

PROSTATE CANCER SURVIVAL STUDY

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Prostate cancer is the most common cancer in men in the United States with 186,320 cases reported to the National Cancer Institute in 2008. In addition, prostate cancer remains the second most common cause of death from cancer in males with 28,660 cases reported in 2008. Prostate cancer has been and remains a significant health problem that affects approximately one in six American males.

The best treatment for localized prostate cancer can be controversial and include expectant management, radical prostatectomy, various forms of radiation therapy, cryotherapy, hormonal therapy, and high intensity focused ultrasound. It is beyond the scope of this article to recommend one course of therapy over another; however, we intend to report the University of Tennessee Medical Center (UTMC) survival data and management of prostate patients who received brachytherapy with or without adjuvant external beam therapy (BRT) and patients treated with or without adjuvant hormone deprivation (AHD).

Methods:

Data of interest was extracted from the UTMC Tumor Registry from the period of January 1998 to December 2007. This data includes the number of new cases of prostate cancer detected by year, mortality from prostate cancer by year, age at diagnosis, stage at diagnosis, Gleason score at diagnosis, and the overall distribution of treatment modalities.

Specifically with regard to brachytherapy modalities, data on survival by stage at diagnosis was extracted and will be compared to other reported data in the literature.

Results:

Prostate Cancer Incidence:

The number of new cases of prostate cancer detected at UTMCK through the Tumor Registry for consecutive ten-year periods is shown in Figure 1. There has been a steady rise since the late 1990s which can be attributed to several factors: (1) increase in urology staff specifically interested in prostate cancer diagnosis and management, (2) multiple prostate cancer screenings per year, (3) the advent of PSA screening, and (4) wider outreach programs increasing referrals to UTMC.

Prostate Cancer Mortality

The number of deaths per year from prostate cancer over a 30 year period is shown in Figure 2. The number of deaths has remained relatively constant except for bumps in 2004 and 2007 which is not directly explainable. Overall in Tennessee for the period 2001-2005 prostate cancer mortality has decreased 3.5% (Figure 3).

Age at Diagnosis of Prostate Cancer.

The age of diagnosis of prostate cancer is shown in Figure 4. Approximately 94% of diagnoses occurred between the ages of 50 and 80. When comparing this data to the previous 20 year period (Figure 4a), more men in their 40s were diagnosed. This phenomenon is probably based on more public awareness, screening activities, and age adjustment to normal PSA values.

Stage at Diagnosis of Prostate Cancer.

TNM classification of prostate cancer is shown in Figure 5. Basically, T₁ and T₂ (Stage I or II) is organ confined disease. Stage T₃ (III) means extra prostatic capsule extension of disease and Stage IV is metastatic disease. Over the past 30 years, there has been significant stage migration such that now 84% of diagnosed cases are prostate gland confined compared to 32% in 1978 (Figure 5a). Remarkably, the incidence of men presenting with metastatic disease is now 3.2% compared to 47% in 1978.

Gleason Score.

The Gleason score is determined by pathology for grading prostate cancer. Separate areas of tumor are graded 1 to 5 and the sum equals the Gleason score. We only have Gleason data beginning in 2004 but most cases were classified as 6 or 7 (85%) as shown in Figure 6. It should be mentioned that Gleason score evaluation has recently changed and newer data will show higher rates of 7 and 8. Likewise, Gleason score is important in risk stratification of prostate cancer (see Table 1) and is an important factor in the management algorithm.

Prostate Cancer Treatment

Trends in prostate cancer treatment have certainly changed by decade. In 2008, the most common options would include (1) expectant management, (2) hormone deprivation, (3) radiation therapy to include external beam (ERT), brachytherapy, combined ERT and brachytherapy, combined ERT and high dose brachytherapy and CyberKnife, (4) radical prostatectomy, (5) cryotherapy, and (6) high intensity focused ultrasound (HIFU). It should be noted that HIFU is not yet FDA approved in the United States and not offered at UTMC. Likewise, cryotherapy is an option but also not offered at UTMC.

Figure 7 shows the treatment options broken down by per cent over the last ten years. Surgical extirpation is approximately 37% while radiation modalities constitute approximately 60% of the cases. This is a significant change when compared to 1997 when surgery constituted 54% of treated cases and radiation only 22% (Figure 7a). The major reason these numbers changed was the initiation of the brachytherapy protocol in 1998. With the advent of minimally invasive radical prostatectomies (Da Vinci Robot) in 2006, it is likely that a review in another ten years will also reflect different trends.

Prostate Cancer Survival by Stage.

Overall, prostate cancer survival by stage at UTMC is shown in Figure 8. Compared to national data from 138 programs for the same period, there is no significant difference stage by stage. If one compares these results to the curves published in 1990, Figure 9, there is across the board improvement. The survival curves for brachytherapy with or without adjuvant external beam therapy and hormones are shown in Figure 10. At 5 years, there is no significant difference in survival; however, there is drop-off at 10 years as would be expected. Patients treated with adjuvant hormones had higher stage disease and higher Gleason scores portending a poorer prognosis.

Discussion:

Brachy in Greek stands for being close or a short distance. In contrast to conventional EBRT, the radiation sources are in or near the targeted organ. Therefore, brachytherapy can provide high intraprostatic doses of radiation that are not achievable with EBRT while sparing toxic effects on the surrounding tissue. Likewise, since the radiation sources are in the targeted organ, organ movement during treatment does not affect efficacy or toxicity.

Encapsulated radiation sources have been available since the 1970s. Originally, Au¹⁰³ was used but exposure to personnel was unacceptable and adjuvant EBRT was always necessary. With the introduction of iodine¹²⁵ and subsequently Pd¹⁰³ radiation sources, brachytherapy became more acceptable. However, the newer techniques with careful computer dosimetry mapping and real time planning only appeared on the scene in the last 15 years or so. In the 21st century, brachytherapy with or without EBRT is an acceptable treatment modality with low morbidity and is well accepted as successful therapy stage for stage with other treatment modalities.

Patients with localized prostate cancer are now stratified according to risk category with well documented treatment regimens published per stratification. Brachytherapy as monotherapy is suitable for patients with clinical Stage T₁ or T₂ disease, Gleason sum of ≤ 6 and PSA < 10 mg/ml. Brachytherapy following EBRT is indicated for high risk patients with clinical Stage T_{2b} or T_{2c} disease and Gleason sums of ≥ 20 mg/ml. With regard to intermediate risk patients with low volume low PSA and Gleason 3+4, brachytherapy alone can be considered; however, those with higher PSAs and more extensive disease are better treated with combined therapy.

Exclusion criteria for brachytherapy are also well known and include patients with life expectancy of less than 5 years, large or poorly healed transurethral defects, unacceptable operative risks, and distant metastases. Relative contraindicators to brachytherapy include patients with high I-PSS scores, previous pelvic radiation, large median lobes and severe diabetes with healing problems. Likewise, technical problems exist with prostate size >60 gms and seminal vesical invasion.

In patients with large glands, ADT in the form of LHRH analog or bicalutamide and dutasteride may be used with mean prostatic volume reduction of 33% after an average of 3.7 months. It should be noted, however, that although neoadjuvant ADT is routinely used for downsizing large glands, there is no definite survival benefit for continued therapy and it may significantly reduce quality of life.

Overall, complications and toxicity with modern brachytherapy regimens are low. Mild irritative urinary symptoms including dribbling, frequency or urgency occur in many for one to two months and gradually subside. Potency rates overall run as high as 70% with the help of PDE⁵ inhibitors. Incontinence and severe anorectal toxicities or morbidities are also uncommon and range from 0-2% in most published series.

It should be emphasized that most modern trials indicate biochemical control rates with brachytherapy approach or are equivalent to those seen with radical prostatectomy. Brachytherapy is a safe, highly effective therapy that is administered on an outpatient basis, is associated with easy recovery, and has a shorter overall treatment time. High volume institutions or centers of excellence will achieve high success rates with the least morbidity. UTMC fits these criteria having performed in excess of 1500 implants to date.