DETERMINANTS OF LONG-TERM SEXUAL HEALTH OUTCOME AFTER RADICAL PROSTATECTOMY MEASURED BY A VALIDATED INSTRUMENT

BRENT K. HOLLENBECK, RODNEY L. DUNN, JOHN T. WEI, JAMES E. MONTIE AND MARTIN G. SANDA

From the Department of Urology and Cancer Center Biostatistics Core, University of Michigan, Ann Arbor, Michigan

ABSTRACT

Purpose: We combined the strengths of previous patient reported studies (that is use of a validated instrument) with the assets of previous single surgeon, physician reported series (that is prospective collection of operative data) by performing a multiple surgeon study to identify demographic and operative determinants of post-prostatectomy sexual health related quality of life outcomes.

Materials and Methods: Sexual outcome was measured after prostatectomy in 671 prostate cancer cases with a followup of 4 to 52 months treated by any of 7 urologists at a high volume medical center and 112 age matched controls by cross-sectional health related quality of life assessment using the Expanded Prostate Cancer Index Composite validated questionnaire. Multivariable ANCOVA was done to identify the baseline determinants affecting post-prostatectomy sexual health outcomes among 17 clinical and demographic factors.

Results: Factors independently associated with better sexual health outcome in patients included younger age (p < 0.0001), nerve sparing technique (p < 0.0001), time since prostatectomy (p = 0.0001), smaller prostate size (p = 0.003), higher education level (p = 0.02), and higher household income (p = 0.02). Orgasm was achieved at a higher rate than erection. In controls only age (p = 0.0004) and having a partner (p = 0.04) were significantly associated with sexual health.

Conclusions: Larger prostate size adversely affected sexual health outcome after radical prostatectomy independent of all other measured factors. Patient sexual outcome did not differ significantly among surgeons who performed a broad range of such procedures yearly, suggesting that surgical expertise cannot be measured simply by the number of such operations that a surgeon performs. Stratifying patient reported sexual function by the principal determinants of age, nerve sparing and prostate size provides a basis for counseling patients.

KEY WORDS: prostatic neoplasms, impotence, quality of life, questionnaires, prostatectomy

Health related quality of life in prostate cancer survivors is subject to increasing scrutiny due to improved cancer-free survival.1-4 In particular sexual health is more commonly affected after prostate cancer therapy than other health related quality of life domains.5-8 Physician reported data regarding erection recovery after prostatectomy were initially described in a few series limited to single surgeons.9-11 Conversely available patient reported data elicited using validated health related quality of life instruments are limited by small sample size, lack of detail on surgical technique or early post-prostatectomy followup.5-7,12-18 Consequently relating patient characteristics and surgical factors to long-term post-prostatectomy sexual recovery requires further characterization. Validated health related quality of life instruments facilitate such characterization by measuring outcomes via patient report, thereby, circumventing possible investigator bias, and by providing summary scores that convert qualitative information into a continuous format, which can improve statistical sensitivity to clinically relevant covariates.

We identified patient characteristics and surgical technique components that affect long-term sexual health outcome using a validated health related quality of life instrument, that is the Expanded Prostate Cancer Index Composite (EPIC), in a large cohort of men who underwent prostatectomy performed treated by 1 of several surgeons at a single, high volume referral center.5,9,19 Sexual health was concurrently measured in age matched male controls to provide a context for observed sexual functioning in patients with prostate cancer. Responses on specific elements of sexual function, including erection reliability and ability to achieve orgasm, were stratified by variables affecting long-term sexual health outcome. Our findings provide a basis for guiding long-term sexual outcome expectations based on patient age, prostate size and nerve sparing technique.

MATERIALS AND METHODS

Subjects. All 896 patients who underwent radical retropubic prostatectomy as primary therapy for localized prostate cancer between June 1, 1995 and May 31, 1999, and 142 age matched males without prostate cancer identified from a community based registry of volunteers for observational research studies were mailed an institutional review board approved, cross-sectional health related quality of life survey. Of these patients and controls 75% consented to participate, completed the EPIC questionnaire privately and returned it to anonymous research staff. Demographic characteristics of participants have been described previously.8 Briefly, average participant age was 64 years, 86% of the patients who underwent prostatectomy and 78% of controls
were married, 94% of patients reported a significant relationship with a partner, and 94% of patients and 96% of controls were white. Prostate cancer was stages T1 and T2 or greater in 62% and 37% of cases, while biopsy Gleason score was 6 or less, 7 and 8 or greater in 60%, 37% and 3%, respectively.

Prostatectomy was performed using the retropubic technique described by Quinlan et al with the cavernous nerves spared at surgeon discretion. Clinical factors and operative data collected prospectively included patient age, clinical stage, preoperative prostate specific antigen (PSA), neoadjuvant hormonal therapy, anesthesia type (general or regional), operative blood loss, transfusion requirement, nerve sparing technique (bilateral, unilateral, or none) and surgeon (7 urologists accrued patients into this study). Measured socioeconomic factors included race, income, marital status, a partner and education level.

Measures. Sexual health outcome was measured using the EPIC instrument by mail, as previously described. The 13-item EPIC sexual item set was derived by augmenting the 9-item University of California-Los Angeles prostate cancer index sexual item set with items regarding orgasm and a multi-item set regarding bother. EPIC was validated for use as a stand-alone sexual health questionnaire or as part of a multidimensional instrument (EPIC sexual summary score Cronbach’s α = 0.95 and 0.93, test-retest correlation r = 0.89 and 0.91, respectively). The EPIC sexual summary score and its function (α = 0.92) and bother (α = 0.84) subscales are scored from 0 to 100 with higher scores representing better sexual health.

Statistical analyses. Multivariable ANCOVA was used to test the association of demographic and perioperative factors with post-prostatectomy sexual outcome. These factors included age, followup duration (linear and quadratic terms), prostate size, preoperative serum PSA, biopsy Gleason score (2 to 6, 7 or 8 to 10), clinical stage (T1 or greater than T1), neoadjuvant hormonal therapy, transfusion requirement, blood loss, bilateral or unilateral nerve sparing, bladder neck sparing, type of anesthetic (general or regional), race, income ($30,000 or less, or greater than $30,000 yearly), significant relationship status, education (high school graduate or not) and surgeon experience. Four urologists with the lowest number of participating patients (18 or fewer on study each) were considered a single category to attain appropriate model sensitivity. This group served as the reference group. The effect of age and the nerve sparing technique on tangible elements of sexual health outcome were shown in patient responses to specific EPIC survey questions (table 2). The effects of age and nerve sparing were consistent across multiple elements of sexual health outcome, including erection reliability, the ability to achieve orgasm and overall sexual function.

Table 1. Baseline factors independently associated with sexual health outcome after radical prostatectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. Pts.</th>
<th>Mean Postop. EPIC Sexual Score</th>
<th>Multivariate ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger than 59</td>
<td>162</td>
<td>45</td>
<td>-5.33</td>
</tr>
<tr>
<td>59–69</td>
<td>329</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Older than 69</td>
<td>164</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Nerve sparing:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilat.</td>
<td>427</td>
<td>42</td>
<td>15.05</td>
</tr>
<tr>
<td>Unilat.</td>
<td>96</td>
<td>35</td>
<td>7.60</td>
</tr>
<tr>
<td>None</td>
<td>148</td>
<td>23</td>
<td>-1.30</td>
</tr>
<tr>
<td>Prostate size (gm.):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 59</td>
<td>491</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>59 or Greater</td>
<td>168</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Income greater than $30,000/yr.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>534</td>
<td>39</td>
<td>6.43</td>
</tr>
<tr>
<td>No</td>
<td>94</td>
<td>28</td>
<td>Reference value</td>
</tr>
<tr>
<td>High school graduate education:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>606</td>
<td>38</td>
<td>8.88</td>
</tr>
<tr>
<td>No</td>
<td>46</td>
<td>25</td>
<td>Reference value</td>
</tr>
</tbody>
</table>

Results

The relationship of sexual health outcome to patient and operative factors was evaluated by multivariate ANCOVA, adjusting for time from prostatectomy to cross-sectional sexual outcome assessment. In order of significance independent determinants of post-prostatectomy sexual health outcome included nerve sparing technique, patient age, prostate size, time from prostatectomy to health related quality of life assessment, income and education level (table 1). Sexual health outcome was better with a longer interval since prostatectomy from 1 to 4 years after surgery (p <0.003). The mean EPIC sexual score after prostatectomy was 28, 36, 37 and 40 in years 1 to 4 after prostatectomy, respectively. Longer time since prostatectomy was associated with improved function and bother sexual domain subscales (each p <0.01). The observed 12-point difference in EPIC sexual summary score improvement from 1 to 4 years after prostatectomy met the criteria for a clinically significant change (0.3 to 0.5 times the standard deviation) but the predominant differences related to followup duration were observed in the first 2 years. Although cancer severity measures showed marginal association with sexual outcome on univariate assessments (univariate clinical stage p = 0.1 and Gleason score p = 0.08), they were not significant on multivariate analysis. In controls the mean EPIC sexual summary score ± SD was 63 ± 23 and determinants of sexual health on EPIC included age and relationship status.

The negative impact of increasing prostate size on sexual function and its tendency to increase impairment postopera-
tively were novel findings. To determine these deleterious effects the responses to specific EPIC items of patients who underwent bilateral nerve sparing were stratified by prostate size and age (see figure). The modest but significant adverse effect of increasing prostate size on the ability to attain erection or orgasm postoperatively in any given age group was most profound in men with a prostate of 59 gm. or greater, which was the largest quartile of prostate size. For example, 67% of the patients younger than 64 years with a prostate of less than 38 gm. reported at least fair ability to achieve erection or orgasm postoperatively in any given age group. These findings reiterate that erection, ejaculation and orgasm are distinct elements of sexual health. The observation that prostate size can be a significant independent determinant of post-prostatectomy sexual health outcome has not been previously characterized. The figure suggests that much of the adverse prostate size effect is in the largest prostate quartile of 59 gm. or greater. This observation is relevant because large prostate size is commonly used to exclude patients from alternative interventions, such as brachytherapy. A possible explanation for this effect is that more extensive dissection may be required for a large prostate to spare the cavernous nerves. Another possibility is that larger prostates may preclude optimal visualization, predisposing to unrecognized neural injury. The possibility that men with a larger prostate had worse sexual function preoperatively cannot be excluded. However, we subsequently evaluated a cohort of 264 patients with prostate cancer before prostatectomy and noted no significant association of prostate size with the baseline EPIC sexual summary score (Pearson correlation r = –0.03, p = 0.62).

There is a paucity of published information on the ability to attain orgasm after radical prostatectomy. This lack of knowledge limits the ability to counsel patients regarding an important element of sexuality. Many patients and some physicians assume that men who are not able to attain erection cannot achieve orgasm. In contrast, we observed that after prostatectomy the ability to achieve orgasm was retained more commonly than the ability to achieve erection. These findings reiterate that erection, ejaculation and orgasm are distinct elements of sexual health. The observation that satisfactory ability to achieve orgasm can be retained even after prostatectomy in patients who lack erection may be of interest to men with prostate cancer and their physicians. An additional novel aspect of our study design was evaluating the role of surgical expertise in sexual health outcome by including all patients from each of 7 surgeons who performed prostatectomy at our institution during the study period. This aspect extends beyond the design of previous studies that evaluated only patients of a single surgeon or did not mention analysis of different surgeons as a discrete variable. We did not detect an effect related to the operating surgeon in regard to sexual health outcome. The covariate adjusted mean sexual summary score was 32 after surgery by high volume surgeons to 26 for surgeons performing fewer than 15 prostatectomies yearly (p = 0.48). The sample size conferred 80% power for detecting a 1/2 SD difference in sexual summary score in patients grouped by surgeon. These findings imply a similar level of competency among participating surgeons and suggest that surgical expertise cannot be measured simply by the number of such cases that a surgeon performs. A larger study may be necessary to detect surgical expertise effects on sexual outcome. Few studies have evaluated the relationship of socioeconomic factors to post-prostatectomy sexual health outcome. Stanford et al observed that higher education level, involvement in a relationship and race were associated study provides a comprehensive assessment of parameters associated with post-prostatectomy sexual health recovery.

Our findings extend the characterization of post-prostatectomy sexual health in several respects. We noted that prostate size can be a significant independent determinant of post-prostatectomy sexual health outcome. Also, we provide further evidence regarding orgasm after radical prostatectomy. In addition, we evaluated the effect of the surgeon. Furthermore, we extended the observation that nerve sparing and younger patient age are independently associated with better sexual health outcome to methodology using a validated health related quality of life instrument, while adjusting for other factors by multivariate analysis. Our findings also confirm the previous observation that sexual health can continue to improve beyond year 1 after radical prostatectomy.

To our knowledge the adverse effect of larger prostate size on sexual health recovery after radical prostatectomy has not been previously characterized. The figure suggests that much of the adverse prostate size effect is in the largest prostate quartile of 59 gm. or greater. This observation is relevant because large prostate size is commonly used to exclude patients from alternative interventions, such as brachytherapy. A possible explanation for this effect is that more extensive dissection may be required for a large prostate to spare the cavernous nerves. Another possibility is that larger prostates may preclude optimal visualization, predisposing to unrecognized neural injury. The possibility that men with a larger prostate had worse sexual function preoperatively cannot be excluded. However, we subsequently evaluated a cohort of 264 patients with prostate cancer before prostatectomy and noted no significant association of prostate size with the baseline EPIC sexual summary score (Pearson correlation r = –0.03, p = 0.62).

There is a paucity of published information on the ability to attain orgasm after radical prostatectomy. This lack of knowledge limits the ability to counsel patients regarding an important element of sexuality. Many patients and some physicians assume that men who are not able to attain erection cannot achieve orgasm. In contrast, we observed that after prostatectomy the ability to achieve orgasm was retained more commonly than the ability to achieve erection. These findings reiterate that erection, ejaculation and orgasm are distinct elements of sexual health. The observation that satisfactory ability to achieve orgasm can be retained even after prostatectomy in patients who lack erection may be of interest to men with prostate cancer and their physicians.

An additional novel aspect of our study design was evaluating the role of surgical expertise in sexual health outcome by including all patients from each of 7 surgeons who performed prostatectomy at our institution during the study period. This aspect extends beyond the design of previous studies that evaluated only patients of a single surgeon or did not mention analysis of different surgeons as a discrete variable. We did not detect an effect related to the operating surgeon in regard to sexual health outcome. The covariate adjusted mean sexual summary score was 32 after surgery by high volume surgeons to 26 for surgeons performing fewer than 15 prostatectomies yearly (p = 0.48). The sample size conferred 80% power for detecting a 1/2 SD difference in sexual summary score in patients grouped by surgeon. These findings imply a similar level of competency among participating surgeons and suggest that surgical expertise cannot be measured simply by the number of such cases that a surgeon performs. A larger study may be necessary to detect surgical expertise effects on sexual outcome.

Few studies have evaluated the relationship of socioeconomic factors to post-prostatectomy sexual health outcome. Stanford et al observed that higher education level, involvement in a relationship and race were associated...
with a better sexual health outcome after prostatectomy. Litwin et al reported that income and race were associated with urinary outcome but did not detect an association of these factors with sexual health. We noted that education and income were significantly associated with better sexual health outcome. Although education and income have been described as determinants of general or urinary health related quality of life domains by previous groups, they did not identify these factors as significantly associated with sexual health related quality of life outcome on multivariable analysis that also controlled for age and nerve sparing status. Socioeconomic factors may influence health related quality of life outcome indirectly, such as by affecting expectations, access to information and supportive care, but our study did not address these mechanisms. Socioeconomic factors merit further study as possible sexual health determinants.

This cross-sectional study is limited, in that it was administered at a single institution and baseline data on sexual health were not collected. We compensated somewhat by measuring the sexual health of age matched controls to provide a proxy of baseline function for the post-prostatectomy cohort. The lack of baseline assessment affects some of our interpretations. For example, it is possible that socioeconomic factors may not affect the recovery of sexual health after controlling for baseline impairment. Nevertheless, the fact that cross-sectional studies serve a key role in health related quality of life assessment is well established. For example, our cross-sectional design provided unique insight into the adverse effects of larger prostate size on sexual recovery.

CONCLUSIONS

We observed that age, nerve sparing technique and prostate size are significant independent determinants of sexual health outcome after radical prostatectomy. When adjusting for these significant factors, post-prostatectomy sexual health outcome did not differ significantly among surgeons who performed a broad range of such procedures yearly, suggesting that surgical expertise cannot be measured simply by the number of such cases that a surgeon performs. This evidence challenges the notion that surgeon surgical case volume is the principal determinant of superior sexual health outcome. Our findings extend the observation of nerve
sparing benefit, which has previously been reported only in single surgeon series, to a setting in which multiple surgeons were included in a study using a validated health related quality of life instrument. These data provide a basis for counseling patients on long-term post-prostatectomy sexual function expectations based on age, prostate size and nerve sparing technique by any of multiple surgeons at an academic referral center.

Operating surgeons included 2 of us (M. S. and J. M.), and urologists Drs. William Belville, Gary Faerber, John Konnak, Joseph Oesterling and Dana Ohl. Carol Galofaro and Karen King performed data entry and management, and Linda Agius coordinated regulatory concerns.

REFERENCES