**Purpose of the Study**
The purpose of the study was to evaluate factors that predict death from prostate cancer in men who have a rapid rise in PSA levels soon after radical prostatectomy or external beam radiation therapy.

**Study Population**
The analysis population for this study consisted of 1,159 men chosen from 8,669 patients treated with radical prostatectomy or radiation therapy between Jan. 1, 1988-Jan. 1, 2002. All 8,669 patients provided consent forms and pretreatment, treatment and follow-up information to either of two databases – the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) or the Center for Prostate Disease Research (CPDR).

The 1,159 men were chosen because they all shared the following characteristics: their prostate cancer at diagnosis had not spread to distant areas of the body by way of the lymph system or bloodstream, so therefore was “localized” or locally advanced only; all in the group developed PSA failure after treatment with radical prostatectomy or radiation therapy and all received hormone therapy (up to 3 months only) at some point after PSA failure and before their bone scan was positive. “PSA failure“ is identified as three rises in PSA levels that occur one after the other following treatment for men with radiation therapy and as two consecutive PSA levels greater than or equal to 0.2 ng/mL for men with radical prostatectomy.

The study groups’ median age was 64.3 for those treated with radical prostatectomy (498 men), and 71.1 years for those treated with radiation therapy (661 men). All study patients provided a medical history, had a physical examination including a digital rectal exam, had a PSA test, and a transrectal ultrasound-guided needle biopsy of the prostate to determine the Gleason grading score (a method of classifying the projected growth rate of prostate cancer cells) and cancer staging. Their median follow-up time – starting the first day of treatment – was more than 6 years.

**Results.** Some study findings were:
PSA failure may occur in up to 30% of patients up to 10 years after radical prostatectomy or radiation therapy. However, only a small subset of these patients will develop prostate cancer that spreads beyond the prostate. And because of other possible causes of mortality, even a smaller percentage will die of prostate cancer.

Patients at high risk for prostate cancer-specific mortality (PCSM) after PSA failure can be identified based on how quickly after radical prostatectomy or radiation therapy their PSA value doubles (“PSA doubling time”), and based on their biopsy Gleason score.
Results (continued)

♦ The following factors were significantly associated with PCSM: a PSA doubling time of less than 3 months after radical prostatectomy, a PSA doubling time of less than 3 months after radiation therapy, and a biopsy Gleason score of 8 to 10 for patients treated with radiation therapy.

♦ Post-radical prostatectomy estimated rates of death 5 years after PSA failure were 31% for patients with PSA doubling time of less than 3 months. Post-radiation therapy estimated rates of death 5 years after PSA failure were 75% for patients with a biopsy Gleason score of more than 8 and PSA doubling time of less than 3 months.

♦ Only PSA doubling time was a significant predictor of time to PCSM after PSA failure post-radical prostatectomy. (Neither Gleason score nor time from treatment to time to PSA failure was significantly associated with time to death from prostate cancer.)

♦ Post-radiation therapy, all three predictors – PSA doubling time, biopsy Gleason score, and time from treatment to time to PSA failure – were significantly associated with time to PCSM after PSA failure.

Study Limitations
Determining the precise factors associated with PCSM after PSA failure is difficult because of the long development course of prostate cancer and because of other causes of death.

The median follow-up time of the study was almost 7 years, which is still a relatively short period given the long natural history of prostate cancer.

Only 25 patients died of prostate cancer in the post radical prostatectomy group indicating a lack of significance of a prostatectomy Gleason score of 8 to 10 to predict PCSM in surgically managed patients.

Pretreatment patient testosterone levels were not available leading to the question of pretreatment functional castration in some of the study patients.

Conclusion
A rapidly rising PSA level after treatment in men with localized disease is a significant problem in the management of prostate cancer. Because patients are very different from each other with regard to their risk of dying from prostate cancer or from other competing causes, it is important to identify the group of patients who have PSA failure soon after treatment and who are therefore at highest risk of prostate cancer mortality. These patients can be identified based on their PSA doubling time after surgery or their PSA doubling time and biopsy Gleason score after radiation therapy. Such patients would be suited for additional treatment and involvement in studies comparing the use of hormonal therapy alone with hormonal therapy plus a chemotherapy that targets hormone-resistant prostate cancer.

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