

## Prospective Multicenter Comparison of Open and Robotic Radical Prostatectomy: The PROST-QA/RP2 Consortium

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**Study Need and Importance:** The rapid adoption of robot-assisted laparoscopic prostatectomy (RALP) over open radical prostatectomy (ORP) has outpaced quality evidence comparing the 2 surgical approaches. Most studies have been retrospective. The 1 published randomized trial was limited by being a single-center study comparing 2 surgeons. We present the results of a prospective multicenter study comparing RALP and ORP in subjects from 11 large academic centers in the United States that used centralized patient-reported outcome collection to assess baseline and postoperative quality of life.

**What We Found:** Surgical approach was not a significant factor in longitudinal patient-reported quality of life change in any health domain. Positive surgical margin rates were similar between approaches. RALP subjects had less pain, less interference with activity,

less blood loss/transfusions, and shorter lengths of stay. Bladder neck contractures were more common in ORP subjects (8.3% vs 1.6% in RALP), as were deep vein thromboses (1.9% vs 0.5% in RALP).

**Limitations:** The study is limited by its non-randomized trial design, and its accrual from 2 separate cohorts that were separated by time, institution composition, and surgical approach distribution.

**Interpretations for Patient Care:** With an experienced surgeon, men undergoing radical prostatectomy can expect similar long-term quality of life outcomes, regardless of surgical approach. The robotic approach does not eliminate the risk of quality of life deficits, but does offer superior perioperative and short-term recovery outcomes. Men undergoing open surgery are more likely to need intervention to treat bladder neck contractures.

## Prospective Multicenter Comparison of Open and Robotic Radical Prostatectomy: The PROST-QA/RP2 Consortium

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**Purpose:** To evaluate the comparative effectiveness of robot-assisted laparoscopic prostatectomy (RALP) and open radical prostatectomy (ORP) in a multicenter study.

**Materials and Methods:** We evaluated men with localized prostate cancer at 11 high-volume academic medical centers in the United States from the PROST-QA (2003–2006) and the PROST-QA/RP2 cohorts (2010–2013) with a pre-specified goal of comparing RALP (549) and ORP (545). We measured longitudinal patient-reported health-related quality of life (HRQOL) at pre-treatment and at 2, 6, 12, and 24 months, and pathological and perioperative outcomes/complications.

**Results:** Demographics, cancer characteristics, and margin status were similar between surgical approaches. ORP subjects were more likely to undergo lymphadenectomy (89% vs 47%;  $p < 0.01$ ) and nerve sparing (94% vs 89%;  $p < 0.01$ ).

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Attestation: Dr. Chang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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### Abbreviations and Acronyms

DVT = deep venous thrombosis

EPIC = Expanded Prostate Cancer Index Composite

HRQOL = health-related quality of life

LAPPRO = Laparoscopic Prostatectomy Robot Open

ORP = open radical prostatectomy

PQA = PROST-QA

RALP = robot-assisted laparoscopic prostatectomy

RP2 = PROSTQA-RP2

RALP vs ORP subjects experienced less mean intraoperative blood loss (192 vs 805 mL;  $p < 0.01$ ), shorter mean hospital stay (1.6 vs 2.1 days;  $p < 0.01$ ), and fewer blood transfusions (1% vs 4%;  $p < 0.01$ ), wound infections (2% vs 4%;  $p = 0.02$ ), other infections (1% vs 4%;  $p < 0.01$ ), deep vein thromboses (0.5% vs 2%;  $p = 0.04$ ), and bladder neck contractures requiring dilation (1.6% vs 8.3%;  $p < 0.01$ ). RALP subjects reported less pain ( $p = 0.04$ ), less activity interference ( $p < 0.01$ ) and higher incision satisfaction ( $p < 0.01$ ). Surgical approach (RALP vs ORP) was not a significant predictor of longitudinal HRQOL change in any HRQOL domain.

**Conclusions:** In high-volume academic centers, RALP and ORP patients may expect similar long-term HRQOL outcomes. Overall, RALP patients have less pain, shorter hospital stays, and fewer post-surgical complications such as blood transfusions, infections, deep venous thromboses, and bladder neck contractures.

**Key Words:** prostatectomy, quality of life

WHILE radical prostatectomy has remained a treatment mainstay for localized prostate cancer since the turn of the century, there has been a seismic shift from open radical prostatectomy (ORP) to robot-assisted laparoscopic prostatectomy (RALP). Driven largely by market forces and patient preference, RALP utilization in the United States has increased from less than 5% in 2003 to 85% in 2013,<sup>1</sup> outpacing evidence supporting its comparative effectiveness.<sup>2</sup>

Most studies have suggested comparable cancer control and survival outcomes between surgical approaches, and an advantage for RALP regarding perioperative outcomes such as blood loss and hospital stay.<sup>3</sup> Given generally favorable oncologic outcomes after radical prostatectomy, increasing emphasis has been placed on longer-term changes in urinary and sexual health-related quality of life (HRQOL). However, definitive conclusions regarding comparison of HRQOL between surgical approaches have been elusive. While longitudinal patient-reported outcome assessment has become the gold standard for evaluating HRQOL in prostate cancer,<sup>4</sup> most reports comparing ORP and RALP have depended primarily on physician-reported outcomes or claims based data<sup>5</sup> or have been single-center studies.<sup>6,7</sup>

We previously described a multicenter, longitudinal, prospective study evaluating HRQOL outcomes after localized prostate cancer treatment.<sup>8</sup> Accrued from 2003–2006, the PROST-QA (PQA) cohort defined the burden of prostate cancer treatment on HRQOL but was less well-equipped to evaluate comparative effectiveness between ORP and RALP given that adoption of robot-assisted surgery for radical prostatectomy was in its earlier stages. Building on our prior experience and research infrastructure, we accrued a second multicenter cohort—the PROSTQA-RP2 cohort (RP2)—between 2010–2013, after widespread dissemination of RALP. This study was specifically powered to evaluate whether surgical approach is a significant predictor of longitudinal differences in patient-reported HRQOL. Secondly, we assessed for differences in perioperative outcomes, including surgery-associated complications.

## METHODS

### Study Design

Study design and analytical plan were approved through a peer-reviewed funding process. Study subjects were participants in 2 prospective, longitudinal, multi-center cohorts, PQA and RP2 (supplementary table 1, <https://www.jurology.com>). The PQA consortium has been previously described,<sup>8</sup> made up of 9 university-affiliated hospitals, from which subjects were accrued between 2003–2006. From the 1,201 subjects who underwent prostate cancer treatment in PQA, 493 men fit the inclusion criteria in this study of having undergone open or robotic radical prostatectomy, with complete surgical data collected. Of these, 382 underwent ORP and 111 underwent RALP. The RP2 cohort, accrued between 2010–2013, and also made up of 9 university-affiliated hospitals (supplementary table 1, <https://www.jurology.com>), consisted of 601 men with localized prostate cancer, of whom 163 underwent ORP and 438 underwent RALP. The final analytical cohort consisted of 545 ORP subjects and 549 RALP subjects (fig. 1).

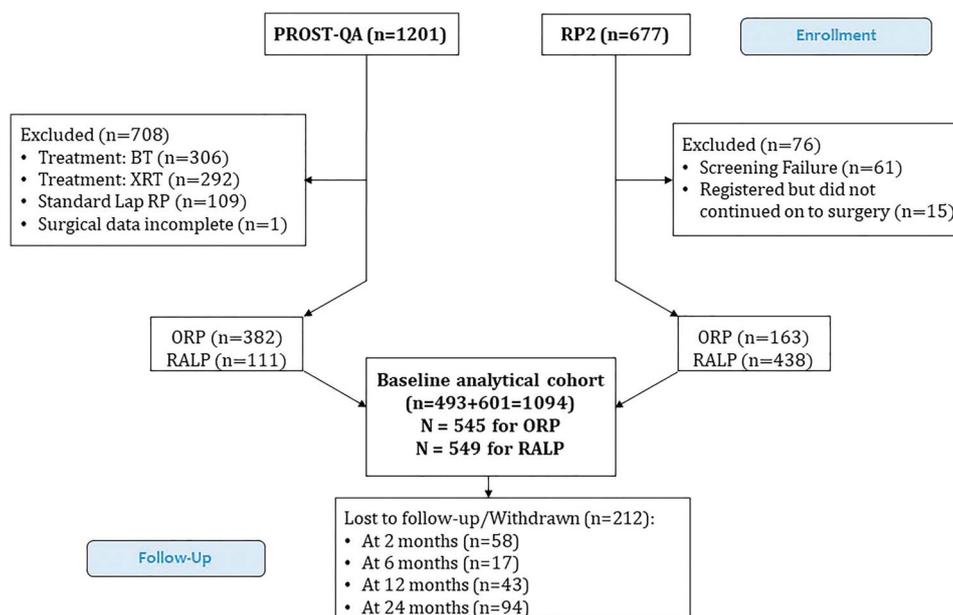
### Study Subjects and Outcome Assessment

Subjects were men with previously untreated clinical stage T1 or T2 prostate cancer who elected to undergo either open or robot-assisted radical prostatectomy at a university-affiliated hospital and provided informed consent to enroll in an IRB-approved prospective, longitudinal study (IRB No. 05-178). The participating surgeon determined surgical approach and extent of nerve-sparing/lymphadenectomy.

HRQOL outcome measures were collected using the Expanded Prostate Cancer Index Composite (EPIC-26)<sup>9</sup> and the Service Satisfaction for Cancer Care<sup>10</sup> by a third-party phone survey facility at pre-treatment baseline and at 2, 6, 12, and 24 months post-treatment for all analyzed subjects. Incisional and pain outcomes were collected 2 months post-treatment, while the postoperative complications encompassed the first 6 months following prostatectomy.

### Statistical Considerations

To assess the effect of surgical approach (ORP or RALP) on HRQOL over time, we used generalized estimating equations to model time profiles of each HRQOL domain. An all-inclusive base model was used that included, in addition to surgical approach, baseline HRQOL domain score, age, race, education, cohabitation, prostate size, Gleason score, tumor stage, baseline prostate specific



**Figure 1** CONSORT diagram. *BT*, brachytherapy. *Lap RP*, laparoscopic radical prostatectomy. *XRT*, radiation therapy.

antigen, comorbidities, body mass index, and nerve sparing. Lastly, the models also accounted for cohort (PQA or RP2) as a clustering factor for which the institutions and time periods of enrollment differed. Differences between ORP and RALP in distributions of categorical and continuous surgical outcomes and complications were compared using the Fisher's exact test and the Wilcoxon sum-rank test, respectively, with the Cochrane-Mantel-Haenszel test used to control for cohort. All statistical analyses were performed using SAS® version 9.4 (SAS, Cary, North Carolina).

## RESULTS

Our analytical cohort consisted of 545 subjects who underwent ORP and 549 subjects who underwent RALP. At 2, 6, 12, and 24 months, 1,036 (95%), 1,019 (93%), 976 (89%), and 882 (81%) remained in both clinical and HRQOL followup, respectively (fig. 1). Mean age at treatment surgery was 60 for ORP and 61 for RALP. Subjects from the PQA cohort were more likely to have lower disease severity than those in the RP2 cohort (supplementary table 2, <https://www.jurology.com>). Still, observed significant differences in subjects between surgical approaches in categories such as clinical T-stage, Gleason score, and D'Amico risk group<sup>11</sup> (table 1) were not statistically significant after controlling for cohort (supplementary table 2, <https://www.jurology.com>).

We assessed HRQOL outcomes using EPIC-26 at baseline, and at 2, 6, 12, and 24 months. As expected, significant HRQOL changes after both ORP and RALP, stratified by whether nerve-sparing was performed, were observed in the urinary incontinence and sexual domains, similarly to previously

described (fig. 2).<sup>8</sup> All statistically or clinically significant HRQOL changes from baseline observed in ORP subjects were also observed in RALP subjects. Satisfaction with cancer outcome did not vary significantly by surgical approach. On multivariable longitudinal analysis, age, baseline HRQOL domain score, and having more than 2 comorbid conditions were factors most frequently associated with a significant change in HRQOL (supplementary table 3, <https://www.jurology.com>). Nerve-sparing and larger prostate size predicted improved post-surgical HRQOL in the urinary irritation-obstruction domain. Surgical approach (ORP vs RALP) was not found to be a significant predictor of longitudinal patient-reported HRQOL change in any domain.

Pathological outcomes were similar between groups (table 2). The rate of positive margins trended towards being higher in RALP subjects ( $p=0.080$ ), although a higher proportion of RALP subjects had extraprostatic disease than ORP subjects (23% vs 19%, respectively;  $p=0.05$ ). Subjects who underwent RALP were far less likely to undergo lymphadenectomy (47% vs 89% in ORP;  $p<0.001$ ). RALP subjects were also more likely to undergo bilateral nonnerve sparing surgery (11% vs 6%;  $p=0.008$ ). Mean length of stay and estimated blood loss were lower in RALP subjects (1.6 days, 192 cc) than in ORP subjects (2.1 days, 805 cc, respectively). Two months postoperatively, subjects who underwent RALP reported lower pain scores (56% of RALP subjects with no pain vs 45% of ORP subjects;  $p=0.009$ ), were less likely to have pain-related moderate to extreme interference with activity (7% for RALP vs 12% for ORP;  $p=0.004$ ), and

**Table 1.** Pre-treatment subject characteristics by surgical approach

	ORP	RALP	Total	p Value
No. pts	545	549	1,094	
No. yrs age (%):				0.08
<60	276 (51)	242 (44)	518 (47)	
60–69	229 (42)	256 (47)	485 (44)	
70+	40 (7)	51 (9)	91 (8)	
No. race (%):				0.97
Caucasian	475 (91)	496 (91)	971 (91)	
African American	35 (7)	36 (7)	71 (7)	
Other	10 (2)	9 (2)	19 (2)	
No. college or post-graduate education (%)	365 (67)	351 (64)	716 (65)	0.31
No. married/cohabiting (%)	478 (88)	481 (88)	959 (88)	0.93
Median kg/m <sup>2</sup> body mass index (IQR):				0.79
<35	515 (95)	515 (94)	1,030 (94)	
35+	30 (5)	33 (6)	63 (6)	
No. comorbidities (%):				0.47
0–2	511 (94)	508 (93)	1,019 (93)	
3+	34 (6)	41 (7)	75 (7)	
No. mL prostate vol (%):				<b>0.005</b>
<30 cc	123 (27)	143 (31)	266 (29)	
30–53 cc	226 (50)	248 (55)	474 (52)	
>53 cc	100 (22)	64 (14)	164 (18)	
No. ng/mL prostate specific antigen (%):				0.14
<4	126 (23)	107 (20)	233 (21)	
4–10	341 (63)	375 (68)	716 (65)	
>10	78 (14)	67 (12)	145 (13)	
No. clinical T-stage (%):				<b>0.006</b>
cT1	405 (74)	445 (81)	850 (78)	
cT2	140 (26)	102 (19)	242 (22)	
No. Gleason score on init biopsy (%):				<b>&lt; 0.001</b>
6 or less (grade group 1)	299 (55)	234 (43)	533 (49)	
7 (grade group 2–3)	214 (39)	272 (50)	486 (44)	
8–10 (grade group 4–5)	32 (6)	43 (8)	75 (7)	
No. D'Amico risk group (%):				<b>0.007</b>
Low	255 (47)	211 (39)	466 (43)	
Intermediate–high	290 (53)	336 (61)	626 (57)	

p Value is calculated by the Fisher's exact test.

were more likely to be mostly to completely satisfied with the appearance of their surgical incisions (95% for RALP vs 89% for ORP;  $p < 0.001$ ).

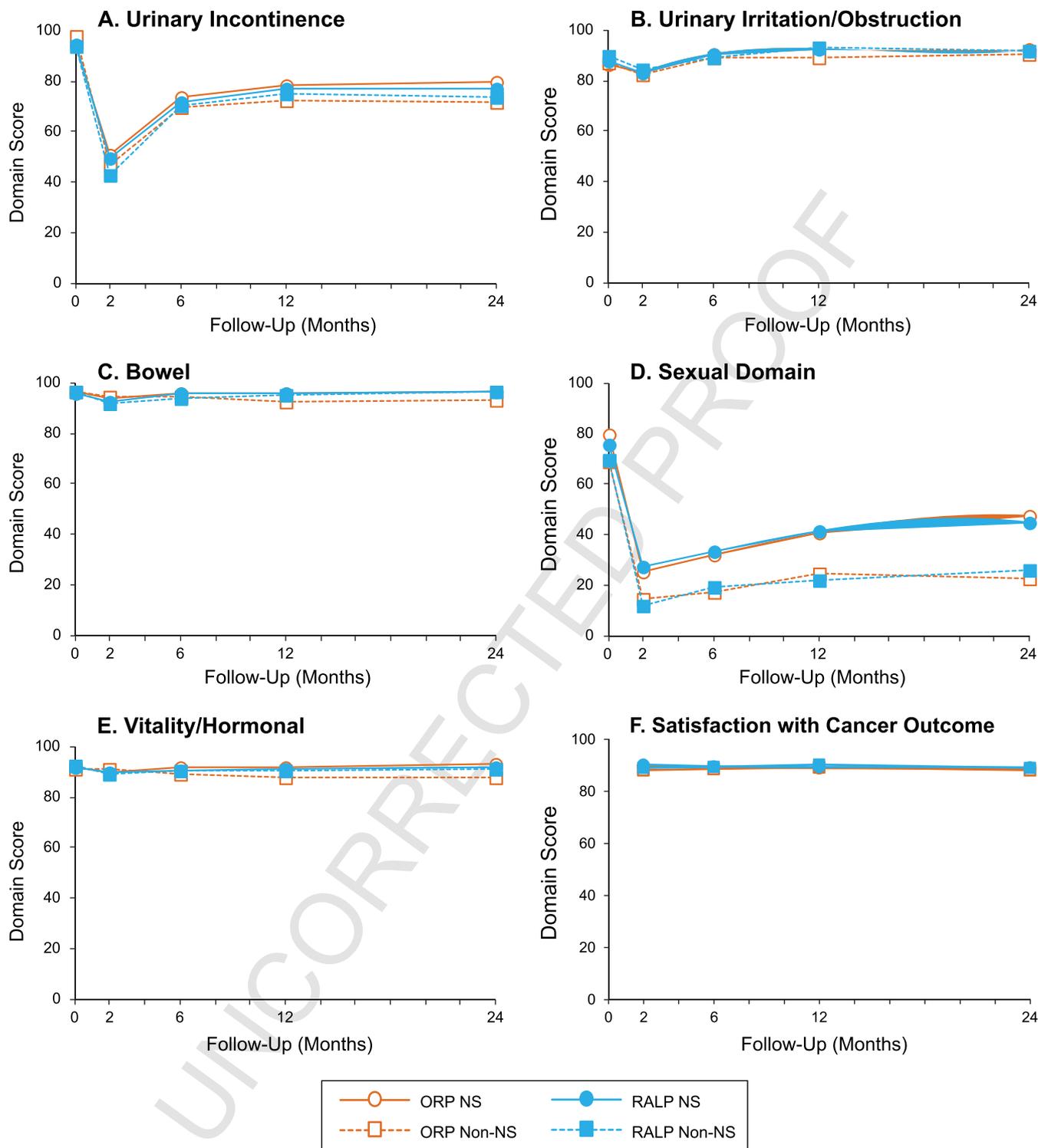
Post-surgical complications were uncommon across both surgical approaches (table 3). Blood transfusions were more common in subjects who underwent ORP (6.2% vs 1.3% in RALP;  $p = 0.006$ ), as were postoperative infections. The rate of bladder neck contracture requiring dilation/treatment was significantly higher in men undergoing ORP (8.3% vs 1.6% in RALP;  $p < 0.001$ ). Thromboembolic events were rare in both approaches, but the incidence of deep venous thrombosis (DVT) was higher in men undergoing ORP (1.9% vs 0.5% in RALP;  $p = 0.04$ ). Cohort factors (other than type of surgical approach) may have contributed to some of the observed differences (although bladder neck contracture remained significantly higher after ORP regardless of cohort), though such post-hoc analysis was further limited by reduction in sample power (supplementary table 4, <https://www.jurology.com>).

## DISCUSSION

The rapid adoption and eventual predominance of robot-assisted radical prostatectomy in the last

decade has presented unique challenges to researchers seeking to supplement the dearth of high-quality evidence evaluating the comparative effectiveness of ORP and RALP. Most early reports were single-surgeon series from high-volume centers that either lacked or featured a retrospective ORP comparator group<sup>6,7</sup> and often featured surgeons at various stages of the substantial RALP learning curve.<sup>12</sup>

Since the first reported robotic prostatectomy in 2001,<sup>13</sup> only 1 trial has successfully randomized subjects to ORP and RALP. This single-center Australian study randomized 326 patients by surgical approach and found no significant differences between ORP and RALP in patient-reported EPIC urinary or sexual function domain scores at 6 and 12 weeks as well as 24 months postoperatively.<sup>14,15</sup> However, RALP subjects had superior physical function scores 6 weeks postoperatively, corroborating our findings in which RALP subjects had less pain-induced interference with physical activity. Despite the rigor of its randomized approach, its generalizability is limited by it being a single-center comparison of 1 open surgeon to 1 robotic surgeon with a significant surgeon experience differential.



**Figure 2** Longitudinal patient-reported HRQOL and satisfaction with cancer outcome after radical prostatectomy, stratified by surgical approach and nerve-sparing (NS) status. A–E, health domains of EPIC-26 HRQOL instrument.<sup>9</sup> F, satisfaction with cancer outcome, domain of Service Satisfaction Scale for Cancer Care instrument.<sup>10</sup> Surgical approach (ORP vs RALP) was not found to be significant predictor of longitudinal patient-reported HRQOL change in any domain.

Attempts at a multi-center randomized controlled trial have been unsuccessful.<sup>16</sup>

Efforts at comparing RALP and ORP have used different methods to tackle the analytical moving

target in which the proportion of radical prostatectomies performed robotically in the United States changed from 15% to 85% within 10 years.<sup>1</sup> A population-based analysis compared RALP subjects

**Table 2.** Perioperative and incisional outcomes

	ORP	RALP	Total	p Value
No. pts	545	549	1,094	
No. pathological stage (%):				0.05
pT2 (gland-confined disease)	436 (81)	419 (77)	855 (79)	
pT3+ (locally advanced disease)	99 (19)	128 (23)	227 (21)	
No. pos margins (%):				0.08
pT2 (gland-confined disease)	83 (16)	109 (20)	192 (18)	
pT3+ (locally advanced disease)	47 (11)	53 (13)	100 (12)	0.46
No. lymphadenectomy performed (%)	36 (36)	56 (43)	92 (40)	0.28
No. nonnerve-sparing (%)	478 (89)	260 (47)	738 (68)	< 0.001
Mean days length of stay (SD)	35 (6)	60 (11)	95 (9)	<b>0.008</b>
Mean estimated blood loss (SD)	2.1 (7.7)	1.6 (7.8)	1.9 (7.7)	< 0.001
No. pain at surgical site (%):*	805 (525)	192 (142)	498 (491)	< 0.001
0				<b>0.009</b>
1–3	232 (45)	287 (56)	519 (50)	
4–6	233 (45)	189 (37)	422 (41)	
7–10	37 (7)	30 (6)	67 (7)	
No. pain interfered with activity (%):*	12 (2)	9 (2)	21 (2)	
None/slightly				<b>0.004</b>
Moderately–extremely	449 (88)	478 (93)	927 (90)	
No. appearance of surgical incision (%):*	64 (12)	37 (7)	101 (10)	
Completely satisfied—mostly satisfied				< 0.001
Mixed—completely unsatisfied	455 (89)	485 (95)	940 (92)	
	55 (11)	26 (5)	81 (8)	

\* Assessed 2 months postoperatively.

from the Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study group (2011–2012) to ORP subjects primarily from the historical Prostate Cancer Outcomes Study (PCOS) (1994–1995) and found RALP subjects to have a small but statistically significant advantage in patient-reported sexual function at 6 and 12 months postoperatively.<sup>17</sup> While this analysis did control for baseline HRQOL, it could not control for the almost 20 year between-group time period differences in surgical technique and the availability of sexual function recovery aids including phosphodiesterase-5 inhibitors. A multi-center prospective Swedish trial (2008–2011), the Laparoscopic Prostatectomy Robot Open (LAPPRO) study, compared 778 subjects from 7 centers that exclusively performed ORP to 1,847 subjects from a second group of 7 centers performing RALP and found no significant difference in urinary outcomes between surgical approaches, but a modest advantage in erectile

dysfunction rates in favor of RALP over ORP; however, this analysis did not control for baseline sexual HRQOL, a strong predictor of postoperative outcome.<sup>18</sup>

Our study used the existing rigorous PQA core infrastructure—prospective third-party administration of patient-report HRQOL surveys, centralized data coordinating center, and high-volume university-affiliated member institutions—to accrue the RP2 cohort and form the only American multi-center prospective trial designed and powered to detect a longitudinal difference in patient-reported HRQOL outcomes between RALP and ORP. In contrast to the PCOS/CEASAR and LAPPRO studies, we found no significant effect of surgical approach on longitudinal HRQOL change (in all domains) from pre-treatment baseline to 2 years post-treatment after adjusting for other factors, including baseline HRQOL. The most likely explanation for our difference in results from the above 2

**Table 3.** Post-surgical complications

	No. ORP (%)	No. RALP (%)	No. Total (%)	p Value
Pts	545	549	1,094	
Blood transfusion	21 (4.0)	7 (1.3)	28 (2.6)	<b>0.006</b>
Urinary tract infection requiring treatment	33 (6.2)	23 (4.2)	56 (5.2)	0.14
Unplanned urinary catheterization	35 (6.6)	17 (3.1)	52 (4.8)	<b>0.007</b>
Bladder neck contracture requiring dilation	45 (8.3)	9 (1.6)	54 (4.9)	< 0.001
Wound infection	23 (4.3)	10 (1.8)	33 (3.1)	<b>0.02</b>
Other infection	23 (4.3)	6 (1.1)	29 (2.7)	<b>0.001</b>
DVT*	10 (1.9)	3 (0.5)	13 (1.2)	<b>0.04</b>
Pulmonary embolism	3 (0.6)	4 (0.7)	7 (0.7)	0.74
Rectal bleeding requiring treatment	3 (0.6)	2 (0.4)	5 (0.5)	0.63
Hematuria requiring treatment	13 (2.5)	12 (2.2)	25 (2.3)	0.78
Unplanned hospital admission	27 (5.1)	24 (4.4)	51 (4.8)	0.59

\* Routine imaging assessment for deep vein thrombosis was not protocol-mandated in the absence of symptoms.

studies, in addition to the already mentioned differences in confounding adjustment, is that PCOS/CEASAR and LAPPRO were population-based cohorts while PQA/RP2 subjects received their care at high-volume academic institutions.<sup>19</sup>

The rate of positive surgical margins varies widely both within series and between series,<sup>20,21</sup> and is influenced by many factors, especially cancer severity, which is readily subject to selection bias between groups. Similar to the Australian randomized controlled trial<sup>14</sup> and the LAPPRO study,<sup>18</sup> we did not find a significant difference in positive surgical margin rates between ORP and RALP for organ-confined disease, a metric considered to be an oncologic care quality measure in radical prostatectomy. In our study, the rate of lymphadenectomy in ORP subjects was disproportionately high (89%) considering the number of subjects with low-risk disease, while lymphadenectomy utilization in RALP subjects (47%) was more appropriately matched with disease severity, a commonly observed finding in other registry-based series.<sup>22</sup> This overutilization of lymphadenectomy in our ORP subjects, especially considering the proportion of subjects with low-risk disease, may be related to the tradition of considering routine lymphadenectomy as a pedagogical opportunity during ORP in our participating academic medical centers.

While prior single-center reports have suggested a lower incidence of bladder neck contracture in RALP compared to ORP,<sup>23</sup> to our knowledge this is the first multicenter prospective study that has shown this finding, which was demonstrated independent of cohort (PQA vs RP2) despite RALP being performed relatively early in its evolution compared to ORP in the PQA cohort. While this finding did not translate into a significant overall difference in longitudinal urinary HRQOL between surgical approaches, it did represent an additional burden of post-surgical intervention in men undergoing ORP.

We found that ORP subjects had a higher incidence of post-surgical DVT than RALP subjects. While the magnitude of this finding was more pronounced in PQA than RP2 subjects, suggesting cohort effects, the trend was maintained across cohorts. Possible explanations include further evolution of DVT prophylaxis over time, a higher surgeon/institutional heterogeneity in the PQA cohort, or that this increased thrombotic risk is conferred by the disproportionately high incidence of lymphadenectomy in the ORP group. Indeed, 10/13 (77%) of men who experienced DVT underwent lymphadenectomy; however, the overall incidence of DVT was small enough in our study that we cannot rigorously test these hypotheses. A separate analysis of thromboembolic events in the LAPPRO study suggested that both open surgery (RR 12.67, 95% CI

5.05–31.77) and lymphadenectomy (7.80, 95% CI 3.51–17.32) were independent predictors of thromboembolic events.<sup>24</sup>

Perioperatively, RALP subjects had a shorter hospital stay, less blood loss, fewer blood transfusions, reported less pain, and were more satisfied with the appearance of their incisions than ORP subjects. These advantages, commonly associated with a minimally invasive surgical approach, were also observed by Yaxley et al.<sup>14</sup> While the differences in postoperative pain between groups are limited to the initial weeks after surgery, the nationwide opioid crisis has illustrated that the societal impact of post-surgical pain and its potential downstream effects should not be underestimated.<sup>25</sup>

Our study has several limitations. Subjects were accrued from academic, university-affiliated institutions, which may limit the generalizability of our results. However, with growing regionalization and centralization of cancer care,<sup>26</sup> and multiple studies suggesting that higher-volume radical prostatectomy centers provide superior outcomes independent of surgical approach,<sup>1,27,28</sup> our results gathered from 11 of the highest-volume academic centers in the United States represents an idealized comparison of ORP and RALP in settings of high care quality.

Our study is nonrandomized and accrued subjects from 2 cohorts—PQA and RP2—separated by time, institution composition, and surgical approach distribution, which introduces confounding that cannot be completely accounted for by statistical adjustment. The temporal difference may introduce between-cohort subject variability (overall cancer severity was higher in RP2, likely because active surveillance was not as prevalent in 2003–2006), surgeons' experiential learning curve, and technical<sup>29</sup> or perioperative advancements.<sup>30</sup> Institutional variability between cohorts was small (5/8 institutions in PQA and RP2 were in both cohorts) but also contributes to unadjusted confounding. While confounding cannot be fully eliminated, given how this is a highly controlled prospective study in which extensive pre-treatment baseline characteristics, including cohort, were known and controlled for, significant unadjusted confounding is less likely.

## CONCLUSIONS

In this multicenter, prospective, longitudinal study, we found that RALP subjects had superior incisional/pain outcomes, shorter hospital stays, and fewer post-surgical complications such as blood transfusions, infections, DVTs, and bladder neck contractures. Long-term postoperative patient-reported HRQOL outcomes were similar between open and robotic surgical approaches. These results

should help guide treatment counseling and be integrated into future cost analyses.

## THE PROSTQA AND PROSTQA-RP2 CONSORTIUM

The PROSTQA and PROSTQA-RP2 Consortium includes contributions in cohort design, patient accrual and followup from the following investigators: Meredith Regan (Dana Farber Cancer Institute, Boston, Massachusetts); Matthew Cooperberg, Peter Carroll, and Leslie Wilson (University of California San Francisco, San Francisco, California); Larry Hembroff and Douglas Roberts (Michigan State University, East Lansing, Michigan); John T. Wei, Dan Hamstra, Daniel Spratt, Rodney Dunn, Laurel Northouse and David Wood (University of Michigan, Ann Arbor, Michigan); Eric A Klein and Jay Ciezki (Cleveland Clinic, Cleveland, Ohio); Misop Han and Alan Partin (Johns Hopkins Medical Institutions, Baltimore, Maryland); Joseph Smith (Vanderbilt University Medical Center, Nashville, Tennessee); Jeff Michalski and Gerald Andriole (Washington University, St. Louis, Missouri); Mark Litwin and Chris Saigal (University of California, Los Angeles Medical Center, Los Angeles, California); Thomas Greenfield, PhD

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## REFERENCES

- Leow JJ, Chang SL, Meyer CP et al: Robot-assisted versus open radical prostatectomy: a contemporary analysis of an all-payer discharge database. *Eur Urol* 2016; **70**: 837.
- Makarov DV, Li H, Lepor H et al: Teaching hospitals and the disconnect between technology adoption and comparative effectiveness research: the case of the surgical robot. *Med Care Res Rev* 2017; **74**: 369.
- Hu JC, O'Malley P, Chughtai B et al: Comparative effectiveness of cancer control and survival after robot-assisted versus open radical prostatectomy. *J Urol* 2017; **197**: 115.
- Barry MJ, Fowler FJ Jr, O'Leary MP et al: The American Urological Association symptom index for benign prostatic hyperplasia. The measurement committee of the American Urological Association. *J Urol* 1992; **148**: 1549.
- Hu JC, Gu X, Lipsitz SR et al: Comparative effectiveness of minimally invasive vs open radical prostatectomy. *JAMA* 2009; **302**: 1557.
- Ahlering TE, Woo D, Eichel L et al: Robot-assisted versus open radical prostatectomy: a comparison of one surgeon's outcomes. *Urology* 2004; **63**: 819.
- Ficarra V, Novara G, Fracalanza S et al: A prospective, non-randomized trial comparing robot-assisted laparoscopic and retropubic radical prostatectomy in one European institution. *BJU Int* 2009; **104**: 534.
- Sanda MG, Dunn RL, Michalski J et al: Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med* 2008; **358**: 1250.
- Szymanski KM, Wei JT, Dunn RL et al: Development and validation of an abbreviated version of the expanded prostate cancer index composite instrument for measuring health-related quality of life among prostate cancer survivors. *Urology* 2010; **76**: 1245.
- Shah NL, Dunn RL, Greenfield TK et al: Development and validation of a novel instrument to measure patient satisfaction in multiple dimensions of urological cancer care quality (abstract 41). *J Urol, suppl.*, 2003; **169**: 11.
- D'Amico AV, Whittington R, Malcovic SB et al: Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998; **280**: 969.
- Thompson JE, Egger S, Böhm 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.
- Binder J and Kramer W: Robotically-assisted laparoscopic radical prostatectomy. *BJU Int* 2001; **87**: 408.
- Yaxley JW, Coughlin GD, Chambers SK et al: Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomized controlled phase 3 study. *Lancet* 2016; **388**: 1057.
- Coughlin GD, Yaxley JW, Chambers SK et al: Robot-assisted laparoscopic prostatectomy versus open retropubic prostatectomy: 24-month outcomes from a randomised controlled study. *Lancet Oncol* 2018; **19**: 1051.
- Prospective Randomized Trial Comparing Robotic versus Open Radical Prostatectomy (NCT01365143), [ClinicalTrials.gov](http://ClinicalTrials.gov) 2015.
- O'Neil B, Koyama T, Alvarez J et al: The comparative harms of open and robotic prostatectomy in population based samples. *J Urol* 2016; **195**: 321.
- Haglund E, Carlsson S, Stranne J et al: LAPPRO steering committee. Urinary incontinence and erectile dysfunction after robotic versus open radical prostatectomy: a prospective, controlled, nonrandomised trial. *Eur Urol* 2015; **68**: 216.
- Begg CB, Riedel ER, Bach PB et al: Variations in morbidity after radical prostatectomy. *N Engl J Med* 2002; **346**: 1138.

20. Yossepowitch O, Briganti A, Eastham JA et al: Positive surgical margins after radical prostatectomy: a systematic review and contemporary update. *Eur Urol* 2014; **65**: 303.
21. Suardi N, DellOglio P, Gallina A et al: Evaluation of positive surgical margins in patients undergoing robot-assisted and open radical prostatectomy according to preoperative risk groups. *Urol Oncol* 2016; **34**: 57.
22. Wang EH, Yu JB, Gross CP et al: Variation in pelvic lymph node dissection among patients undergoing radical prostatectomy by hospital characteristics and surgical approach: results from the National Cancer Database. *J Urol* 2015; **193**: 820.
23. Webb DR, Sethi K and Gee K: An analysis of the causes of bladder neck contracture after open and robot-assisted laparoscopic radical prostatectomy. *BJU Int* 2009; **103**: 957.
24. Tyrirtzis SI, Wallerstedt A, Steineck G et al: Thromboembolic complications in 3,544 patients undergoing radical prostatectomy with or without lymph node dissection. *J Urol* 2015; **193**: 117.
25. Dowell D, Noonan RK and Houry D: Underlying factors in drug overdose deaths. *JAMA* 2017; **318**: 2295.
26. Anderson CB, Penson DF, Ni S et al: Centralization of radical prostatectomy in the United States. *J Urol* 2013; **189**: 500.
27. Sammon JD, Karakiewicz PI, Sun M et al: Robot-assisted versus open radical prostatectomy: the differential effect of regionalization, procedure volume and operative approach. *J Urol* 2013; **189**: 1289.
28. Trinh QD, Bjartell A, Freedland SJ et al: A systematic review of the volume-outcome relationship for radical prostatectomy. *Eur Urol* 2013; **64**: 786.
29. Egan J, Marhamati S, Carvalho FLF et al: Retzius-sparing robot-assisted radical prostatectomy leads to durable improvement in urinary function and quality of life versus standard robot-assisted radical prostatectomy without compromise on oncologic efficacy: single-surgeon series and step-by-step guide. *Eur Urol* 2021; **79**: 839.
30. Abou-Haidar H, Abourbih S, Braganza D et al: Enhanced recovery pathway for radical prostatectomy: implementation and evaluation in a universal healthcare system. *Can Urol Assoc J* 2014; **8**: 418.