PSA levels after treatment may not be reliable predictor of survival for patients with prostate cancer

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A UCLA-led study has found treatments that reduce the risk of being diagnosed with a cancer recurrence based on rising prostate-specific

antigen (PSA) levels after radiotherapy, commonly referred to as biochemical recurrence, do not necessarily improve a patient's long-term overall survival.

The team of investigators found that while biochemical recurrence was associated with a higher risk of death, it still did not meet the criteria to be a reliable surrogate endpoint for overall survival. As defined by the FDA, a clinical outcome directly measures whether people in a trial feel or function better, or live longer. A surrogate endpoint is a specific, relatively early outcome that reliably predicts for a clinical outcome that occurs in the longer-term.

Biochemical recurrences occur much earlier in the disease course than metastases or survival, and could potentially be the ideal surrogate endpoint for prostate cancer. Therefore, the team evaluated whether biochemical recurrence could be a useful surrogate endpoint for death. This has implications for not only designing clinical trials, but also for evaluating the benefit of various forms of treatment intensification and for counseling patients.

"One reason for our finding could be that many patients in the study died from causes unrelated to prostate cancer," said Dr. Amar Kishan, an associate professor of radiation oncology at the David Geffen School of Medicine at UCLA and a researcher at the UCLA Health Jonsson Comprehensive Cancer Center, and senior author of the study published in the *Journal of Clinical Oncology*.

"The strength of the correlation between biochemical recurrence and overall survival varied depending on how deaths from non-cancer-related causes were accounted for. However, it is important to note that we looked specifically at death, and not at quality of life. Certainly, biochemical recurrence could impact quality of life. Unfortunately, high-level data tracking this are lacking, and it is something our group, and

others, are hoping to explore further."

Biochemical recurrence develops in almost one-third of men with prostate cancer after treatment with prostatectomy or radiation therapy for localized prostate cancer. It often occurs early on in the course of prostate cancer and indicates the cancer might be coming back. Because of this, it has been theorized to be a potential marker to predict a patient's overall survival outcome. However, previous analyses have yielded conflicting conclusions about whether or not biochemical recurrence could be a reliable predictor of overall survival for patients treated for prostate cancer.

The researchers collected and analyzed data from 11 different studies evaluating radiation therapy dose escalation, the use of androgen deprivation therapy and androgen deprivation therapy prolongation to evaluate the potential of biochemical recurrence as a predictor of survival. Overall, 10,741 patients were included in the analysis.

Despite the potential of using biochemical recurrence as a potential marker to predict overall survival in patients with prostate cancer, the results of the study indicates that it should not be the main focus or primary measure in future clinical trials for localized prostate cancer. Instead, metastasis-free survival, which refers to the period without cancer spreading to other parts of the body, is a more suitable endpoint for future trials involving radiation therapy in localized prostate cancer cases.

More information: Soumyajit Roy et al, Biochemical Recurrence Surrogacy for Clinical Outcomes After Radiotherapy for Adenocarcinoma of the Prostate, *Journal of Clinical Oncology* (2023). DOI: 10.1200/JCO.23.00617 , ascopubs.org/doi/10.1200/JCO.23.00617