Quality of Life Following Prostatectomy as a Function of Surgery Type and Degree of Nerve Sparing

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Key Words

Prostate cancer • Quality of life • Sexual function •
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Abstract

Objectives: To compare robotic-assisted laparoscopic prostatectomy with conventional retropubic radical prostatectomy in maintaining pre-surgery levels of urinary and sexual functioning and to evaluate the efficacy of nerve sparing in prostatectomies in protecting urinary functioning. **Material and Methods:** Patients (n = 385) receiving both surgical procedures were surveyed prior to surgery. Multiple measures, including the Expanded Prostate Cancer Index Composite, the Sexual Health Inventory for Men, and the International Prostate Symptom Score, assessed sexual and urinary function at an average of 12 months post-surgery. **Results:** Across multiple measures, while controlling for pre-surgical sexual functioning, robotic-assisted surgery did not offer an advantage in maintaining sexual or urinary function an average of a year following the prostatectomy. Bilateral nerve sparing offered a strong and reliable advantage in the maintenance of sexual function, but not so regarding urinary function. **Conclusion:** While robotic-assisted prostatectomies may offer a number of medical advantages over open procedures, we found no significant effect on important quality of life outcomes associated with the technique.

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Introduction

While the incidence of prostate cancer in the U.S. has remained fairly constant (i.e., about 25% of all new cancers yearly) and continues to be the second leading cause of death among men [1], the last 2 decades have seen significant decreases both in mortality rates [2, 3] and age at detection [4]. With decreased mortality and earlier detection, men and their partners are increasingly interested not only in a cure for their cancer, but in the quality of life (QoL) implications of their treatment choice as well. The greatest QoL concerns usually involve sexual and urinary functioning [5]. The importance of these functions to many men is illustrated in a study [6] in which in a sample of men age 45–70, without prostate cancer, 68% expressed the willingness to give up 10% of their survival time if it meant they were more likely to maintain their pre-surgical erectile and urinary functioning. Further, urologists may tend to underestimate their patients' distress concerning the maintenance of sexual function following treatment for prostate cancer [7].

Currently, the most common forms of treatment for prostate cancer, prostatectomies, carry significant risk for erectile dysfunction (ED) and some risk for incontinence [8]. The multiple surgical approaches to treating prostate cancer differ primarily in whether or not robotics are used and degree of nerve sparing achieved.

While many studies have demonstrated that nerve sparing is strongly and positively associated with maintenance of erectile function [9], the empirical evidence is less clear on its impact on urinary function. Currently, while less true world-wide, the vast majority of prostatectomies in the U.S. are performed robotically [10]. There is evidence that, compared to other types of prostate surgery, robotic-assisted laparoscopic prostatectomy (RALP) can shorten hospital stays, reduce intraoperative blood loss, require shorter catheterizations, and produce fewer perioperative complications [11–16]. However, the empirical evidence for the post-operative superiority of RALP over laparoscopic approaches regarding QoL variables, i.e., eventual sexual and urinary functioning, is less clear [16–22].

The present study compared the QoL (urinary and sexual functioning) outcomes in radical prostatectomies as a function of surgery type [robotic-assisted laparoscopic prostatectomy (RALP) vs. retropubic radical prostatectomy (RRP)] and degree of nerve sparing achieved.

The aims of this study were (1) to compare RALP with conventional RRP in the maintaining of pre-surgery levels urinary and sexual functioning and (2) to evaluate the efficacy of nerve sparing in prostatectomies in protecting urinary functioning.

Materials and Methods

Patients

In this retrospective study, participants were up to 385 men (numbers varied as not all patients completed all measures), ages 47–79 years ($M = 61.0$, $SD = 6.46$, median = 61) having undergone a radical prostatectomy, performed by either of 2 urological oncologists, at a major university cancer hospital.

Measures

Several self-report measures of urinary and sexual functioning were utilized, each of which consisted of multiple items. In order to more meaningfully capture the multiple elements of some of our measures (as opposed to their total scores), they were first subjected to factor analysis, with subsequent analyses utilizing the resulting factor scores as the dependent measures.

Sexual Function

Sexual Health Inventory for Men (SHIM) SHIM, an abbreviated version of the International Index of Erectile Function 5 [23], is commonly used in both research and clinical settings [24]. It consists of 5 items, each rated on a 5-point scale, covering the last 6 months of the participant's life. Items include: (1) confidence in getting and keeping an erection, (2) how often erections were hard enough for penetration, (3) how often an erection could be maintained after penetration, (4) how difficult it was to maintain an erection after penetration, and (5) how often intercourse was "satisfactory". At each time period of this study (see Procedures), par-

ticipants completed the SHIM twice, once describing their erectile functioning without the use of erectile dysfunction medications (e.g. sildenafil) and once describing their functioning when using such a drug (for those having done so). When used as a dependent measure, a total SHIM score was computed based on the sum of all 5 questionnaire items.

Expanded Prostate Cancer Index Composite (EPIC) The EPIC-Sex questionnaire consisted of 13 items taken from EPIC [25], each item inquiring about a commonly assessed element of sexual functioning (in the "last 4 weeks") on a 4- or 5-point scale. A principal components (varimax rotation) factor analysis of the 13 EPIC-Sex items yielded 3 factors which we termed: (1) erection/sexual function (items included ability to have an erection, ability to reach an orgasm, quality of erections, frequency of erections, morning erections, frequency of sexual activity, frequency of intercourse, ability to function sexually), (2) how big a problem (i.e., "How big a problems was...": getting an erection, reaching orgasm, overall sexual functioning), and (3) sexual desire (level of desire, how big a problem was your level of sexual desire).

QoL-Erection Another measure of erectile capacity included 4 items assessing current functioning taken from a broader QoL questionnaire, including firmness of erection, ability to maintain erection, achieving an erection when wanted, and confidence in ability to achieve an erection. A principal components (varimax rotation) factor analysis of these 4 items yielded a single factor. As with the SHIM, participants completed the QoL-Erection twice, describing their erectile functioning both with and without the use of erectile dysfunction medications. When used as a dependent measure, a total QoL-Erection score was computed based on the sum of all 4 items.

Urinary Function

International Prostate Symptom Score (IPSS) IPSS is a brief self-report measure of urinary function created by the American Urological Association [26]. It consists of 8 items, each scored on a 5-point scale, including incomplete bladder emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia, as well as one urinary quality of life item. Each item refers to functioning in the previous month. A principal components factor analysis (varimax rotation) of the 8 items yielded 2 factors as follows: factor 1 (incomplete emptying, difficulty stopping/starting, weak stream, push/strain) and factor 2 (frequency of urination, difficulty postponing, nighttime urination, and feeling about urinary functioning).

EPIC-Urine The EPIC-Urine questionnaire consisted of 12 items taken from the EPIC [25], each item inquiring about a commonly assessed element of urinary functioning, in the last 4 weeks. A principal components factor analysis (varimax rotation) of these items yielded 4 factors as follows: (1) control (leaking/dripping urine, urinary control, pads/diapers, frequent urination, overall urinary functioning), (2) frequency (frequent urination, nocturia, weak/incomplete urine stream), (3) bleeding (urinating blood), and (4) pain (pain or burning with urination).

Procedure

In 2009, as part of ongoing research and clinical programs, prostate surgery patients of 2 urological oncologists at a major cancer center began completing a battery of QoL questionnaires (focusing on urinary and sexual functioning) starting just prior to surgery and again at, what was intended to be, regular intervals

(i.e., 3 months, 6 months, 1 year, then yearly). As is often the case with such research, there were differences (sometimes considerably so) among participants in how routinely this schedule was followed. To be included in this study, participants would have had to complete questionnaires on at least 4 occasions, with the fourth assessment occurring at least 9 months after surgery. This time frame was chosen so as to allow for at least minimally sufficient time for sexual and urinary function to have returned post-surgery while maintaining sufficient numbers of participants for statistical analysis. The time to this fourth set of ratings ranged from 9 to 61 months (mean = 15.0 months, median = 11.5 months).

Following each prostatectomy, surgeons completed a questionnaire describing various elements of the surgery, including an estimate of the degree of nerve sparing that was achieved as falling into 1 of 4 groups: (1) complete bilateral nerve sparing, (2) unilateral nerve sparing, (3) modified nerve sparing (i.e., a degree of nerve sparing measurably less than complete), and (4) non-nerve-sparing. Because of the small number of participants in Group 4 and the difficulty in establishing the nature and reliability of Group 2 ratings, it was decided to combine participants in Groups 2 through 4, resulting in 2 groups, Bilateral Nerve Sparing (BNS) and Other.

Results

Sexual Function

SHIM total score without medication was treated as a dependent measure in a 2 (surgery type: RALP vs. RRP) by 2 (nerve sparing: BNS vs. Other) ($n = 276$) analysis of covariance (ANCOVA). Given that pre-surgery sexual functioning has routinely been demonstrated to predict post-surgery functioning [27], this analysis included the pre-surgery score on the first item on the SHIM (SHIM 1, confidence you can get and keep an erection) as a covariate. The analysis revealed a significant effect for nerve sparing (BNS scoring higher than Other), $F(1,271) = 14.26$, $p < 0.001$, and non-significant effects for surgery type, $F(1,271) = 1.05$, $p = 0.31$ and the nerve-sparing by surgery type interaction, $F(1,271) = 0.18$, $p = 0.68$. The same ANCOVA was conducted with SHIM total score with medication as the dependent measure ($n = 200$). The analysis again revealed a significant effect favoring nerve sparing, $F(1,196) = 9.34$, $p < 0.005$, and non-significant effects for surgery type, $F(1,196) = 0.32$, $p = 0.57$ and the nerve sparing by surgery type interaction, $F(1,196) = 0.64$, $p = 0.42$.

A 2 (surgery type: RALP vs. RRP) by 2 (nerve sparing: BNS vs. Other) ($n = 264$) multivariate analysis of covariance was also conducted with the 3 EPIC-Sex factor scores as the dependent measures and pre-surgery SHIM 1 score (confidence you can get and keep an erection) as the covariate. The analysis revealed significant multivariate effects for nerve sparing, $F(3,257) = 8.12$, $p < 0.001$

and non-significant effects for surgery type, $F(3,257) = 0.09$, $p = 0.96$ and the nerve sparing by surgery type interaction ($F(3,257) = 1.91$, $p = 0.13$). Three follow-up univariate analyses of covariance were then conducted comparing the BNS and Other group on each of the 3 EPIC-Sex factors, again with the pre-surgery SHIM 1 score as a covariate. The BNS group scored significantly higher (i.e., better sexual functioning), $F(1,259) = 21.77$, $p < 0.001$, on Factor 1 (erection/sexual function), and marginally higher, $F(1,259) = 3.69$, $p < 0.056$ on Factor 2 (how big a problem). The effect of nerve sparing was non-significant, $F(1,259) = 1.63$, $p = 0.20$, on Factor 3 (sexual desire).

A 2 (surgery type: RARP vs. RRP) by 2 (nerve sparing: BNS vs. Other) ($n = 385$) ANOVA was conducted with the QoL-Erection, without medication, factor score as the dependent measure. The analysis revealed a significant effect for nerve sparing (BNS group scoring higher than Other), $F(1,381) = 30.43$, $p < 0.001$, and non-significant effects for surgery type, $F(1,381) = 0.045$, $p = 0.83$ and the nerve sparing by surgery type interaction, $F(1,381) = 1.91$, $p = 0.17$. The same analysis conducted using QoL-Erection, with medication ($n = 177$), as the dependent measure again yielded a significant effect for nerve sparing, $F(1,173) = 4.66$, $p < 0.05$ (better erections for the BNS group). Again, the effect for surgery type was non-significant, $F(1,173) = 2.91$, $p = 0.09$ (the difference favoring the RRP group), as was the nerve sparing by surgery type interaction, $F(1,173) = 0.33$, $p = 0.57$.

Taken as a whole, these findings, consistent with a large body of literature, indicate that across multiple measures, even when controlling for pre-surgery sexual function, bilateral nerve sparing offers a strong and reliable advantage in the maintenance of sexual functioning (particularly erectile capacity), with or without the use of erection enhancing medication. The evidence here is equally clear that robotic-assisted surgery did not offer an advantage in maintaining sexual function.

Urinary Function

Urinary function was first assessed with IPSS. Two 2 (surgery type: RALP vs. RRP) by 2 (nerve sparing: BNS vs. Other) ($n = 250$) ANOVAs were conducted with IPSS Factor 1 and Factor 2 scores as the dependent measures. The analysis on Factor 1 revealed non-significant effects for surgery type, $F(1,246) = 0.02$, $p = 0.9$, nerve sparing, $F(1,246) = 0.46$, $p = 0.5$, and the nerve sparing by surgery type interaction, $F(1,246) = 0.77$, $p = 0.38$. While the analysis on Factor 2 also revealed non-significant ef-

fects for surgery type, $F(1,246) = 1.13$, $p = 0.29$, and the nerve sparing by surgery type interaction, $F(1,246) = 0.98$, $p = 0.32$, there was a modest but statistically significant effect for nerve sparing, $F(1,246) = 3.93$, $p < 0.05$, favoring the BNS group.

A 2 (surgery type: RALP vs. RRP) by 2 (nerve sparing: BNS vs. Other) ($n = 374$) multivariate analysis of variance was conducted with the 4 EPIC-Urine factors as the dependent variables. This yielded non-significant multivariate effects for nerve sparing, $F(4,371) = 0.38$, $p = 0.82$, surgery type, $F(4,371) = 1.32$, $p = 0.82$, and their interaction, $F(4,371) = 0.87$, $p = 0.48$. None of the follow-up univariate effects even approached reaching statistical significance.

Overall, neither degree of nerve sparing nor surgery type proved to be reliably related to urinary functioning.

Discussion

Men diagnosed with prostate cancer today have many treatment options. Even when choosing only among surgical alternatives, there are several options, primarily involving the degree of nerve sparing to be attempted and whether or not to utilize a robotic approach. As more men are being diagnosed with prostate cancer earlier than ever, the issue of QoL, particularly regarding sexual and urinary functioning, associated with these treatment alternatives becomes increasingly important.

While there are undoubtedly medical advantages to robotic surgery (e.g., less blood loss), the research evidence regarding QoL implications of choosing this approach is less clear. In our sample, across multiple measures and when controlling for pre-surgery sexual functioning, robotic-assisted surgery did not offer an advantage in maintaining sexual function an average of a year following the prostatectomy. In contrast, and consistent with much previous research, bilateral nerve sparing offered a strong and reliable advantage over lower degrees of nerve sparing in the maintenance of sexual functioning, with or without the use of erection enhancing medication.

The existing empirical evidence regarding the impact of robotics and nerve sparing on post-prostatectomy urinary and sexual functioning is also mixed. Taken as a whole, our findings indicated that neither the type of surgery (RRP vs. RALP) nor the degree of nerve sparing reliably impacted the urinary functioning of our participants.

There are several features of this study that may limit the generalizability of our findings and conclusions. First, our outcomes were limited to surgeries conducted

by only 2 surgeons, and some of the robotic procedures were conducted while the surgeons were still early in the learning curve for the technique. In addition, patients were not randomly assigned to surgery condition. It is also the case that the non-nerve sparing condition was a somewhat heterogeneous group, including a variety of degrees of nerve sparing, ranging from unilateral-nerve-sparing to no nerve sparing. A more detailed division of degrees of nerve sparing might have revealed additional effects for this variable. Finally, there were other pre-surgery variables (e.g., urinary function, tumor features) which we were unable to control.

Conclusion

As clinicians and patients consider and weigh the likely advantages and disadvantages of the various options currently available for treating prostate cancer, QoL outcomes, particularly those involving sexual and urinary functioning, continue to be important elements of this decision-making process. This is especially true as the diagnosis of prostate cancer is made increasingly earlier in men's lives. Findings of studies like this, especially as the findings become replicated, can and should play an important role in this decision-making process.

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References

- 1 Baade PD, Youlten DR, Krnjacki LJ: International epidemiology of prostate cancer: geographical distribution and secular trends. *Mol Nutr Food Res* 2009;53:171–184.
- 2 Byers T, Wender RC, Jemal A, Baskies AM, Ward EE, Brawley OW: The American Cancer Society challenge goal to reduce US cancer mortality by 50% between 1990 and 2015: results and reflections. *CA Cancer J Clin* 2016;66:359–369.
- 3 Wong MC, Goggins WB, Wang HH, Fung FD, Leung C, Wong SY, Ng CF, Sung JJ: Global incidence and mortality for prostate cancer: analysis of temporal patterns and trends in 36 countries. *Eur Urol* 2016;70:862–874.
- 4 Zhou CK, Check DP, Lortet-Tieulent J, Laversanne M, Jemal A, Ferlay J, Bray F, Cook MB, Devesa SS: Prostate cancer incidence in 43 populations worldwide: an analysis of time trends overall and by age group. *Int J Cancer* 2016;138:1388–1400.
- 5 Wittmann D, Northouse L, Foley S, Gilbert S, Wood DP Jr, Balon R, Montie JE: The psychosocial aspects of sexual recovery after prostate cancer treatment. *Int J Impot Res* 2009;21:99–106.
- 6 Singer P, Tasch E, Stocking C, Rubin S, Siegler M, Weichselbaum R: Sex or survival: trade-offs between quality and quantity of life. *J Clin Oncol* 2009;9:328–334.
- 7 Chartier-Kastler E., Amar E, Chevallier D, Montaigne O, Coulangue C, Joubert JM, Giuliano F: Does management of erectile dysfunction after RP meet patients' expectations? Results of a national survey (REPAIR) by the French Urological Association. *J Sex Med* 2008;5:693–704.
- 8 Adam M, Tennstedt P, Lanwehr D, Tilki D, Steuber T, Beyer B, Thederan I, Heinzer H, Haese A, Salomon G, Budäus L, Michl U, Pehrke D, Stattin P, Bernard J, Klaus B, Pompe RS, Petersen C, Hülndt H, Graefen M, Schwarz R, Huber W, Loeb S, Schlömm T: Functional outcomes and quality of life after radical prostatectomy only versus a combination of prostatectomy with radiation and hormonal therapy. *Eur Urol* 2017;71:330–336.
- 9 Sopko NA, Burnett AL: Erection rehabilitation following prostatectomy - current strategies and future directions. *Nat Rev Urol* 2016;13:216–225.
- 10 Ficarra V, Novara G, Artibani W, Cestari A, Galfano A, Graefen M, Guazzoni G, Guillonnet B, Menon M, Montorsi F, Patel V, Rassweiler J, Van Poppel H: Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. *Eur Urol* 2009;55:1037–1063.
- 11 Murphy DG, Bjartell A, Ficarra V, Graefen M, Haese A, Montironi R, Montorsi F, Moul JW, Novara G, Sauter G, Sulser T, van der Poel H: Downsides of robot-assisted laparoscopic radical prostatectomy: limitations and complications. *Eur Urol* 2010;57:735–746.
- 12 Asimakopoulos AD, Fraga P, Annino F, Pasqualetti P, Calado AA, Mugnier C: Randomized comparison between laparoscopic and robot-assisted nerve-sparing radical prostatectomy. *J Sex Med* 2011;8:1503–1512.
- 13 Krambeck AE, DiMarco DS, Rangel LJ, Bergstralh EJ, Myers RP, Blute ML, Gettman MT: Radical prostatectomy for prostatic adenocarcinoma: a matched comparison of open retropubic and robot-assisted techniques. *BJU Int* 2009;103:448–453.
- 14 Tewari A, Sooriakumaran P, Bloch A, Seshadri-Kreaden U, Hebert AE, Wiklund P: Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: a systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. *Eur Urol* 2012;62:1–15.
- 15 Trinh QD, Sammon J, Sun M, Sun M, Ravi P, Ghani KR, Bianchi M, Jeong W, Shariat SF, Hansen J, Schmitges J, Jeldres C, Rogers CG, Peabody JO, Montorsi F, Menon M, Karakiewicz PI: Perioperative outcomes of robot-assisted radical prostatectomy compared with open radical prostatectomy: results from the nationwide inpatient sample. *Eur Urol* 2012;61:679–685.
- 16 Ploussard G, de la Taille A, Moulin M, Hoznek A, Abbou CC, Salomon L: Comparisons of the perioperative, functional, and oncologic outcomes after robot-assisted versus pure extraperitoneal laparoscopic radical prostatectomy. *Eur Urol* 2014;65:610–619.
- 17 Porpiglia F, Morra I, Chiarissi MC, Manfredi M, Mele F, Grande S, Ragni F, Poggio M, Fiori C: Randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. *Eur Urol* 2013;63:606–614.
- 18 Nason GJ, O'Kelly F, White S, Dunne E, Smyth GP, Power RE: Patient reported functional outcomes following robotic-assisted (RARP), laparoscopic (LRP), and open radical prostatectomies (ORP). *Ir J Med Sci* 2016;1–6.
- 19 Davison BJ, Matthew A, Gardner AM: Prospective comparison of the impact of robotic-assisted laparoscopic radical prostatectomy versus open radical prostatectomy on health-related quality of life and decision regret. *Can Urol Assoc J* 2014;8:E68–E72.
- 20 Ludovico GM, Dachille G, Pagliarulo G, D'Elia C, Mondaini N, Gacci M, Detti B, Malossini G, Bartoletti R, Cai T: Bilateral nerve sparing robotic-assisted radical prostatectomy is associated with faster continence recovery but not with erectile function recovery compared with retropubic open prostatectomy: the need for accurate selection of patients. *Oncol Rep* 2013;29:2445–2450.
- 21 Hakimi AA, Blitstein J, Feder M, Shapiro E, Ghavamian R: Direct comparison of surgical and functional outcomes of robotic-assisted versus pure laparoscopic radical prostatectomy: single-surgeon experience. *Urology* 2009;73:119–123.
- 22 Barry M, Gallagher P, Skinner J, Fowler F: Adverse effects of robotic-assisted laparoscopic versus open retropubic radical prostatectomy among a nationwide random sample of medicare-age men. *J Clin Oncol* 2012;30:513–518.
- 23 Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM: Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11:319–326.
- 24 Victorson DE, Schuetz S, Schalet BD, Kundu SD, Helfand BT, Novakovic K, Sufrin N, McGuire M, Brendler C: Factors affecting quality of life at different intervals after treatment of localized prostate cancer: unique influence of treatment decision making satisfaction, personality and sexual functioning. *J Urol* 2016;196:1422–1428.
- 25 Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG: Development and validation of the Expanded Prostate Cancer Index Composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 2000;56:899–905.
- 26 Barry MJ, Fowler FJ Jr, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, Cockett AT: The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148:1549–1557.
- 27 Krishnan R, Katz D, Nelson CJ, Mulhall JP: Erectile function recovery in patients after non-nerve sparing radical prostatectomy. *Andrology* 2014;2:951–954.