

SURGICAL RESULTS OF PROSTATE CANCER TREATMENT

By: Gil Lederman, MD

One of the great debates ongoing in oncology is the role of surgery versus sophisticated radiation for treatment of apparently localized prostate carcinoma.

While new treatment techniques have been developed for those with prostate carcinoma, the so-called "gold standard" - at least by some - has been the radical prostatectomy.

A recent analysis by D'Amico et al and published in The Journal of Clinical Oncology evaluated the results of 341 men who have undergone radical prostatectomy over recent years (between 1989 and 1995) with at least one year follow-up. An important criterion was that all patients had to have pathologically organ-confined disease as well as margins of surgical resection free of cancer.

Obviously since many men at the time of surgery had cancer that extended to or beyond the margin, these patients did not qualify for this study. The purpose of the study in this select group of patients was to determine the rate of treatment failure when allegedly "all the cancer was seemingly removed."

Work-up prior to treatment included history and physical examination, blood testing, CT scans or MRI scans as well as bone scans and needle biopsy of the prostate. If there was evidence of cancer spread beyond the prostate including involvement of seminal vesicles or extracapsular disease, these patients were excluded from the analysis. Furthermore, all patients underwent lymph node sampling and if lymph nodes were involved, then these patients were also excluded. Any patient who had any hormonal therapy was, as well, excluded from the study.

According to the authors, all patients were seen at least on an every three-month follow-up for the first two years and then regularly thereafter with "no patient lost to follow-up examination."

Post-operatively PSA (Prostatic Specific Antigen) levels were said to be detectable if they were greater than or equal to 0.2 nanogram (ng) per cubic centimeter (cc). One month after surgery, patients with elevated PSA were said to have persistent PSA; and those with two consecutive detectable PSA levels after a non-detectable level were called an increasing PSA.

The authors noted that the time of PSA failure was the time of the first of the rising PSA levels post-operatively. The date of surgery was time zero. For example, if the first PSA at three months was elevated, it was called a PSA failure at time zero. Since this is a recent analysis, the median follow-up was only 36 months.

Of 341 men thus analyzed, 13% had initial PSA levels (prior to surgery) of zero to 4, 62% had PSA levels of 4 to 10, 20% had PSA levels of 10 to 20, and 5% had PSA levels greater than 20.

Of Gleason pathologic scores in men evaluated, 18% had scores of 2 to 4, 51% had scores of 5 to 6 and 31% had scores 7 or greater.

The authors found that PSA level and pathologic Gleason score were "significant predictors of early post-operative PSA failure (i.e., within the first post-operative year)." If patients had Gleason score of 7 or greater and a PSA of 10 or greater, 40% had already relapsed at only three years after surgery.

This is quite a large number of patients relapsing especially since those who had either one or both of these high risk characteristics totaled 156 of the 341 men analyzed or 46% of the total group. It must be remembered that these failures occurred despite all margins being allegedly free of cancer.

The group with Gleason scores of 6 or less and PSA levels of 10 or less did better - having a four year freedom from relapse of 90%. Of course, this group would be expected to do well in most any event because of the low risk potential for recurrence.

While it is commonly thought that patients whose cancer is totally removed should fare well, this study would negate that notion. Complete surgical removal in these situations is not associated with high freedom from relapse rates.

In fact because of the high relapse rates, the authors suggested that these identified risk factors serve as a basis for patients to be treated in other manners than just pure surgery.

Others have found that even with negative margins in pathologically-confined prostate cancer as well as negative bone scans at the time of rising post-operative PSA levels, 20% of patients have a biopsy-proven local recurrence - that is, cancer that has recurred in the tumor bed despite surgery.

A possibility raised by the authors was whether "consideration should be given to combining local field post-operative external beam radiation therapy (which can sterilize both androgen independent and dependent cells) with total androgen suppression. The adjuvant use of radiotherapy (i.e., when the post-operative PSA level is usually undetectable), as opposed to giving the treatment at the time of a rising PSA level, is a potentially important distinction. Several retrospective studies have shown that long-term freedom from PSA failure in post-prostatectomy setting is strongly associated with the delivery of post-operative radiation therapy to patients with a low (less than or equal to 1.1ng per cc) or undetectable post-operative PSA level."

The authors concluded that "Therefore, it is possible that the delivery of adjuvant androgen suppression and/or radiation therapy to patients with pathologically organ-confined and margin negative disease who have the clinical and/or pathologic predictors of early PSA failure may improve survival. The results of this study support the selection of pathologically organ-confined and margin-negative patients with high grade (pathological Gleason score greater than or equal to 7) or high PSA level (greater than 10ng per cc) disease for entry onto a Phase III adjuvant therapy trial."

Of course, other investigators are directing attention in other less invasive directions. The role of sophisticated external beam radiation therapy as well as radiation seed implantation offers great appeal in avoiding both the radical prostatectomy and its post-operative complications and convalescence. Early data shows at least equivalence if not superiority, avoiding the known surgical risks for these minimally invasive approaches.

Addendum:

What is so impressive about this paper is the high recurrence rate in men who have surgery even when it seems all the cancer has been removed. There have been ongoing theories for many years that, in fact, the surgeon may well spread the cancer cells at the time of surgery. It is such a paradox that at the time of treatment to remove the cancer cell, in fact, cancer cells are spread and the disease is made more difficult to treat.

Personally, comparing our results to surgery even in the so-called best hands showing advantage to our patients undergoing seeds plus body radiosurgery makes one believe that surgery spreads

cancer cells. Since surgery supposedly removes all the prostate cancer, surgery should also seemingly have the best outcome. The fact that it does not speaks for itself. The fact that we can radiate and get a better outcome in terms of cancer-free survival than the surgeon suggests that one should attempt to AVOID manipulation of the prostate. This is especially true with high risk cancers. This data is compelling and is another reason to consider avoiding radical prostatectomy for treatment of prostate cancer. Other reasons to avoid radical prostatectomy are the morbidity and mortality. Some men even die during surgery or the immediate post-op period. Additionally, quality of life issues such as urinary control and sexual function appear to be superior in men undergoing radiation compared to surgical treatment.