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Research Highlights

Outcomes of prostate cancer treatments

This month's column focuses on outcomes associated with the treatment of prostate cancer. Unger et al. chronicled long-term treatment-related adverse effects and complications occurring in patients diagnosed with localised prostate cancer and compared them to a general population of older men. They linked data available in Medicare claims records with data from two large randomised clinical trials: The Prostate Cancer Prevention Trial and the Selenium and Vitamin-E Cancer Prevention Trial. They were able to identify 3946 men with localised prostate cancer of which 655 underwent radical prostatectomy and 1056 underwent radiation therapy. They compared these men to 25 150 untreated controls. The mean age of the study sample was 68.7 years. They found the 12-year hazard risk of urinary or sexual complications was 7.23 times greater for men undergoing prostatectomy and 2.76 times greater for men undergoing radiation therapy than for controls. Men receiving radiation therapy had a 2.78-times greater risk of developing bladder cancer and a 100-fold increase in the risk of radiation cystitis or proctitis. The incidence of any one of 10 treatment related complications was 124.26 per 1000 person years for prostatectomy, 62.15 for radiotherapy and 23.61 for untreated participants. The authors concluded that considering the uncertain benefits of treatment for many patients, their findings highlight the importance of detailed patient counselling before prostate cancer screening and treatment.

Unger JM, Till C, Tangen CM et al. Long-term adverse effects and complications after prostate cancer treatment. *JAMA Oncol.* 2024; https://doi.org/10.1001/jamaoncol.2024.4397.

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"This study highlights the importance of detailed patient counselling before prostate cancer screening and treatment"

Holmberg et al. recently reported 30-year results for men enrolled in the Scandinavian Prostate Cancer Group Study number 4. They enrolled 695 men between 1989 and 1999 in a randomised trial comparing radical prostatectomy or watchful waiting following the diagnosis of localised low to intermediate grade prostate cancer. At baseline 88% had clinically detected disease. Among men undergoing surgery, 47% had extracapsular extension. After 30 years of follow up 85% of the men randomised to surgery had undergone a radical prostatectomy and 15% of the men in the watchful waiting arm had undergone curative intent. Deaths from prostate cancer occurred up to 30 years after randomisation in both trial groups. Men undergoing radical prostatectomy had a 48% lower risk of death from prostate cancer compared to watchful waiting and a 26% lower risk of death from any cause. These men gained a mean of 2.2 life-years. At 30 years, six men needed to be treated to prevent one cancer death. The authors cautioned that these results do not apply to men with screen detected disease. The trial showed that radical prostatectomy can save lives in men presenting with more advanced localised disease, but the lead time associated with contemporary prostate cancer diagnosis following PSA detection makes it difficult to estimate the efficacy of surgery for many men.

Holmberg L, Adami HO, Bill-Axelson A. Radical prostatectomy or watchful waiting in early prostate cancer. *N Eng J Med* 2024; 391:1362–4.

Van As et al. conducted a phase 3 trial of stereotactic body radiotherapy for

localised prostate cancer. They randomised 874 patients in an international open-label, randomised controlled trial comparing stereotactic body radiotherapy (SBRT) against conventional or moderately hypo-fractionated intensity-modulated radiotherapy. Men included had stage T1 or T2 disease, a Gleason score of 3 + 4 or less, and a PSA score ≤ 20 ng/mL. SBRT was delivered in five fractions of 36.25 Gy over a period of one to two weeks. Conventional therapy was given in 39 fractions of 78 Gy given over 7.5 weeks or 20 fractions of 62 Gy given over 4 weeks. None of the men received androgen deprivation therapy. At a median follow up of 74.0 months, 95.8% of men receiving SBRT were free from biochemical relapse or clinical failure compared with 94.6% of the men receiving conventional therapy. The cumulative incidence of grade 2 or higher toxicity was 26.9% in the SBRT group and 18.3% in the conventionally treated group. The authors concluded that five fraction SBRT is an equivalent option for patients with low to intermediate risk localised prostate cancer.

Van As N, Griffin C, Tree A, et al. Phase 3 trial of sterotactic body radiotherapy in localized prostate cancer. *N Eng J Med* 2024; 391:1413–25.

Daskivich et al. performed a cohort study of men with clinically localised prostate cancer treated in the Veterans Affairs health system between 2000 and 2019 to address the question whether overtreatment of prostate cancer among men with limited longevity still occurred. Life expectancy was estimate using the age-adjusted Prostate Cancer Comorbidity Index. The study population numbered 243 928. The mean age was 66.8 years. Twenty percent of the cohort had a life expectancy less than 10 years. From 2000 to 2019 the proportion of men treated who had a limited life expectancy and low-risk disease decreased from 37.4% to 14.7% but the proportion of men treated with intermediate grade disease increased from 37.6% to 59.8%. Radiotherapy was utilised in 78% of these cases. The authors concluded that radiotherapy was still commonly given to men with limited life expectancy and localised disease if they had and intermediate or high-risk disease.

Daskivish TJ, Luu M, Heard J et al. Overtreatment of prostate cancer among men with limited longevity in the active surveillance era. *JAMA Intern Med* 2024; 10:1001/Jamainternmed.2024.5994.

Research highlights is written by Peter Albertsen.