0.63
Q3	0.62(0.53–0.73)	<0.01	0.82(0.66–1.01)	0.07
Q4	0.50(0.42–0.59)	<0.01	0.72(0.56–0.92)	<0.01
Surgeon Volume (vs. Q1)				
Q2	0.99(0.85–1.16)	0.93	0.99(0.85–1.15)	0.85
Q3	1.00(0.86–1.18)	0.95	1.04(0.88–1.22)	0.67
Q4	0.82(0.67–0.99)	0.04	0.90(0.73–1.11)	0.32
SEER Region (vs. NA)				
Midwest	0.86(0.46–1.61)	0.64	0.77(0.43–1.39)	0.38
Northeast	0.63(0.33–1.19)	0.16	0.68(0.38–1.23)	0.21
South	1.18(0.64–2.17)	0.59	0.97(0.55–1.70)	0.92
West	0.90(0.50–1.64)	0.74	0.87(0.50–1.54)	0.64
T Stage (vs. T1)				
T2	0.66(0.44–0.98)	0.04	0.73(0.49–1.10)	0.13
T3	1.08(0.72–1.61)	0.71	1.03(0.69–1.55)	0.88
T4	2.08(1.27–3.40)	<0.01	1.87(1.13–3.10)	0.02
Unknown	0.57(0.34–0.97)	0.04	0.63(0.37–1.05)	0.08
N Stage (vs. N0)				
N1	3.05(2.40–3.88)	<0.01	2.04(1.57–2.65)	<0.01
Unknown	0.94(0.61–1.46)	0.79	1.01(0.66–1.53)	0.98
Histology				
Other vs. Adenocarcinoma	0.65(0.48–0.88)	<0.01	0.71(0.53–0.96)	0.03
Grade (vs. Grade I)				

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
Grade II	0.73(0.40–1.33)	0.30	0.90(0.49–1.67)	0.74
Grade III/IV	1.12(0.61–2.06)	0.71	1.18(0.63–2.22)	0.60
Not Determined	1.28(0.50–3.26)	0.61	1.45(0.57–3.71)	0.43
No. Comorbidities (vs. 0)				
1	1.31(1.06–1.62)	0.01	1.26(1.00–1.59)	0.05
2–3	1.57(1.29–1.92)	<0.01	1.28(0.98–1.67)	0.07
4	3.13(2.56–3.82)	<0.01	1.77(1.25–2.50)	<0.01
Comorbidities (Ref=No)				
Pulmonary Circulatory Disease	2.10(1.43–3.08)	<0.01	1.40(0.93–2.11)	0.11
CHF	2.38(1.95–2.90)	<0.01	1.48(1.21–1.83)	<0.01
CAD	1.49(1.34–1.67)	<0.01	1.09(0.95–1.24)	0.21
Valve Disease	1.27(1.10–1.47)	<0.01	0.93(0.79–1.09)	0.37
COPD	1.92(1.70–2.17)	<0.01	1.41(1.23–1.62)	<0.01
PVD	1.92(1.66–2.22)	<0.01	1.36(1.16–1.59)	<0.01
Renal Failure	2.23(1.71–2.92)	<0.01	1.38(1.04–1.84)	0.03
Hypertension	1.31(1.17–1.47)	<0.01	0.92(0.78–1.08)	0.29
CVD	1.61(1.37–1.89)	<0.01	1.02(0.85–1.21)	0.86
AMI	1.47(1.18–1.82)	<0.01	0.99(0.78–1.26)	0.93
Hypothyroidism	1.00(0.85–1.17)	1	0.80(0.67–0.95)	0.01
Diabetes (uncomplicated)	1.53(1.37–1.71)	<0.01	1.11(0.96–1.27)	0.15
Diabetes (complicated)	2.09(1.71–2.55)	<0.01	1.30(1.04–1.62)	0.02
Paralysis	2.25(1.29–3.94)	<0.01	1.13(0.63–2.05)	0.68
Other Neurological Disorders	2.53(2.02–3.16)	<0.01	1.57(1.21–2.05)	<0.01
HIV/AIDS	1.34(0.20–9.15)	0.76	0.98(0.13–7.22)	0.98
Coagulopathy	1.21(0.96–1.53)	0.11	0.97(0.76–1.26)	0.84
Weight Loss	2.01(1.48–2.74)	<0.01	1.33(0.98–1.82)	0.07
Electrolyte Disorders	1.63(1.36–1.95)	<0.01	1.08(0.89–1.31)	0.45
Deficiency Anemia	1.33(1.16–1.53)	<0.01	1.02(0.87–1.20)	0.76
Blood Loss Anemia	1.36(1.00–1.85)	0.05	1.02(0.74–1.40)	0.91
Ulcer with Bleeding	1.82(0.77–4.29)	0.17	0.99(0.38–2.58)	0.98
Alcohol Abuse	2.44(1.75–3.41)	<0.01	1.59(1.12–2.25)	<0.01
Drug Abuse	4.04(2.03–8.04)	<0.01	1.84(0.83–4.10)	0.13
Depression	1.48(1.18–1.85)	<0.01	1.12(0.89–1.42)	0.33

CHF=Congestive Heart Failure, CAD=Coronary Artery Disease, PVD=Peripheral Vascular Disease, CVD=Cerebrovascular Disease, AMI=Acute Myocardial Infarction,

Appendix Table 6

Predictors of cancer specific mortality

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
RARP vs. ORP	0.48(0.33–0.68)	<0.01	0.81(0.56–1.17)	0.26

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
Age Group (vs. 65–69)				
70–74	1.49(1.09–2.04)	0.01	1.48(1.06–2.07)	0.02
75–79	1.83(1.08–3.11)	0.02	1.82(1.06–3.12)	0.03
80	6.86(2.62–17.97)	<0.01	6.46(2.42–17.24)	<0.01
Hispanic vs. Non-Hispanic	0.77(0.39–1.50)	0.44	0.62(0.27–1.41)	0.25
Race (vs. Unknown)				
White	1.47(0.20–10.56)	0.70	1.02(0.14–7.44)	0.98
Black	2.58(0.35–19.27)	0.35	1.40(0.18–10.89)	0.75
Other	0.21(0.01–3.50)	0.28	0.15(0.01–2.55)	0.19
Non-Metro vs. Metro	0.91(0.61–1.35)	0.63	0.69(0.44–1.07)	0.09
Unmarried vs. Married	1.24(0.85–1.83)	0.27	1.19(0.82–1.72)	0.36
Year of Procedure (vs. 2003–2004)				
2005–2006	0.83(0.59–1.16)	0.26	0.81(0.57–1.17)	0.27
2007–2008	0.50(0.32–0.79)	<0.01	0.54(0.34–0.84)	<0.01
2009–2012	0.22(0.10–0.49)	<0.01	0.21(0.09–0.49)	<0.01
Educated ≥12yr (vs. 75%)				
76%–85%	0.96(0.64–1.43)	0.82	0.87(0.55–1.39)	0.57
86%–90%	0.64(0.40–1.04)	0.07	0.65(0.35–1.20)	0.17
91%–100%	0.58(0.39–0.86)	<0.01	0.69(0.36–1.31)	0.26
Median Income (vs. Q1)				
Q2	0.92(0.64–1.32)	0.64	1.12(0.71–1.76)	0.64
Q3	0.74(0.50–1.10)	0.14	0.98(0.57–1.68)	0.94
Q4	0.52(0.33–0.82)	<0.01	0.81(0.40–1.65)	0.56
Surgeon Volume (vs. Q1)				
Q2	0.73(0.51–1.06)	0.10	0.73(0.49–1.09)	0.13
Q3	0.55(0.36–0.85)	<0.01	0.59(0.38–0.90)	0.02
Q4	0.56(0.38–0.83)	<0.01	0.65(0.42–0.99)	0.05
SEER Region (vs. NA)				
Midwest	0.31(0.12–0.80)	0.02	0.32(0.13–0.80)	0.01
Northeast	0.30(0.11–0.80)	0.02	0.34(0.13–0.88)	0.03
South	0.40(0.16–1.03)	0.06	0.39(0.15–0.97)	0.04
West	0.28(0.12–0.70)	<0.01	0.29(0.12–0.71)	<0.01
T Stage (vs. T1)				
T2	0.50(0.15–1.59)	0.24	0.47(0.15–1.52)	0.21
T3	2.29(0.71–7.37)	0.17	1.43(0.45–4.56)	0.55
T4	7.95(2.23–28.33)	<0.01	4.27(1.15–15.83)	0.03
Unknown	2.16(0.53–8.81)	0.28	1.83(0.42–7.89)	0.42
N Stage (vs. N0)				
N1	11.77(8.09–17.13)	<0.01	5.39(3.63–8.02)	<0.01
Unknown	0.42(0.06–3.01)	0.38	0.34(0.07–1.64)	0.18

	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
Histology				
Other vs. Adenocarcinoma	1.66(0.81–3.40)	0.17	1.34(0.58–3.09)	0.49
Grade (vs. Grade I/II)				
Grade III/IV	1.66(0.81–3.40)	0.17	0.42(0.06–2.75)	0.36
Not Determined	0.32(0.04–2.34)	0.26	1.01(0.16–6.46)	0.99
No. Comorbidities (vs. 0)				
1	1.60(0.89–2.90)	0.12	1.74(0.93–3.24)	0.08
2–3	1.32(0.76–2.30)	0.33	1.47(0.73–2.96)	0.29
4	1.61(0.91–2.84)	0.10	1.78(0.62–5.11)	0.28
Comorbidities (Ref=No)				
Pulmonary Circulatory Disease	2.02(0.76–5.40)	0.16	1.83(0.60–5.59)	0.29
CHF	1.61(0.91–2.87)	0.10	1.39(0.76–2.53)	0.29
CAD	1.17(0.84–1.63)	0.35	0.98(0.66–1.47)	0.92
Valve Disease	0.93(0.57–1.50)	0.76	0.82(0.48–1.41)	0.48
COPD	1.55(1.10–2.19)	0.01	1.20(0.80–1.81)	0.37
PVD	1.39(0.91–2.13)	0.13	1.13(0.69–1.84)	0.62
Renal Failure	1.06(0.39–2.83)	0.91	1.18(0.39–3.59)	0.76
Hypertension	0.84(0.61–1.15)	0.28	0.68(0.44–1.04)	0.08
CVD	1.01(0.58–1.73)	0.98	0.91(0.52–1.61)	0.76
AMI	1.49(0.85–2.63)	0.17	1.49(0.79–2.81)	0.22
Hypothyroidism	0.80(0.49–1.32)	0.39	0.84(0.49–1.46)	0.54
Diabetes (uncomplicated)	0.95(0.66–1.37)	0.79	0.98(0.61–1.58)	0.95
Diabetes (complicated)	0.84(0.38–1.88)	0.68	0.84(0.35–2.02)	0.69
Paralysis	–	–	0.51(0.14–1.81)	0.30
Other Neurological Disorders	0.62(0.20–1.93)	0.41	10.07(1.11–91.16)	0.04
HIV/AIDS	9.22(1.36–62.57)	0.02	2.16(1.14–4.09)	0.02
Coagulopathy	1.75(0.95–3.21)	0.07	0.87(0.30–2.47)	0.79
Weight Loss	0.90(0.30–2.68)	0.85	0.87(0.43–1.77)	0.70
Electrolyte Disorders	1.04(0.55–1.98)	0.90	0.71(0.44–1.15)	0.16
Deficiency Anemia	0.90(0.59–1.38)	0.62	1.38(0.60–3.15)	0.45
Blood Loss Anemia	1.64(0.74–3.66)	0.22	2.47(0.96–6.32)	0.06
Ulcer with Bleeding	–	–	1.13(0.16–8.22)	0.90
Alcohol Abuse	2.80(1.29–6.08)	<0.01	0.47(0.19–1.17)	0.11
Drug Abuse	2.79(0.37–21.33)	0.32	1.83(0.60–5.59)	0.29
Depression	0.51(0.19–1.34)	0.17	1.39(0.76–2.53)	0.29

CHF=Congestive Heart Failure, CAD=Coronary Artery Disease, PVD=Peripheral Vascular Disease, CVD=Cerebrovascular Disease, AMI=Acute Myocardial Infarction,

Glossary

RARP Robot assisted radical prostatectomy

ORP	open radical prostatectomy
SEER	Surveillance, Epidemiology, and End Results
HR	Hazard Ratio
ADT	androgen deprivation
IQR	Interquartile Range

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Figure 1.
Patient selection

Figure 2.
Increasing Utilization of RARP vs. ORP over time ($p < 0.001$).

Figure 3. Kaplan Meier survival estimates for A) full and B) propensity matched cohorts. Overall survival (top panel), Prostate cancer specific survival (middle panel), and Additional treatment-free survival (bottom panel). RARP: Black with dark gray Hall-Wellner bands; ORP: Gray with light gray bands.

Table 1

Patient baseline demographics and pathological characteristics. Full sample and propensity score matched cohorts.

Variable	Full Sample				PS- Matched Cohort			
	RARP n=6430	ORP n=9161	Std. Diff	RARP n=4164	ORP n=4164	Std. Diff		
Age Mean (SD)	70.0 (3.1)	70.0 (3.1)	0.1%	70.0 (3.2)	70.0 (3.1)	-0.3%		
Age Group			3.5%			1.3%		
65-69	3333 (51.8%)	4824 (52.7%)		2144 (51.5%)	2140 (51.4%)			
70-74	2513 (39.1%)	3448 (37.6%)		1608 (38.6%)	1626 (39.0%)			
75-79	541 (8.4%)	831 (9.1%)		381 (9.1%)	368 (8.8%)			
80	43 (0.7%)	58 (0.6%)		31 (0.7%)	30 (0.7%)			
Year of Procedure			90.1%			6.8%		
2003-2004	522 (8.1%)	3307 (36.1%)		501 (12.0%)	499 (12.0%)			
2005-2006	1398 (21.7%)	2644 (28.9%)		1090 (26.2%)	1176 (28.2%)			
2007-2008	2430 (37.8%)	2136 (23.3%)		1546 (37.1%)	1548 (37.2%)			
2009-2010	1591 (24.7%)	889 (9.7%)		841 (20.2%)	770 (18.5%)			
2011-2012	489 (7.6%)	185 (2.0%)		186 (4.5%)	171 (4.1%)			
Race			15.8%			3.9%		
White	5601 (87.1%)	8028 (87.6%)		3637 (87.3%)	3654 (87.8%)			
Black	402 (6.3%)	780 (8.5%)		297 (7.1%)	292 (7.0%)			
Other	349 (5.4%)	292 (3.2%)		197 (4.7%)	185 (4.4%)			
Unknown	78 (1.2%)	61 (0.7%)		33 (0.8%)	33 (0.8%)			
Ethnicity			-1.7%			0.2%		
Non-Spanish-Hispanic-Latino	6099 (94.9%)	8455 (92.3%)		3914 (94.0%)	3908 (93.9%)			
Spanish-Hispanic-Latino	331 (5.1%)	706 (7.7%)		250 (6.0%)	256 (6.1%)			
Marital Status			4.2%			1.4%		
Married (incl. common law)	5076 (78.9%)	7386 (80.6%)		3313 (79.6%)	3289 (79.0%)			
Not Married	1354 (21.1%)	1775 (19.4%)		851 (20.4%)	875 (21.0%)			
T Stage			12.3%			3.6%		
T1	169 (2.6%)	136 (1.5%)		90 (2.2%)	93 (2.2%)			
T2	4717 (73.4%)	6587 (71.9%)		3087 (74.1%)	3091 (74.2%)			
T3	1425 (22.2%)	2151 (23.5%)		917 (22.0%)	891 (21.4%)			

Variable	Full Sample				PS- Matched Cohort			
	RARP n=6430	ORP n=9161	Std. Diff		RARP n=4164	ORP n=4164	Std. Diff	
T4	65 (1.0%)	125 (1.4%)			38 (0.9%)	50 (1.2%)		
Unknown	54 (0.8%)	162 (1.8%)			32 (0.8%)	39 (0.9%)		
N Stage				12.4%				2.1%
N0	6214 (96.6%)	8784 (95.9%)			4026 (96.7%)	4010 (96.3%)		
N1	84 (1.3%)	261 (2.8%)			70 (1.7%)	79 (1.9%)		
Unknown	132 (2.1%)	116 (1.3%)			68 (1.6%)	75 (1.8%)		
Histology				3.7%				1.2%
Adenocarcinoma	6167 (95.9%)	8850 (96.6%)			3986 (95.7%)	3996 (96.0%)		
Other	263 (4.1%)	311 (3.4%)			178 (4.3%)	168 (4.0%)		
Grade				18.6%				2.8%
Grade I	20 (0.3%)	61 (0.7%)			13 (0.3%)	11 (0.3%)		
Grade II	2136 (33.2%)	3816 (41.7%)			1430 (34.3%)	1477 (35.5%)		
Grade III/IV	4242 (66.0%)	5239 (57.2%)			2702 (64.9%)	2654 (63.7%)		
Not Determined	32 (0.5%)	45 (0.5%)			19 (0.5%)	22 (0.5%)		
No. of Comorbidities				6.8%				0.9%
0	712 (11.1%)	1109 (12.1%)			489 (11.7%)	478 (11.5%)		
1	1479 (23.0%)	2234 (24.4%)			985 (23.7%)	992 (23.8%)		
2-3	2517 (39.1%)	3614 (39.4%)			1625 (39.0%)	1625 (39.0%)		
4	1722 (26.8%)	2204 (24.1%)			1065 (25.6%)	1069 (25.7%)		
Location				18.3%				0.3%
Metropolitan	5693 (88.5%)	7518 (82.1%)			3578 (85.9%)	3574 (85.8%)		
Non-Metropolitan	737 (11.5%)	1639 (17.9%)			586 (14.1%)	590 (14.2%)		
Census Tract Year 2000				34.8%				1.4%
Median Income								
Quartile 1	1215 (18.9%)	2678 (29.3%)			956 (23.0%)	939 (22.6%)		
Quartile 2	1428 (22.2%)	2528 (27.6%)			1023 (24.6%)	1041 (25.0%)		
Quartile 3	1746 (27.2%)	2136 (23.4%)			1059 (25.4%)	1070 (25.7%)		
Quartile 4	2032 (31.6%)	1803 (19.7%)			1126 (27.0%)	1114 (26.8%)		
Census Tract Year 2000 %				20.5%				1.5%
High School Educated								

Variable	Full Sample			PS- Matched Cohort		
	RARP n=6430	ORP n=9161	Std. Diff	RARP n=4164	ORP n=4164	Std. Diff
0%–75%	1078 (16.8%)	2154 (23.6%)		809 (19.4%)	793 (19.0%)	
76%–85%	1317 (20.5%)	2025 (22.1%)		841 (20.2%)	855 (20.5%)	
86%–90%	1242 (19.3%)	1761 (19.3%)		809 (19.4%)	824 (19.8%)	
91%–100%	2784 (43.4%)	3205 (35.0%)		1705 (40.9%)	1692 (40.6%)	
SEER Registry Region			24.8%			1.9%
Midwest	1009 (15.7%)	1023 (11.2%)		556 (13.4%)	567 (13.6%)	
Northeast	998 (15.5%)	880 (9.6%)		491 (11.8%)	508 (12.2%)	
South	1238 (19.3%)	2156 (23.5%)		849 (20.4%)	838 (20.1%)	
West	3114 (48.4%)	5028 (54.9%)		2224 (53.4%)	2203 (52.9%)	
Not Applicable	71 (1.1%)	74 (0.8%)		44 (1.1%)	48 (1.2%)	
Surgeon Volume Quartile			75.8%			6.3%
Quartile 1	816 (12.7%)	2864 (31.3%)		780 (18.7%)	863 (20.7%)	
Quartile 2	1164 (18.1%)	2893 (31.6%)		1053 (25.3%)	1092 (26.2%)	
Quartile 3	1803 (28.0%)	2104 (23.0%)		1260 (30.3%)	1193 (28.7%)	
Quartile 4	2646 (41.2%)	1300 (14.2%)		1071 (25.7%)	1016 (24.4%)	

Table 2

Hazard ratios of long term outcomes following RARP and ORP before and after matching.

Outcome (RARP vs. ORP)	Full Sample		PS- Matched Cohort	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
All-cause Mortality	0.76 (0.66–0.87)	<0.001	0.85 (0.72–1.01)	0.07
Cancer Specific Mortality	0.48 (0.33–0.68)	<0.001	0.85 (0.50–1.43)	0.54
Additional Treatment	0.76 (0.69–0.83)	<0.001	0.78 (0.70–0.86)	<0.001
Additional ADT Treatment	0.71 (0.64–0.80)	<0.001	0.84 (0.72–0.98)	0.03
Additional Radiation Therapy	0.80 (0.72–0.90)	<0.001	0.77 (0.69–0.86)	<0.001