Management of Prostate Cancer After Prostatectomy

Treating the Patient, Not the PSA

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MEASUREMENT OF THE LEVEL OF PROSTATE-specific antigen (PSA) in the blood has had a profound impact on the management of prostate cancer. Heated debates surround early detection and screening.[1-5] Equally controversial is the use and interpretation of serial changes in PSA values for assessing outcomes and determining prognosis.[6] For the patient who has undergone a radical prostatectomy, a persistent PSA value is a sign of residual disease, but an undetectable value does not necessarily mean cure. But what if the PSA value had been undetectable and then becomes detectable and continues to increase? A rising PSA value can predate other signs of progression by months or even years.[7] Misinterpretation of the significance of the change in PSA levels can create havoc for patients who are profoundly concerned with their PSA determinations and for physicians who must address the anxieties and fears of their patients. Unfortunately, documentation of rising values also often triggers a cascade of expensive testing that can prompt the administration of treatments that may be unnecessary and, perhaps, more detrimental to the patient than the disease itself.

The article by Pound et al[8] in this issue of THE JOURNAL begins to provide information on how to place in perspective "treatment failure" signified first by the detection and later by serial increases in PSA values in the patient treated by a radical prostatectomy. The initial importance of this study is that it provides evidence that a rising PSA level after surgery is not a death warrant for all patients. Patients and physicians must place these results in context, recognizing that left untreated, the natural history of prostate cancer is to progress. However, doing so requires never losing focus of the reasons for treating cancer in patients, by concentrating on clinical objectives and not solely on the PSA level.

The objectives of treating a rising PSA level are to prevent metastases, symptoms, or death due to prostate cancer. Central to this approach is the ability to define and to redefine continually the prognosis of patients as the natural and treated course of their disease unfolds. Not all patients with relapsing disease have an equal risk of death due to prostate cancer and only some will develop clinical metastatic disease or symptoms of disease in their lifetimes. Do all need immediate intervention? No. Do all need any treatment? No.

The study by Pound et al provides some order to the chaos associated with the management of the patient whose PSA value increases after radical surgery by distinguishing *advanced* (PSA level increase only) from *lethal* (metastases detected on imaging studies) disease in a more objective manner. Recognizing that all men with detectable metastatic disease in the series who have died did so of prostate cancer stresses the need to ensure that the therapeutic objective in treating such patients is to avoid their developing metastatic disease.

Pound et al report the outcomes of 1997 men who underwent a radical prostatectomy by the same surgeon over a 15-year period. Pathologic findings were consistently classified, and follow-up routines were standardized. But perhaps the most difficult and unique aspect of this series was that, after their prostatectomies, patients were not offered treatment solely on the basis of rising PSA values. Treatment was offered only when metastases or symptoms of disease were documented. This analysis was possible in large part because of the rigorous treatment policy by which interventions were deferred until metastatic disease was documented. Adherence to such a policy is extremely difficult given the anxieties of patients and the pressures on physicians to provide treatment for a cancer that is "growing."

The median follow-up was 5.3 years (range, 0.5 to 15 years). At the time of analysis, 315 patients' disease had recurred to an advanced state, defined as a detectable PSA value but with no clinical evidence of metastasis. Of these, 136 patients had experienced biochemical recurrence within 2 years and 108 between 2 and 5 years. Seventy-one had been biochemically free for more than 5 years and some of these for more than 10 years. The late recurrences contrast with the results of others[9] and show the importance of continued follow-up. In univariate analysis, only 4% (60/1345) of patients with organ-confined disease or capsular penetration experienced recurrence vs 62% (151/653) of patients with a Gleason tumor score of between 8 and 10. That only

See also p 1591.

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