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# The Comparative Harms of Open and Robotic Prostatectomy in Population Based Samples

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**Purpose:** Robotic assisted radical prostatectomy has largely replaced open radical prostatectomy for the surgical management of prostate cancer despite conflicting evidence of superiority with respect to disease control or functional sequelae. Using population cohort data, in this study we examined sexual and urinary function in men undergoing open radical prostatectomy vs those undergoing robotic assisted radical prostatectomy.

**Materials and Methods:** Subjects surgically treated for prostate cancer were selected from 2 large population based prospective cohort studies, the Prostate Cancer Outcomes Study (enrolled 1994 to 1995) and the Comparative Effectiveness Analysis of Surgery and Radiation (enrolled 2011 to 2012). Subjects completed baseline, 6-month and 12-month standardized patient reported outcome measures. Main outcomes were between-group differences in functional outcome scores at 6 and 12 months using linear regression, and adjusting for baseline function, sociodemographic and clinical characteristics. Sensitivity analyses were used to evaluate outcomes between patients undergoing open radical prostatectomy and robotic assisted radical prostatectomy within and across CEASAR and PCOS.

## Abbreviations and Acronyms

CEASAR = Comparative Effectiveness Analysis of Surgery and Radiation

EPIC = Expanded Prostate Cancer Index Composite-26

PCOS = Prostate Cancer Outcomes Study

PD5 = phosphodiesterase type 5

PROM = patient reported outcome measures

RALP = robotic assisted radical prostatectomy

RRP = open radical prostatectomy

SEER = Surveillance, Epidemiology, and End Results

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**Editor's Note:** This article is the third of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 530 and 531.

**Results:** The combined cohort consisted of 2,438 men, 1,505 of whom underwent open radical prostatectomy and 933 of whom underwent robotic assisted radical prostatectomy. Men treated with robotic assisted radical prostatectomy reported better urinary function at 6 months (mean difference 3.77 points, 95% CI 1.09–6.44) but not at 12 months (1.19, –1.32–3.71). Subjects treated with robotic assisted radical prostatectomy also reported superior sexual function at 6 months (8.31, 6.02–10.56) and at 12 months (7.64, 5.25–10.03). Sensitivity analyses largely supported the sexual function findings with inconsistent support for urinary function results.

**Conclusions:** This population based study reveals that men undergoing robotic assisted radical prostatectomy likely experience less decline in early urinary continence and sexual function than those undergoing open radical prostatectomy. The clinical meaning of these differences is uncertain and longer followup will be required to establish whether these benefits are durable.

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**Key Words:** prostatectomy, robotics, patient outcome assessment

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ROBOTIC assisted radical prostatectomy for the treatment of prostate cancer has largely supplanted open radical prostatectomy despite a lack of evidence demonstrating superior oncologic or functional outcomes.<sup>1</sup> Various studies of RALP have reported benefits over RRP, including less blood loss and shorter length of hospital stay, with inconsistent findings of fewer bladder neck contractures, positive surgical margins, and quicker recovery of erectile function and urinary control.<sup>2–8</sup>

Many of these reports are based on data from single surgeon/institution reports, lack controls for patient comorbidities and evaluate short-term outcomes. In some studies the functional outcomes have been excluded altogether, are assessed too early postoperatively or are measured using nonstandard instruments. Community based analyses are a more representative method to assess the real-world use of these techniques rather than idealized comparisons in tertiary referral centers. To date, such studies have consistently demonstrated shorter hospital stay and less blood loss with RALP, but with variable rates of perioperative complications and positive surgical margins.<sup>9–15</sup> Additionally, assessments of PROM using validated and reliable instruments are often lacking, and investigators have relied on administrative data sources to extrapolate disease specific function. However, it remains unknown whether this adequately reflects the patient survivorship experience.<sup>9</sup>

Despite more than a decade of experience, considerable uncertainty remains surrounding the comparative effectiveness and harms of RALP and RRP in the context of the questionable cost-effectiveness of RALP.<sup>15,16</sup> Unfortunately, a prospective randomized trial (NCT01365143) designed to address many of these shortcomings was closed due to lack of accrual.<sup>17</sup> A single-institution randomized trial is ongoing in Australia but may be limited by methodological concerns.<sup>18</sup>

The goal of this study was to compare sexual and urinary function between men with prostate cancer selected in a population based manner undergoing RRP or RALP, using established measurement strategies while controlling for a large number of potential confounders. We used data from the PCOS and CEASAR, both of which are population based cohorts of men treated for prostate cancer, and contain data using validated and reliable PROM.

## METHODS

### Patients

Data were obtained from 2 large, population based, prospective cohort studies. The PCOS enrolled patients with incident prostate cancer from 6 participating SEER sites between October 1, 1994 and October 31, 1995. Details of PCOS methods have been previously reported.<sup>19</sup>

CEASAR recruited men from 5 SEER registries from January 2011 to February 2012 with a small proportion of subjects from CaPSURE™, an observational prostate cancer registry.<sup>20</sup> Details and objectives for the CEASAR study have also been previously reported.<sup>21</sup> Institutional review boards at all participating sites including the Vanderbilt University coordinating site approved the studies.

In total, PCOS initially enrolled 5,672 subjects while CEASAR enrolled 3,691 subjects. We selected men in either parent study who underwent radical prostatectomy and completed baseline PROM.

Upon enrollment, PCOS subjects completed a baseline survey including items regarding clinical and sociodemographic variables, comorbidities and disease specific outcomes using the UCLA Prostate Cancer Index, a reliable and validated PROM of sexual function, urinary incontinence and bowel function related to prostate cancer and its treatment.<sup>22</sup> CEASAR participants completed a similar baseline assessment using the EPIC, valid and reliable PROM developed from and containing many similar/identical items as the UCLA Prostate Cancer Index. Previous work has reported similar psychometric performance for these instruments.<sup>23</sup> To minimize bias from differences in the 2 PROM, we included 4 common

measures of urinary incontinence and 3 common measures of sexual function, and derived modified domain summary scores scaled 0 to 100, with 100 representing optimal function.<sup>24</sup>

All subjects in PCOS who had surgery underwent RRP because RALP was first introduced more than 5 years after enrollment ended.<sup>25</sup> The majority of CEASAR participants who had surgery underwent RALP (78%).

### Statistical Analysis

We compared differences between baseline characteristics including inflation adjusted income for PCOS participants using nonparametric tests. In addition to standard socio-demographic and clinical characteristics, we evaluated differences in number of comorbidities, baseline general health and whether nerve sparing (any degree vs none) was performed.

### Primary Outcomes

To assess differences in function between patients undergoing RRP vs RALP, we fit 4 multivariable linear regression models, one for each domain summary score (sexual and urinary function) and time point (6 and 12-month surveys). Covariate adjustment was used to control for age (continuous), race, income, education, marital and health insurance status, study site, days since treatment, PSA, Gleason score, margin and nerve sparing status, pathological stage (pT2c or lower vs pT3 or higher), use of androgen deprivation, self-reported overall health and baseline function. Sexual function models also adjusted for use of erectile dysfunction treatments such as injections, vacuum pump, penile prosthesis or medications. Missing values for baseline characteristics included in these models were multiply imputed through predictive mean matching.

To account for documented differences in baseline function between PCOS and CEASAR subjects,<sup>24</sup> mean function was modeled with an interaction term between baseline function and surgical procedure (RRP vs RALP). Primary comparisons were assessed using these models, estimating the mean difference in function between patients undergoing the 2 procedures. Model based contrast tests using t-statistics were used at varying levels of baseline function to identify a threshold, above which between-group differences were significant.

### Secondary Analyses

A second set of 4 multivariable linear regression models was developed by adding study cohort (CEASAR and PCOS) to the models used for the primary analysis. Sensitivity analyses were performed to evaluate differences attributable to the lack of availability of PD5 inhibitors during PCOS, and to mitigate possible confounding associated with differences in baseline reporting of baseline function.<sup>24</sup> This enabled the exploration of between-group differences in outcomes for 3 comparisons of 1) RRP in PCOS vs RRP in CEASAR, 2) RRP in CEASAR vs RALP and 3) RRP in PCOS vs RALP. If observed differences in primary outcomes were explained by differences in surgical technique, one would expect within-group differences between study cohorts not to be significant in comparison 1, but between-group differences to remain significant in comparisons 2 and 3.

To better characterize the impact of surgical approach on treatment in a fashion more meaningful to patients, we fit logistic regression models using each of the 7 individual items aggregated for the domain specific scores. These items were dichotomously recoded from the original Likert-type scales using clinically relevant cut points.

All p values were 2-sided and  $p < 0.05$  was considered statistically significant. Confidence intervals are all 95 percent. The analysis was completed using R software v.3.1.2 (R Foundation, Vienna, Austria).

## RESULTS

The study cohort comprised 2,438 men, of whom 933 underwent RALP while 1,505 underwent RRP (82.6% from PCOS and 17.4% from CEASAR). All sociodemographic characteristics between the groups were different except for marital status. Participants who underwent RALP were younger, and more likely to be white, employed full-time, and have higher income and education, and private insurance (table 1). Differences were also noted for baseline clinical characteristics. Unadjusted negative margin rate and nerve sparing rate were highest in RALP. Baseline scores for sexual and urinary function were highest in the PCOS group, consistent with previous work (table 2).<sup>24</sup>

### Primary Outcomes

Multivariable models revealed that patients undergoing RALP reported higher urinary function scores at 6 months and sexual function at 6 and 12 months (table 3). However, patients undergoing RALP did not report superior urinary function at 12 months. The relationship between the interaction of surgical approach with baseline function and postoperative functional outcome was also significant for the same periods. Age, baseline function and general health were also associated with postoperative functional outcomes, while income and race were not.

We then identified thresholds for baseline function above which there were statistically significant between-group differences in predicted scores (fig. 1). For urinary function (6 months) significant differences were noted for patients whose baseline function score was 94 or greater, above which the majority of men reported baseline function. Above this threshold the magnitude of the difference in favor of RALP over RRP ranged from 2.59 points (95% CI 0.30–5.08) to 3.77 points (1.11–6.44). At 12 months there were no differences in predicted scores at any threshold.

Differences in sexual function were noted for those with a baseline function score of at least 50 at 6 months and 62 at 12 months, values also reported by the majority of men in both studies. The magnitude of this difference ranged from 3.06 points

**Table 1.** Baseline sociodemographic characteristics by surgery type and cohort

	RALP	RRP (total)	RRP (PCOS)	RRP (CEASAR)	p Value*	
					Test 1†	Test 2‡
No. pts	933	1,505	1,243	262		
No. pt age (%):					0.004	0.002
Less than 55	173 (18.5)	239 (15.9)	208 (16.7)	31 (11.8)		
55–59	234 (25.1)	328 (21.8)	272 (21.9)	56 (21.4)		
60–64	244 (26.2)	352 (23.4)	278 (22.4)	74 (28.2)		
65–69	181 (19.4)	376 (25.0)	312 (25.1)	64 (24.4)		
70–74	90 (9.6)	183 (12.2)	150 (12.1)	33 (12.6)		
75 or Greater	11 (1.2)	27 (1.8)	23 (1.9)	4 (1.5)		
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
No. race (%):					<0.001	<0.001
Black	80 (8.6)	243 (16.1)	207 (16.7)	36 (13.7)		
Hispanic	61 (6.5)	191 (12.7)	173 (13.9)	18 (6.9)		
Other	38 (4.1)	11 (0.7)	0 (0.0)	11 (4.2)		
White	739 (79.2)	1,057 (70.2)	863 (69.4)	194 (74.0)		
Missing	15 (1.6)	3 (0.2)	0 (0.0)	3 (1.1)		
No. income (%):					<0.001	<0.001
Less than \$30,000	102 (10.9)	287 (19.1)	228 (18.3)	59 (22.5)		
\$30,000–\$100,000	446 (47.8)	794 (52.8)	673 (54.1)	121 (46.2)		
More than \$100,000	319 (34.2)	322 (21.4)	261 (21.0)	61 (23.3)		
Missing	66 (7.1)	102 (6.8)	81 (6.5)	21 (8.0)		
No. education (%):					<0.001	<0.001
High school or less	229 (24.5)	567 (37.7)	478 (38.5)	89 (34.0)		
Some college	200 (21.4)	365 (24.3)	307 (24.7)	58 (22.1)		
College graduate	224 (24.0)	219 (14.6)	166 (13.4)	53 (20.2)		
Advanced degree	254 (27.2)	334 (22.2)	282 (22.7)	52 (19.8)		
Missing	26 (2.8)	20 (1.3)	10 (0.8)	10 (3.8)		
No. employment (%):					<0.001	<0.001
Other	30 (3.2)	74 (4.9)	54 (4.3)	20 (7.6)		
Part-time	63 (6.8)	141 (9.4)	114 (9.2)	27 (10.3)		
Full-time	557 (59.7)	570 (37.9)	461 (37.1)	109 (41.6)		
Retired	271 (29.0)	710 (47.2)	606 (48.8)	104 (39.7)		
Missing	12 (1.3)	10 (0.7)	8 (0.6)	2 (0.8)		
No. not married (%):	137 (14.7)	230 (15.3)	185 (14.9)	45 (17.2)	0.494	0.844
Missing	28 (3.0)	15 (1.0)	5 (0.4)	10 (3.8)		
No. privately insured (%):	620 (66.5)	842 (55.9)	706 (56.8)	136 (51.9)	<0.001	<0.001
Missing	9 (1.0)	100 (6.6)	98 (7.9)	2 (0.8)		

\* Pearson chi-square test.

† Comparisons are between RALP, RRP (PCOS) and RRP (CEASAR).

‡ Comparisons are between RALP (total) and RRP (total).

(0.14–5.99) to 10.21 points (7.51–12.91) at 6 months and 2.70 points (0.08–5.31) to 10.31 points (7.51–13.13) at 12 months.

### Individual Items

Unadjusted responses to individual PROM items at 6 and 12 months and odds ratios from logistic regression items are presented in figure 2. Several sexual function items at 6 and 12 months were better for RALP and none suggested benefit for RRP. While several urinary function items favored RALP, with the exception of “any urinary incontinence” at 6 months no statistically significant differences were found.

### Sensitivity Analyses

Primary urinary function results favoring RALP were inconsistently supported in the sensitivity analyses (table 4). Consistent with primary results, there were no differences for comparison 1, that is comparing urinary function outcomes between RRP groups from each of the 2 parent studies. Significant

between-group differences persisted when comparing RRP in PCOS to RALP (comparison 3). However, when examining the contemporary cohort (ie between RRP and RALP in CEASAR, comparison 2), significant within-study differences for urinary function were not identified.

Sexual function primary outcomes were consistently supported by the sensitivity analyses. Predicted scores for men undergoing RRP in the contemporary and previous eras (ie CEASAR and PCOS, comparisons 2 and 3) were significantly lower at 6 and 12 months compared to RALP. While within-group differences for those undergoing RRP (comparison 1) were significant at 6 months, by 12 months the differences were not statistically different from zero.

## DISCUSSION

Data from 2 large, prospective, population based cohort studies of prostate cancer survivors

**Table 2. Additional characteristics by surgery type and cohort**

	RALP	RRP (total)		RRP (PCOS)		RRP (CEASAR)		p Value*	
		Test 1*	Test 2†	Test 1*	Test 2†	Test 1*	Test 2†	Test 1*	Test 2†
No. pts	933	1,505		1,243		262			
<i>Clinicopathological characteristics</i>									
No. pathological staging (%):									
pT2	735 (78.8)	1,015 (67.4)	810 (65.2)	205 (78.2)	<0.001‡	<0.001‡			
pT3 (not otherwise specified)	4 (0.4)	105 (7.0)	100 (8.0)	5 (1.9)					
pT3a	114 (12.2)	202 (13.4)	179 (14.4)	23 (8.8)					
pT3b	32 (3.4)	108 (7.2)	92 (7.4)	16 (6.1)					
pT4	0 (0.0)	42 (2.8)	42 (3.4)	0 (0.0)					
Other	3 (0.3)	9 (0.6)	6 (0.5)	3 (1.1)					
Missing	45 (4.8)	24 (1.6)	14 (1.1)	10 (3.8)					
Median ng/ml PSA (IQR)	5.0 (4.1–6.7)	6.6 (4.8–9.9)	6.9 (5.0–10.5)	5.2 (4.2–7.6)	<0.001§	<0.001§			
No. PSA missing (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)					
No. Gleason score (%):					<0.001‡	<0.001‡			
6 or Less	294 (31.5)	762 (50.6)	664 (53.4)	98 (37.4)					
7	557 (59.7)	462 (30.7)	333 (26.8)	129 (49.2)					
8–10	59 (6.3)	126 (8.4)	96 (7.7)	30 (11.5)					
Missing	23 (2.5)	155 (10.3)	150 (12.1)	5 (1.9)					
No. neg margins (%):	710 (76.1)	936 (62.2)	756 (60.8)	180 (68.7)	<0.001‡	<0.001‡			
Missing	28 (3.0)	100 (6.6)	92 (7.4)	8 (3.1)					
No. nerve sparing (%):	728 (78.0)	702 (46.6)	517 (41.6)	185 (70.6)	<0.001‡	<0.001‡			
Missing	145 (15.5)	302 (20.1)	242 (19.5)	60 (22.9)					
No. comorbidities (%):					<0.001‡	0.001‡			
0	355 (38.0)	794 (52.8)	717 (57.7)	77 (29.4)					
1	362 (38.8)	452 (30.0)	344 (27.7)	108 (41.2)					
2	114 (12.2)	163 (10.8)	131 (10.5)	32 (12.2)					
3 or Greater	26 (2.8)	60 (4.0)	51 (4.1)	9 (3.4)					
Missing	76 (8.1)	36 (2.4)	0 (0.0)	36 (13.7)					
<i>Baseline pt reported outcomes</i>									
No. self-reported overall health (%):					<0.001‡	<0.001‡			
Poor	6 (0.6)	21 (1.4)	17 (1.4)	4 (1.5)					
Fair	35 (3.8)	108 (7.2)	90 (7.2)	18 (6.9)					
Good	221 (23.7)	438 (29.1)	351 (28.2)	87 (33.2)					
Very good	429 (46.0)	592 (39.3)	485 (39.0)	107 (40.8)					
Excellent	240 (25.7)	342 (22.7)	296 (23.8)	46 (17.6)					
Missing	2 (0.2)	4 (0.3)	4 (0.3)	0 (0.0)					
Median urinary function summary score (IQR)	100.0 (85.0–100.0)	100 (100.0–100.0)	100.0 (100.0–100.0)	100.0 (88.8–100.0)	<0.001§	<0.001§			
Median sexual function summary score (IQR)	86.7 (58.3–100.0)	88.9 (66.7–100.0)	93.3 (73.3–100.0)	79.2 (51.7–93.3)	<0.001§	<0.001§			

\* Comparisons are among RALP, RRP (PCOS) and RRP (CEASAR).

† Comparisons are between RALP (total) and RRP (total).

‡ Pearson chi-square test.

§ Kruskal-Wallis test.

**Table 3. Multivariable linear regression models for domain summary scores by time of survey**

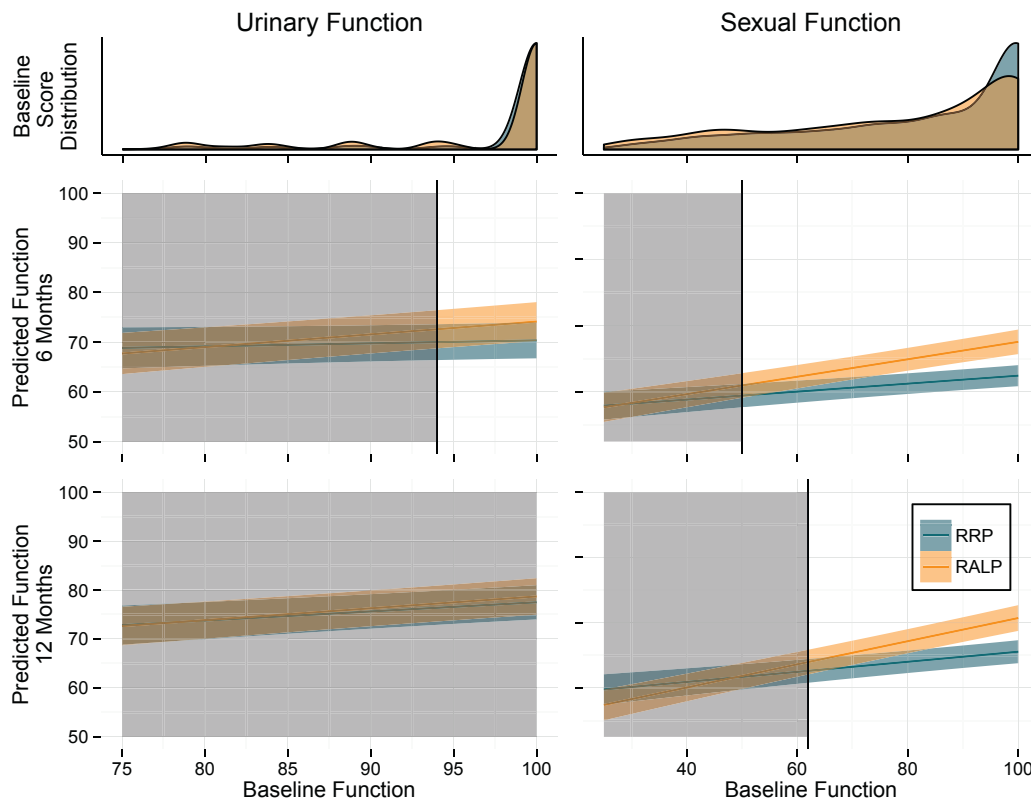
	Urinary Function Summary Scores				Sexual Function Summary Scores*			
	6 Mos		12 Mos		6 Mos		12 Mos	
	Coefficient	p Value	Coefficient	p Value	Coefficient	p Value	Coefficient	p Value
Surgery: RALP vs RRP	3.77	0.005	1.20	0.35	8.31	<0.001	7.64	<0.001
Baseline function (10 pts)†	0.61	0.21	1.87	<0.001	1.20	<0.001	1.54	<0.001
<i>Interactions</i>								
Surgery-baseline function (10 pts)	1.96	0.003	0.55	0.39	1.43	<0.001	2.01	<0.001
Age-10 yrs, continuous	-2.78	0.001	-2.63	0.001	-1.43	0.06	-3.22	<0.001
Race: white vs other	0.75	0.56	-0.06	0.96	-0.33	0.76	-0.65	0.58
<i>Income vs less than \$30,000:</i>								
\$30,000–\$100,000	-0.80	0.59	-0.26	0.86	-1.13	0.39	-0.12	0.93
Greater than \$100,000	3.17	0.09	3.12	0.08	1.75	0.28	1.34	0.45
<i>General health vs excellent:</i>								
Poor	-23.59	<0.001	-24.22	<0.001	-12.15	0.002	-15.94	<0.001
Fair	-6.04	0.008	-6.95	0.002	-5.83	0.003	-10.83	<0.001
Good	-9.38	<0.001	-9.91	<0.001	-4.57	<0.001	-4.15	0.001
Very good	-2.67	0.03	-4.17	<0.001	-1.75	0.09	-3.16	0.004

Adjusted for education, marital and health insurance status, study site, days since treatment, PSA, Gleason score, margin and nerve sparing status, pathological stage, and use of androgen deprivation.

\* Also adjusted for use of erectile dysfunction treatments.

† Refers to baseline summary scores for respective functional domains.





**Figure 1.** Model based predicted postoperative function by baseline function and distribution of baseline function scores. Shaded areas indicate that between-group differences in predicted function are not statistically different at significance level of 0.05. Unshaded areas represent statistically significant differences at  $p < 0.05$ . Colored bands represent 95% CIs for predicted scores. Overlap of intervals does not indicate that differences are nonsignificant.

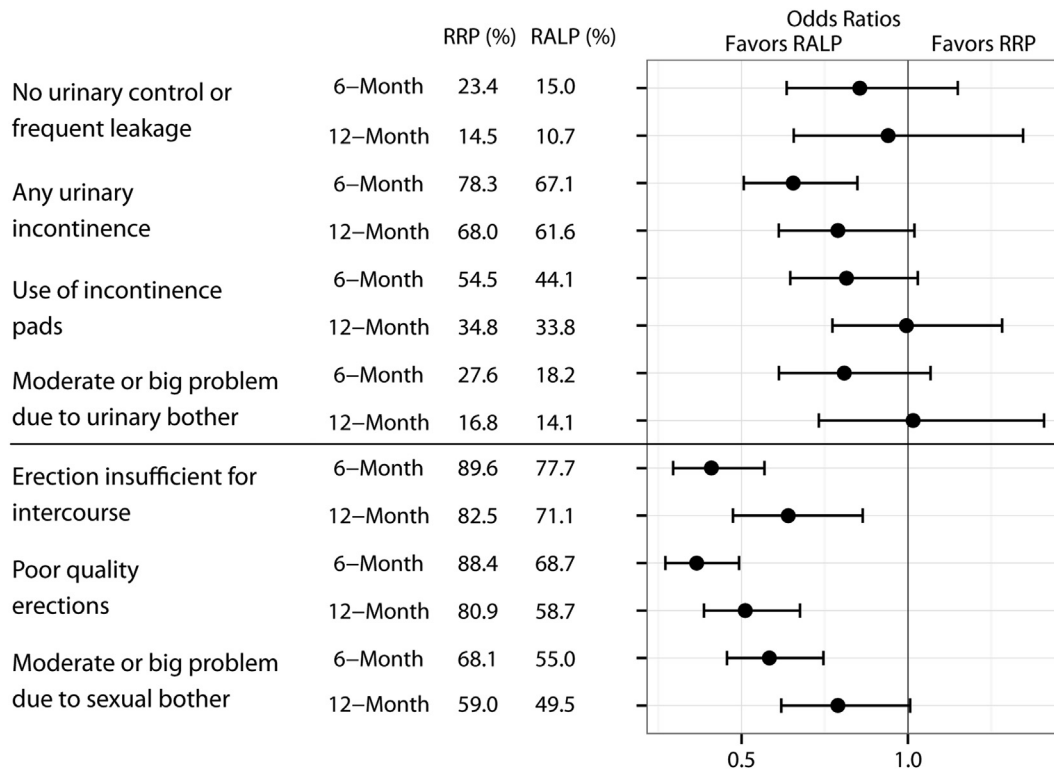
demonstrate that patients treated with RALP report more favorable sexual function at 6 and 12 months as well as more favorable urinary function scores at 6 months. Similar findings were observed when the analysis used responses to individual items. Of note, there were no significant differences in urinary function between the surgical approaches at 12 months, and sensitivity analyses, with less statistical power, provided inconsistent support of differences in urinary function at 6 months.

These possible outcome benefits for sexual function attributed to RALP have not been previously shown in a consistent manner. Many prior studies were undertaken at high volume tertiary referral centers and patients who seek treatment at these institutions may be different from the general population. Furthermore, surgeons who operate in these centers tend to have high operative volumes and their outcomes may be different from surgeons operating in the community.<sup>26</sup> The current study is population based, and includes surgeons from tertiary referral centers and those in community practice and, accordingly, more accurately reflects the experience of prostate cancer survivors undergoing prostatectomy.

Alternatively, the difference between these findings and those of prior studies may be due to our inclusion of baseline function in the multivariable models. Several cross-sectional analyses comparing RRP and RALP that have not demonstrated functional outcome differences failed to adjust for baseline differences,<sup>7,9,12</sup> while a recent study demonstrated sexual function benefit for RALP after doing so.<sup>27</sup>

Differences between RALP and RRP in this study could be due to factors unrelated to robotic technology but from general patterns of prostate cancer care and/or surgical training. During the adoption of RALP, prostate cancer care became more centralized<sup>1</sup> and several reports suggest that better outcomes may be achieved at high volume centers.<sup>26</sup> Furthermore, instruction designed to teach the operation relied heavily on the use of video demonstrations that may have standardized the technique more than was achievable for RRP. Therefore, differences may be due to the reduction of variation in technique rather than intrinsic advantages of the robot.

That PCOS only included RRP limits bias from treatment selection. Surgeons continuing to perform RRP in the CEASAR era may select



**Figure 2.** Unadjusted responses and logistic regression models for individual items comparing RRP to RALP. Values less than 1 favor RALP. Error bars represent 95% CIs.

patients with adverse pathology, potentially confounding data surrounding functional outcomes. We largely adjusted for possible confounders in our multivariable models but acknowledge the prospect of remaining unmeasured confounding.

**Table 4.** Model based predicted scores and contrast tests comparing surgical approach and study cohort stratified by time since treatment

	Predicted Scores	Difference	95% CI	p Value (t-statistics)
<i>Comparison of RRP (PCOS) vs RRP (CEASAR)</i>				
Urinary function:				
6-Mo	69.73 vs 72.76	3.03	-1.19-7.24	0.16
12-Mo	77.67 vs 76.81	-0.86	-4.83-3.10	0.67
Sexual function:				
6-Mo	42.17 vs 48.68	6.52	2.81-10.23	0.001
12-Mo	48.98 vs 50.40	1.42	-2.47-5.31	0.47
<i>Comparison of RRP (CEASAR) vs RALP</i>				
Urinary function:				
6-Mo	72.76 vs 74.67	1.92	-1.76-5.59	0.31
12-Mo	76.81 vs 78.39	1.58	-1.83-4.98	0.36
Sexual function:				
6-Mo	48.68 vs 53.14	4.46	1.30-7.62	0.006
12-Mo	50.40 vs 56.57	6.18	2.88-9.48	<0.001
<i>Comparison of RRP (PCOS) vs RALP</i>				
Urinary function:				
6-Mo	69.73 vs 74.67	4.94	1.75-8.13	0.002
12-Mo	77.67 vs 78.39	0.71	-2.34-3.76	0.65
Sexual function:				
6-Mo	42.17 vs 53.14	10.98	8.16-13.80	<0.001
12-Mo	48.98 vs 56.57	7.60	4.62-10.57	<0.001

Some might suggest that the only way to eliminate selection bias is to perform a randomized trial. A large multicenter trial, required to permit generalizability, is unlikely ever to be done given the current pervasiveness of RALP and a previously failed attempt due to accrual.<sup>17</sup> The only ongoing randomized trial of which we are aware is a single center design comparing a high volume open surgeon to a high volume robotic surgeon resulting in significant questions about external validity.<sup>18</sup>

While this work has demonstrated statistically significant differences, especially for sexual function, it is uncertain if the observed differences achieve clinical significance. A third of the standard deviation has been suggested as an acceptable value for a minimally important difference in EPIC.<sup>28</sup> Using this standard, minimal important differences are 4.77 for urinary function and 7.64 for sexual function. Confidence intervals contained these values even in those with the highest levels of baseline function, limiting conclusions that observed differences are clinically meaningful.

Differences in baseline function between the 2 parent studies have been reported with PCOS patients reporting better baseline function.<sup>24</sup> For this reason, and given that baseline function may be the most important predictor of posttreatment function,<sup>29</sup> we adjusted for this in our models.



Furthermore, better baseline function in the PCOS group favors the opposite outcome than what was observed, suggesting that the benefit of RALP may be underestimated. Nonetheless, PCOS and CEASAR, initiated more than 15 years apart, had similar methodology, and provide a means for determining the comparative effectiveness of the 2 approaches, which has otherwise been elusive.

This study has several limitations. The primary measures of sexual and urinary function were created from common items of the Prostate Cancer Index and EPIC. Psychometric validation of this approach has not been established but single-item analysis appeared consistent with the main results. In addition, the introduction of PD5 inhibitors occurred in 1998, after first year data collection in the PCOS. We adjusted for differences in the use of erectile aids but could not adjust for this qualitative difference in treatment. Sensitivity analyses consistently supported findings of improved sexual function at 12 months in those undergoing RALP, suggesting that even with PD5 inhibitors, patients undergoing RALP enjoyed a sexual function benefit.

While this study reveals improvements in patient reported urinary and sexual function attributable to RALP, this study does not evaluate the value assigned to these between-group differences. The widespread use and uptake of robotic technology

were largely driven by market forces despite associated increased costs and before demonstrable patient benefit.<sup>30</sup> As a society we need to evaluate the value of incremental benefits to determine the appropriateness of innovative technologies to ensure patients are provided with high value care.

## CONCLUSIONS

This population based study reveals that patients undergoing RALP likely experience less functional decline in early urinary continence and sexual function compared to those undergoing RRP, but it is uncertain whether these differences are clinically meaningful. Differences in urinary function between the 2 procedures resolve by 12 months while differences in sexual function persist up to 12 months after surgery. Longer followup will be required to establish whether this benefit is durable beyond 1 year and to assess oncologic outcomes.

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## REFERENCES

- Anderson CB, Penson DF, Ni S et al: Centralization of radical prostatectomy in the United States. *J Urol* 2013; **189**: 500.
- Farnham SB, Webster TM, Herrell SD et al: Intraoperative blood loss and transfusion requirements for robotic-assisted radical prostatectomy versus radical retropubic prostatectomy. *Urology* 2006; **67**: 360.
- Nelson B, Kaufman M, Broughton G et al: Comparison of length of hospital stay between radical retropubic prostatectomy and robotic assisted laparoscopic prostatectomy. *J Urol* 2007; **177**: 929.
- Smith JA Jr, Chan RC, Chang SS et al: A comparison of the incidence and location of positive surgical margins in robotic assisted laparoscopic radical prostatectomy and open retropubic radical prostatectomy. *J Urol* 2007; **178**: 2385.
- Menon M, Shrivastava A, Kaul S et al: Vattikuti Institute prostatectomy: contemporary technique and analysis of results. *Eur Urol* 2007; **51**: 648.
- Rocco B, Matei DV, Melegari S et al: Robotic vs open prostatectomy in a laparoscopically naive centre: a matched-pair analysis. *BJU Int* 2009; **104**: 991.
- Krambeck AE, DiMarco DS, Rangel LJ et al: Radical prostatectomy for prostatic adenocarcinoma: a matched comparison of open retropubic and robot-assisted techniques. *BJU Int* 2009; **103**: 448.
- Thompson JE, Egger S, Bohm M et al: Superior quality of life and improved surgical margins are achievable with robotic radical prostatectomy after a long learning curve: a prospective single-surgeon study of 1552 consecutive cases. *Eur Urol* 2014; **65**: 521.
- Hu JC, Gu X, Lipsitz SR et al: Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA* 2009; **302**: 1557.
- Trinh QD, Sammon J, Sun M et al: Perioperative outcomes of robot-assisted radical prostatectomy compared with open radical prostatectomy: results from the Nationwide Inpatient Sample. *Eur Urol* 2012; **61**: 679.
- Kowalczyk KJ, Levy JM, Caplan CF et al: Temporal national trends of minimally invasive and retropubic radical prostatectomy outcomes from 2003 to 2007: results from the 100% Medicare sample. *Eur Urol* 2012; **61**: 803.
- Alemozaffar M, Sanda M, Yecies D et al: Benchmarks for operative outcomes of robotic and open radical prostatectomy: results from the Health Professionals Follow-up Study. *Eur Urol* 2014; **67**: 432.
- Hu JC, Gandaglia G, Karakiewicz PI et al: Comparative effectiveness of robot-assisted versus open radical prostatectomy cancer control. *Eur Urol* 2014; **66**: 666.
- Wallerstedt A, Tyrizis SI, Thorsteinsdottir T et al: Short-term results after robot-assisted laparoscopic radical prostatectomy compared to open radical prostatectomy. *Eur Urol* 2014; **67**: 660.
- Gandaglia G, Sammon JD, Chang SL et al: Comparative effectiveness of robot-assisted and open radical prostatectomy in the post-dissemination era. *J Clin Oncol* 2014; **32**: 1419.
- Hohwu L, Borre M, Ehlers L et al: A short-term cost-effectiveness study comparing robot-assisted laparoscopic and open retropubic radical prostatectomy. *J Med Econ* 2011; **14**: 403.
- Prospective Randomized Trial Comparing Robotic Versus Open Radical Prostatectomy, [ClinicalTrials.gov](http://ClinicalTrials.gov) 2015 (NCT01365143).

18. Gardiner RA, Yaxley J, Coughlin G et al: A randomised trial of robotic and open prostatectomy in men with localised prostate cancer. *BMC Cancer* 2012; **12**: 189.
19. Potosky AL, Legler J, Albertsen PC et al: Health outcomes after prostatectomy or radiotherapy for prostate cancer: results from the Prostate Cancer Outcomes Study. *J Natl Cancer Inst* 2000; **92**: 1582.
20. Lubeck DP, Litwin MS, Henning JM et al: The CaPSURE database: a methodology for clinical practice and research in prostate cancer. CaPSURE Research Panel. *Cancer of the Prostate Strategic Urologic Research Endeavor. Urology* 1996; **48**: 773.
21. Barocas DA, Chen V, Cooperberg M et al: Using a population-based observational cohort study to address difficult comparative effectiveness research questions: the CEASAR study. *J Comp Eff Res* 2013; **2**: 445.
22. Litwin MS, Hays RD, Fink A et al: The UCLA Prostate Cancer Index: development, reliability, and validity of a health-related quality of life measure. *Med Care* 1998; **36**: 1002.
23. Namiki S, Takegami M, Kakehi Y et al: Analysis linking UCLA PCI with Expanded Prostate Cancer Index Composite: an evaluation of health related quality of life in Japanese men with localized prostate cancer. *J Urol* 2007; **178**: 473.
24. Resnick MJ, Barocas DA, Morgans AK et al: The evolution of self-reported urinary and sexual dysfunction over the last two decades: implications for comparative effectiveness research. *Eur Urol* 2014; **67**: 1019.
25. Menon M, Shrivastava A, Tewari A et al: Laparoscopic and robot assisted radical prostatectomy: establishment of a structured program and preliminary analysis of outcomes. *J Urol* 2002; **168**: 945.
26. Trinh QD, Bjartell A, Freedland SJ et al: A systematic review of the volume-outcome relationship for radical prostatectomy. *Eur Urol* 2013; **64**: 786.
27. Stolzenburg JU, Graefen M, Kriegel C et al: Effect of surgical approach on erectile function recovery following bilateral nerve-sparing radical prostatectomy: an evaluation utilizing data from a randomized, double-blind, double-dummy multicenter trial of tadalafil versus placebo. *BJU Int* 2015; **116**: 241.
28. Skolarus TA, Dunn RL, Sanda MG et al: Minimally important difference for the expanded prostate cancer index composite short form. *Urology* 2015; **85**: 101.
29. Chen RC, Clark JA and Talcott JA: Individualizing quality-of-life outcomes reporting: how localized prostate cancer treatments affect patients with different levels of baseline urinary, bowel, and sexual function. *J Clin Oncol* 2009; **27**: 3916.
30. Barbash GI, Friedman B, Glied SA et al: Factors associated with adoption of robotic surgical technology in US hospitals and relationship to radical prostatectomy procedure volume. *Ann Surg* 2014; **259**: 1.