

## Platinum Priority – Prostate Cancer

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# Ten-year Outcomes of Sexual Function After Radical Prostatectomy: Results of a Prospective Longitudinal Study

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### Abstract

**Background:** The long-term impact of radical prostatectomy (RP) on sexual function (SF) and erectile function (EF) has important implications related to the risk-to-benefit ratio of this treatment.

**Objective:** To determine the long-term effect of RP on male SF and EF over 10 yr of follow-up.

**Design, setting, and participants:** This was a prospective, longitudinal outcomes study in 1836 men following RP at a university hospital. Men were invited to complete the University of California, Los Angeles, Prostate Cancer Index SF survey at baseline, 3, 6, 12, 24, 96, and 120 mo postoperatively and a survey at 4 and 7 yr postoperatively assessing global changes in their EF over the preceding 2 yr.

**Intervention:** All men underwent open RP.

**Outcome measurements and statistical analysis:** Multiple, generalized linear regression models were used to evaluate the association between time following RP and SF and EF scores controlling for age, prostate-specific antigen, Gleason scores, stage, nerve sparing, race, and marital status.

**Results and limitations:** After an expected initial decline, time-dependent improvements in SF and EF were observed through 2 yr postoperatively. Overall, SF and EF were both generally stable between 2 and 10 yr following RP. The subgroups of younger men and men with better preoperative function were more likely to maintain their EF and SF through 10 yr following RP. The primary limitation is the potential bias attributable to nonresponders.

**Conclusions:** The recovery of EF can extend well beyond 2 yr. There is a significant association between younger age and better preoperative function and the likelihood of experiencing improvements beyond 2 yr. Assessing the comparative effectiveness of treatment options for localized prostate cancer must examine SF beyond 2 yr to account for delayed treatment effects and the natural history of SF in the aging male population.

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## 1. Introduction

In the early 1980s, Lepor et al. demonstrated that the cavernous nerves course alongside the prostate, thereby supporting the theory that the etiology for postprostatectomy erectile dysfunction (ED) is inadvertent injury of these nerves during dissection of the prostate [1]. In 1983, Walsh

and associates described the nerve-sparing radical retro-pubic prostatectomy (RRP), designed to avoid injuring these nerves with the intent of preserving erectile function (EF) without compromising oncologic disease control [2]. The first two reported large series of nerve-sparing RRP described potency rates between 63% and 68% at 18 mo of follow-up [3,4]. Over time, a varying proportion of men

regained EF. In a significant proportion of men, however, the nerves are irreversibly injured despite attempts at preservation, and EF never recovers [5–10].

The initial studies examining preservation of EF following radical prostatectomy (RP) assumed that maximum return of EF was achieved at 18 mo, because the proportion of men regaining EF appeared to plateau at this time [7]. Although there is a paucity of studies investigating the impact of RP on EF beyond 2 yr, the few studies that do so report progressive improvements in some men [5–7].

The present study prospectively examines both EF and sexual function (SF) at baseline and sequential time points over 10 yr. To our knowledge, this study represents one of the longest prospective longitudinal studies of outcomes following RP and provides important insights regarding the long-term impact of RP on EF and SF.

## 2. Patients and methods

Between October 2000 and September 2012, 1836 men (97% of men who underwent RP by a single surgeon) signed informed consent to participate in a prospective, institutional review board–approved study of outcomes following RP. Throughout this article, *University of California, Los Angeles Prostate Cancer Index (UCLA-PCI) SF evaluation* refers to the overall composite SF score, and *UCLA-PCI EF evaluation* refers to the single question of the survey concerning the ability to have an erection.

Men were invited to complete the UCLA-PCI at baseline, 3, 6, 12, 24, 96, and 120 mo after RP. The UCLA-PCI SF survey is a validated instrument capturing self-reported ability to have an erection, reach climax, quality of erection, frequency of erections, and ability to function sexually [11]. Both the UCLA-PCI composite SF score and the score on the individual question regarding the ability to have an erection were ascertained at all follow-up intervals. In addition, a self-administered survey at 4 and 7 yr following RP inquired whether patients had experienced marked improvement, moderate improvement, slight improvement, no change, or a decline in EF over the preceding 2 yr. This qualitative assessment of EF has been previously used [5] but not validated. The questionnaires were self-administered during scheduled office visits or returned via mail to the data manager of the outcomes database. Subsequent data collection and analysis were handled without the involvement of the operating surgeon.

A standardized clinical pathway for managing ED was used throughout the study. All potent men were encouraged to take 50 mg of sildenafil daily or 10 mg of tadalafil every other day starting 1 wk after RP. If there was no evidence of partial EF at 3 mo and men were eager to engage in sexual intercourse, penile injection therapy was recommended until adequate return of EF. If penile injections were not effective or tolerated, men were encouraged to undergo implantation of a penile prosthesis at 2 yr.

To evaluate the association of time since RP with SF and EF, we used a generalized, linear model in which the dependent variable was the mean composite SF score or the mean score on the specific question regarding the ability to have an erection. There was one observation per patient per follow-up period for a total of up to six observations (3, 6, 12, 24, 96, and 120 mo following RP). Key independent variables of interest were dummies for each follow-up period. The models controlled for baseline, preoperative UCLA-PCI SF score, age (continuous, in years), preoperative prostate-specific antigen (continuous, in nanograms per milliliter), Gleason score ( $\leq 6$ , 3 + 4, 4 + 3, 7 [unspecified],  $\geq 8$ , missing), pathologic stage (T2a, T2b, T2c, T3a, T3b, T3c, or missing), extent of nerve sparing (unilateral, bilateral, none, or missing), race (white, black, Hispanic, Asian, other, or missing), and marital status (married, single, widowed, divorced, separated, or missing). We also included a random effect for

each man to represent other distinguishing characteristics not controlled for by our independent covariates. In this framework, we allowed for the possibility that SF might differ idiosyncratically from man to man in ways unrelated to questions asked on our follow-up surveys. Specifically, we added an error term specific to each individual, because we allowed for the possibility of additional error. The effect was to widen confidence intervals, making it more difficult to document a change in SF following RP. In addition, the model was stratified by age and preoperative UCLA-PCI (at or above the median vs below the median). A Pearson chi-square analysis of whether changes in the global assessment of EF varied by age at time of RP was also investigated.

When evaluating outcomes, we were concerned about potential bias affecting which patients decided to continue answering surveys over time. We therefore performed  $\chi^2$  and paired *t* tests comparing mean preoperative age and UCLA-PCI SF and EF scores between respondents and nonresponders at 2 yr following RP as compared with 8 yr following RP (the period over which the largest reduction in follow-up rate occurred). Analyses were conducted in Stata/SE v.12.0 statistical software (StataCorp, College Station, TX, USA). Differences were deemed significant at a two-sided  $p < 0.05$ .

## 3. Results

Table 1 displays baseline characteristics for the cohort. At the time of RP, the mean age was 59.2 yr of age (standard

**Table 1 – Baseline characteristics (n = 1836)**

Age, yr, mean (SD)	59.2 (6.8)
Age, yr, range	37–79
Baseline UCLA-PCI SF, mean (SD)	70.2 (24.0)
Baseline UCLA-PCI EF, mean (SD)	72.3 (27.6)
Baseline PSA, ng/ml, mean (SD)	6.0 (4.8)
Race, no. (%)	
White	1649 (89.8)
Black	63 (3.4)
Asian	29 (1.6)
Hispanic	23 (1.3)
Other	20 (1.1)
Missing	2 (0.1)
Pathologic stage, no. (%)	
T2a	293 (15.6)
T2b	650 (35.4)
T2c	433 (23.6)
T3a	331 (18.0)
T3b	99 (5.4)
T3c	4 (0.2)
Missing	26 (1.6)
Gleason score, no. (%)	
$\leq 6$	888 (48.4)
3 + 4	629 (34.3)
4 + 3	167 (9.1)
7 (not specified)	18 (1.0)
8–10	117 (6.4)
Missing	17 (1.0)
Marital status, no. (%)	
Married	1576 (85.8)
Single	117 (6.4)
Widowed	26 (1.4)
Divorced	75 (4.1)
Other	42 (2.3)
Extent of nerve sparing, no. (%)	
Bilateral	1405 (76.5)
Unilateral	278 (15.1)
None	59 (3.2)
Missing	94 (5.1)

SD = standard deviation; UCLA-PCI = University of California, Los Angeles, Prostate Cancer Index; SF = sexual function; EF = erectile function.

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