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Title: You Pays Your Money, You Takes Your Choice: Functional Outcomes Following Curative Treatment for Clinically Localized Prostate Cancer

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You pays your money, you takes your choice: functional outcomes following curative treatment for clinically localized prostate cancer.

Association Between Radiation Therapy, Surgery, or Observation for Localized Prostate Cancer and Patient-Reported Outcomes After 3 Years

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Summary

This prospective, population-based, cohort study compared the functional and oncologic outcomes following radical prostatectomy (RP), external beam radiation therapy (EBRT) and active surveillance (AS) as treatment for localized prostate cancer. This large study included 2550 men aged less than 80 years from 5 Surveillance, Epidemiology, and End Results (SEER) registries with a PSA <50 ng/ml who were diagnosed with cT1/T2N0M0 prostate cancer between 2011 and 2012. Of these, 1523 underwent RP, 598 received EBRT and 429 AS. No patients received brachytherapy. At 3 years 24.2% of patients on AS had received definitive treatment. There were statistically significant differences between treatment groups for almost all baseline patient and disease characteristics. For example, patients receiving EBRT were older and had more co-morbidities.

Surveys were conducted at enrolment, 6, 12 and 36 months. Inclusion required completion of the baseline and one additional survey, although the baseline survey was completed in 46% of cases retrospectively after initiation of treatment. Excellent rates of survey completion were obtained at 6 months (89%), 12 months (86%) and 36 months (78%). The primary outcome measures were domain scores on the 26-item Expanded Prostate Cancer Index Composite (EPIC-26) at 36 months. The minimal clinically important difference (MCID) was estimated in five domains.

Unadjusted domain scores for sexual function at three years were similar between
treatment groups, but the decline was greatest in the RP group since they had better function at baseline. The majority of patients in all three groups did not have erections sufficient for intercourse at three years (70% RP, 71% EBRT, and 51% AS). However, the bother between treatment arms was significantly different: RP 44%, EBRT 35% and AS 28% (P<0.001 on multivariate analysis).

Baseline urinary incontinence and irritative voiding symptom scores were similar across groups. At three years urinary function bother scores were not significantly different between RP vs AS or EBRT vs AS but were higher for RP vs EBRT (12% vs 10%; OR 1.7; 1.1-2.5). Moderate or big problems with urinary incontinence were more common after RP vs AS (OR 2.9 CI 95%, 1.8-4.7) and RP vs EBRT (OR 4.5 CI 95%, 2.7-7.3) at 3 years: 14% RP, 6% AS and 5% EBRT. Irritative voiding symptoms improved for nearly 70% of men after RP; whilst patients undergoing AS or EBRT demonstrated little change. Frequent bothersome urination was similar between RP and EBRT, but higher with AS at 3 years.

Bowel domain scores were fairly constant regardless of treatment. Bothersome bowel symptoms, bloody stools and bowel frequency were observed in 1-8% of patients. RP was associated with less bowel urgency than both EBRT (3% vs 7%, OR 0.3; 95% CI 0.3-0.6) and AS (3% vs 5%, OR 0.5; 95%, 0.3-0.9).

No treatment group experienced a significant decline in health-related quality of life as measured by the SF-36. Only 3 prostate cancer-related deaths were observed after a mean follow-up of 40 months.

Discussion

Contemporary treatments for localized prostate cancer report similar, very low cancer-related deaths at 10 years. Thus the comparative functional outcomes of treatments are important for selecting optimal therapy in any individual patient. This study has illustrated some of the early to medium term differences associated with different treatments. Whilst RP is associated with increased sexual and bladder dysfunction, this dysfunction does improve over the first year, though remains greater than that of EBRT or AS. Data from the ProtecT trial support this study, as do those from a second cohort study published in the same volume of JAMA by Chen et al. Do these studies therefore suggest that patients who require intervention should be treated preferentially with EBRT over RP to reduce the impact of treatment on functional outcome?

Strengths of the study include the large sample size, the use of contemporary treatments, the excellent survey completion rates and the broad spectrum of patient demographics and disease characteristics. Important limitations of this trial include the lack of randomization between treatment arms and the recall bias related to completing the baseline survey after treatment in 54% of patients. A 3-year endpoint is too premature to consider the totality of oncologic, functional, quality of life outcomes and treatment-induced adverse effects, especially considering the
potentially insidious onset of radiation complications. Furthermore, to date the validity and reliability of the specific questionnaires used in this study remain disputed. The MCID used has significant flaws: it has not been validated on patients on AS, it originates from a non-randomized study and changes have variable impact on patients depending on the raw score.

Severe side effects, though rare, were not formally compared between treatment groups. Given that up to 18% of patients with localized prostate cancer are treated with brachytherapy, the omission of this common treatment group in this study is a significant shortcoming.

The most important conclusions to be drawn from this study are that we must continue to address patient reported outcome measures in order to understand the true impact of our various therapies, and we must strive to improve these outcomes. Would surgical outcomes be improved, for example, with some degree of centralization of care so that more RPs are performed by fewer urologists? Population level observations may not reflect the outcomes of individual practitioners, and it is important for us all to track our own outcomes.

References


