

RESEARCH HIGHLIGHT

Can erectile function be predicted after prostate cancer treatment?

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Prostate cancer (PCa) is the most common solid-organ cancer in American males and the second most common cause of cancer-related death in men. With the advent of prostate-specific antigen screening, death from PCa continues to decline. However, recent evidence suggests that there is now a trend towards increasing incidence.¹ Current screening strategies result in increased incidence of low-risk PCa and importantly, the diagnosis of PCa is becoming more common in younger patients.² The majority of early-stage PCa patients have a high likelihood of disease free survival after treatment. Localized disease is most commonly treated with radical prostatectomy, external beam radiation therapy (EBRT) or brachytherapy. Local therapy yields excellent long-term survival results in low-risk patients; however, treatments may result in a significant treatment-related morbidity, and ultimately impact patient health-related quality of life (HRQOL).³ The effects of these treatment modalities on the HRQOL have been evaluated and compared and all three are associated with increased sexual dysfunction.^{4,5}

With better long-term survival, improvement in HRQOL outcomes has become a priority for patients undergoing treatment for localized disease. In addition to type of treatment, other factors influence sexual function outcomes, such as baseline sexual function. It has previously been demonstrated that the quality of patient baseline function significantly influences the degree of treatment-related dysfunction.⁶ It is important to assess pre-treatment sexual function in order to adequately counsel patients regarding outcome expectations.⁷ However,

while there are established methods of measuring and scoring baseline conditions of patients, using these results in combination with treatment and disease-related factors to predict post-treatment function is less clear.

In the 21 September 2011 issue of the *Journal of the American Medical Association*, Alemozaffar *et al.*⁸ reported results for the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment. This was a multicenter prospective study evaluating whether sexual outcomes after treatment for PCa can be accurately predicted based on pretreatment baseline characteristics. The cohort consisted of 1201 men with previously untreated clinical-stage T1 or T2 PCa. The men were treated with radical prostatectomy, EBRT or brachytherapy. Baseline clinical data including sexual quality of life, use of medications or devices for erectile dysfunction, demographics and treatment plans were collected. Patients with implanted penile prosthesis were excluded. Outcome measures were assessed by third-party interviewers. The reported outcomes, specifically functional erections suitable for intercourse, were subjective and included patient responses to the Expanded Prostate Cancer Index Composite (EPIC-26) at baseline and at various time points after treatment up to 2 years. The EPIC-26 is a previously validated instrument for measuring HRQOL for PCa survivors.⁹

Of the original cohort, 86% completed the end of study questionnaire and were included in the final evaluation. The authors created a logistic regression model based on patient and disease characteristics and planned treatment to evaluate erectile function 2 years after treatment. Multivariable model development was used and this was internally validated using comprehensive statistical analysis. The inverse logistic function was used to calculate the individual predicted probabilities of

functional erections at 2 years. It was assumed that the omitted 14% non-responders were completely random and further analysis of this did not reveal any effect on the outcomes estimates. In order to establish the generalizability of the prediction model, the results were externally validated and calibrated using the Cancer of the Prostate Strategic Urologic Research Endeavor cohort registry. Men in this previously described cohort provided information about sexual function before and after PCa treatment by completing the University of California Los Angeles Prostate Cancer Index, a tool from which the EPIC-26 was derived.^{10,11} There were 1655 men from the community-based Cancer of the Prostate Strategic Urologic Research Endeavor registry eligible for evaluation and the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment prediction model was applied to each. The predicted erectile function at 2 years was compared to the patient's actual erectile function.

Model-predicted probabilities of functional erections after prostatectomy, EBRT and brachytherapy were developed. These models were determined to be applicable to the Cancer of the Prostate Strategic Urologic Research Endeavor cohort patients based on analysis of areas under the receiver-operating characteristic curve. From the results of the study, it was concluded that pre-treatment patient characteristics and details of treatment stratification allow prediction of erectile function 2 years after treatment for localized PCa. For example, a 60-year-old man with a sexual HRQOL of 83 and a pretreatment prostate-specific antigen of 6 would have a 38% chance of functional erection after nerve-sparing radical prostatectomy. A man with a sexual HRQOL of 100 and a prostate-specific antigen of 6 who underwent neo adjuvant hormone therapy and EBRT would have a 53% chance of

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functional erection after treatment. A 70-year-old African-American man with a body mass index of 27 and an HRQOL of 83 would have a 73% chance of function erection after brachytherapy.

This study highlights the importance of evaluating pre-treatment erectile function. It provides a way in which this baseline information might be used to counsel patients regarding realistic functional outcomes after treatment. Importantly, the investigators incorporated the presence or absence of nerve-sparing surgery and hormone deprivation into their analysis. However, the use and effects of post-treatment penile rehabilitation protocols, erectile dysfunction medications and devices were not factored in. This may have confounded the erectile function results and make it difficult to determine if predicted outcomes can be expected with or without the use of these regimens. Although this study is observational in design, the large multicenter cohort likely facilitated inclusion of broad range of patient demographics, including race and age. In addition, application and validation of the models to a large external community cohort, further allows for better confidence in the generalizability of the models.

The models derived in this study may help improve the counseling of patients about the impact of localized PCa treatments on sexual quality of life. Using these models, physicians can provide patients with individualized information based on their baseline sexual functional status and the impact of radical prostatectomy, EBRT and brachytherapy on post treatment sexual function. However, because of potential for selection bias in this observational study, one must take caution not to use the models as proof of superiority between treatment modalities.

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