Commentary (Huben): Management of Asymptomatic Rising PSA After Prostatectomy or Radiation Therapy

As the number of cases of newly diagnosed prostate cancer has risen dramatically in the United States during the past decade, the management of a rising prostate-specific antigen (PSA) level following definitive therapy has become an increasingly common dilemma. Waxman and associates provide a concise, focused review of many of the key issues and controversies surrounding this dilemma. Several of these issues warrant particular attention.

Rising PSA Following Surgery

The authors appropriately indicate the critical role of serum PSA in the follow-up of patients with prostate cancer. Regardless of therapy, a rising PSA means disease recurrence or progression. The question of disease status is more obvious following radical prostatectomy, at which point PSA should be undetectable.

Observation may be appropriate in selected patients with a rising PSA following radical prostatectomy, since several articles have shown that a rising PSA is not necessarily associated with other clinical indications of relapse. In a large series from Johns Hopkins, a significant majority of patients managed expectantly had an isolated PSA as the only sign of disease progression, up to an average of 2½ years after detection.[1] However, we often feel compelled to "do something" about a rising PSA, particularly if we believe that adjuvant or adjunctive therapy offers a second chance for cure.

Patients themselves are acutely aware of the implications of a rising PSA following radical prostatectomy; namely--that their surgery has failed to effect a "cure" of their disease. Patients (and their physicians) are often uncomfortable with an expectant approach in this situation and, in many cases, will seek out additional therapy.

Adjuvant Radiation Therapy Following Surgery

A strong argument can be made for administering adjuvant radiation therapy in selected patients with a rising PSA following surgery. As the authors point out, factors such as Gleason score, pathologic stage, and PSA velocity may be useful in predicting the likelihood of benefit from adjuvant radiation. Interestingly, the presence of positive surgical margins does not appear to be a risk factor, since only 30% to 40% of patients with focally positive margins progress at 5 years.[2] A case can therefore be made against the use of adjuvant radiation therapy following radical prostatectomy in the absence of a rising PSA as an indicator of local recurrence. Also, random biopsy of the anastomotic area is of limited value in predicting response to adjuvant radiation therapy, since a significant percentage of patients may demonstrate a reduction in PSA to an undetectable range following radiation therapy even in the face of a negative random biopsy.[3]

Most of these criteria, whether considered singly or in combination, fail to predict response of the individual patient to adjuvant radiation. Consequently, treatment is often empiric. The clear exception, as the authors state, is the patient in whom PSA fails to fall to an undetectable range following surgery, and for whom adjuvant radiation is an exercise in futility.
In our experience, PSA will return to an undetectable range in a clear majority (about 80%) of patients treated with adjuvant radiation following radical prostatectomy, and the response will be durable in about 60%. Thus, nearly 50% of patients will derive a sustained benefit from adjuvant radiation therapy, and this will likely result in cure of their prostate cancer. It has also been our experience that when one weighs the risks of treatment vs the benefits, most patients tolerate adjuvant radiation therapy remarkably well.

**Patients With Persistent Disease After Adjuvant Radiation**

As Waxman et al mention, additional or salvage local therapies for biopsy-proven persistence of prostate cancer following radiation therapy are associated with frequent and serious complications. Candidates for salvage prostatectomy should be very carefully selected and be made fully aware of the probability and nature of these complications. For example, rectal injury will require a diverting colostomy to reduce the risk of a rectourethral fistula. Cryosurgery appears to be an attractive option in this clinical situation, but further experience with this technique is needed before its niche is established.

Given the limited options, hormonal ablation is the usual treatment choice for patients in whom radiation therapy failed. Once again, the rate of climb of the serum PSA is the usual indicator to initiate hormonal therapy. At what PSA value should treatment start? At our institution, we generally recommend that hormone therapy be initiated, without further clinical staging, when the PSA is in the 10- to 12-ng/mL range. At this level, there is little doubt of treatment failure and it is unlikely that symptoms of disease progression have developed that may distress the patient.

**Need to Individualize Treatment**

Lastly, this reviewer is very much in agreement with the authors' emphasis on the necessity to individualize treatment recommendations according to the needs of the patient. Therapeutic interventions must address equally the probability of benefit vs the risk of complications. The key element in ensuring treatment success is careful patient selection. Our desire to intercede must be tempered by the caveat to "first do no harm."

**References**


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