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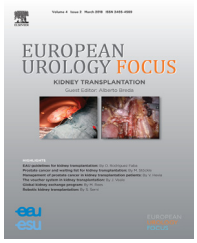

Clinical Trial Update

Functional Recovery Following Primary Treatment for Prostate Cancer: Update from the CEASAR Study

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Treatment for localized prostate cancer is associated with urinary, sexual, and bowel side effects, yet few studies have compared these outcomes among the contemporary management options (robot-assisted radical prostatectomy [RP], intensity-modulated external beam radiation therapy [EBRT], and active surveillance [AS]) [1–3]. Such comparative data are needed to inform shared-decision making. Importantly, these data must be patient-reported to ensure their validity and applicability. We undertook the Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study to address this knowledge gap.

CEASAR is a population-based prospective cohort study [4]. Men aged <80 yr with prostate-specific antigen of <50 ng/ml and clinical stage T1 or T2 disease were enrolled within 6 mo of diagnosis from five Surveillance, Epidemiology and End Results (SEER) sites and the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry between February 2011 and March 2012. At baseline and longitudinally thereafter, patients completed questionnaires regarding clinical and sociodemographic information, disease-specific and general quality of life (QOL), comorbidities, and psychosocial measures. In addition, clinical information was obtained via chart review at 1 yr after enrollment. The primary outcome measure was the Expanded Prostate Cancer Index Composite (EPIC-26), a validated instrument for measuring disease-specific QOL in men with prostate cancer [5]. EPIC-26 assesses urinary incontinence, urinary obstructive/irritative symptoms, sexual function, bowel function, and symptoms related to hormone therapy. Domain scores range from 0 to 100, with higher scores representing better function. Outcomes were compared across treatment groups using multivariate modeling to control for measured confounders. In addition to statistical significance, differences in function were evaluated on the basis of previously published minimum clinically important differences (MCIDs) in domain scores [6].

More than 3000 men were enrolled, of whom 2550 underwent either RP, EBRT, or AS. Approximately 27% of participants were non-white, 55% had D'Amico intermediate or high risk, and there were wide ranges for age and comorbidity status. The mean age at enrollment was 63.8 yr, and 45% of men reported erectile dysfunction at baseline [7]. Some 60% of the cohort underwent RP (77%

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robotic); 23% underwent EBRT (81% intensity-modulated RT, 45% with concurrent androgen deprivation therapy); and 17% chose AS (including 28.6% of all patients with low-risk disease). Men who chose RP were younger and healthier, had lower-risk cancer, and had better baseline sexual function compared to men who chose EBRT.

Surgery patients had a larger decline in sexual function than men who chose EBRT or AS. At 3-yr follow-up, the mean difference in EPIC-26 sexual function domain score between RP and EBRT was 11.9 points (95% confidence interval 15.1–8.7), which is a clinically significant difference (MCID defined as 10–12 points). Among men who had erections sufficient for intercourse at baseline, 43% of RP patients, 53% of EBRT patients and 75% of AS patients reported erections firm enough for intercourse at 3 yr. The difference in sexual function between RP and EBRT was only significant for men in the highest quartile of baseline sexual function; men in the lower three quartiles had similarly poor functional outcomes.

Surgery patients had a larger decline in urinary incontinence scores compared to men who chose RT or AS (3-yr incontinence domain score was 12.7 points lower for RP vs EBRT, higher than the MCID of 6). At 3 yr after treatment, 14% of men who underwent RP reported a moderate or significant problem with urinary incontinence.

Men undergoing EBRT had modest declines in urinary irritative/obstructive symptoms (whereas scores improved for men who had RP), bowel function, and hormone therapy symptom scores. These differences were statistically and clinically significant within the first year after treatment, but attenuated with time. Men who remained on AS had preserved function.

Results from CEASAR inform our understanding of the survivorship experience for men with localized prostate cancer. For other common cancers, physicians and patients focus primarily on the survival benefit of therapy. However, prostate cancer has a long natural history and the differences in oncologic outcomes are small, so comparative effectiveness studies must include QOL as a key outcome. Older studies assessed QOL through physician-reported endpoints [8], chart review, and administrative data [9], despite the obvious limitations of these approaches, including evidence that physicians consistently underestimate patient-reported urinary, sexual, and bowel dysfunction [10]. CEASAR was specifically designed with patient-reported outcomes as the primary endpoints. The population-based design and the focus on contemporary treatments make the CEASAR results relevant and actionable for men facing treatment decisions.

Additional results from CEASAR include identification of disparities in the quality of radiation therapy [11,12], differential functional outcomes by race and disease severity [13,14], and the lack of benefit of nerve-sparing surgery in men with poor baseline function [15]. We are currently preparing to report 5-yr outcomes and to collect 10-yr QOL and clinical outcomes. In addition, we are disseminating results to facilitate shared-decision making and personalized care, including the development of a web-based decision aid (Fig. 1) and incorporation of CEASAR data into the WiserCare platform (www.wisercare.com/).

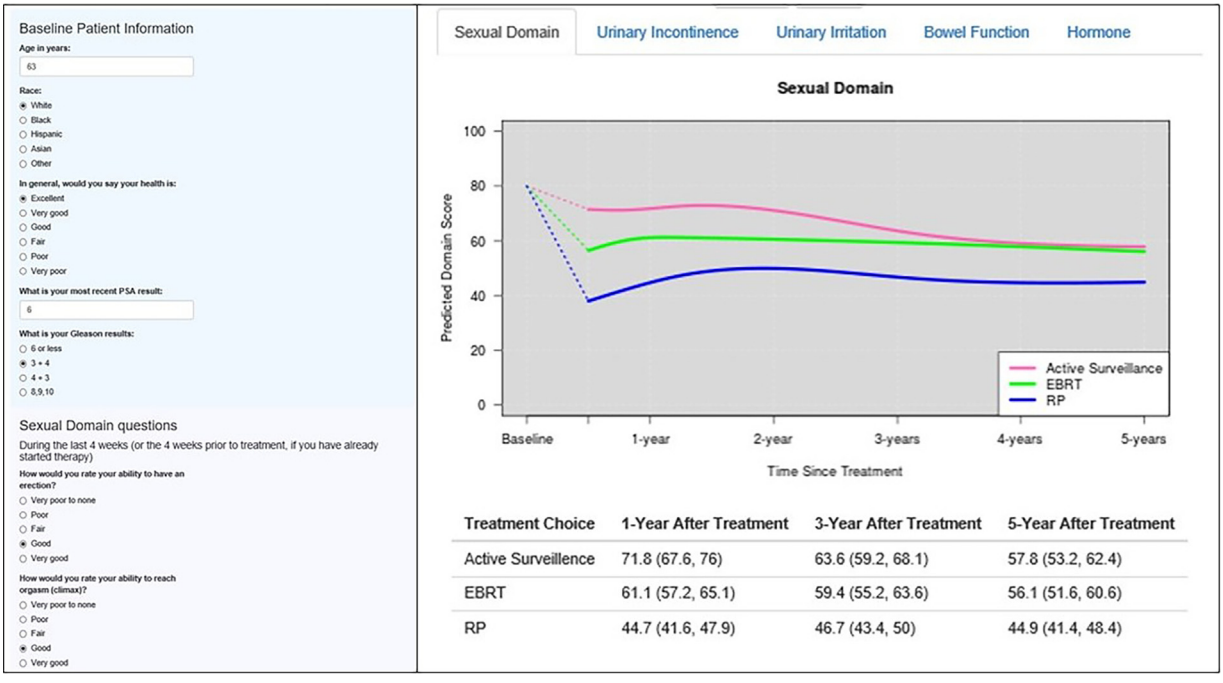

Fig. 1 – Web-based patient-facing decision aid predicting estimated EPIC-26 domain scores following treatment of localized prostate cancer. (Left Panel) Patient data entry module. (Right Panel) Personalized estimate of function after treatment. EBRT = external beam radiation therapy; RP = radical prostatectomy.

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Conflicts of interest: The authors have nothing to disclose.

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