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**Effect of External Beam Radiation versus Radical Prostatectomy
On Patient Mortality and Quality of Life**

By

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Capstone Project

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Introduction

In 2015 there were 183,529 new cases of prostate cancer reported and 28,848 men died from prostate cancer in the United States, according to the Center for Disease Control (CDC). Prostate cancer is the most prevalent cancer in US men, affecting 99 out of every 100,000 with the next highest being lung cancer effecting 66 per 100,000 men. According to the CDC, the rate of new prostate cancer diagnoses has declined from 169 per 100,000 men in 1999 to the current 99 per 100,000 in 2015. This data is affected by the growing and aging population in the US each year. Looking at the number of new cases of prostate cancer beginning in 1999, there were 196,349 cases reported, which is slightly higher than the number in 2015, but not proportional to the change in rate. Prostate cancer rates double every 5 years after the age of 50 and are highest amongst men between 65 and 75 at a rate of 580 per 100,000 in this age group.¹

Since prostate cancer prevalence is so high, multiple treatment modalities have been developed, with a curative goal. The most common prostate cancer treatments include radical prostatectomy (RP), which is simple removal of the prostate; and external beam radiation therapy (EBRT), which is destruction of the cancer cells via direct focused beams of radiation aimed at the tumor from outside the body.² Other treatment modalities for prostate cancer exist, but these two particular modalities are the subject of this literary review. Both treatments have different cancer related mortality outcomes; and both have varying side effects, which can affect the patient's quality of life. These side effects most commonly include urinary incontinence and erectile dysfunction, but may also include rectal pain, dysuria, fatigue, depression and secondary malignancy.³⁻⁴ There have been many studies identifying the efficacy and patient mortality rates associated with each treatment modality. However, there have been conflicting

findings, and they do not incorporate the effects on quality of life. The aim of this literary review is to examine men over 60 years old with localized prostate cancer; then determine the effect of external beam radiation on quality of life and mortality compared to radical prostatectomy. The hope is to paint a clearer picture, so that a single treatment modality can be the primary choice for these patients in the future.

Prostate Cancer Mortality After Treatment

One of the most valuable statistics, when assessing treatment modalities, is the mortality rate after treatment with each type. More specifically, the mortality rates of patients with localized prostate cancer treated with radical prostatectomy, external beam radiation therapy or another modality. There have been numerous primary, population-based and retrospective studies identifying mortality rates of these treatments, but there has been a large variation in these results. It is important to note that there is a variable application with each modality. Regarding radical prostatectomy, there are different approaches surgeons can take, including robotically assisted procedures. External radiation will have different doses of radiation, and the precision at which the radiation is delivered represents a variable. The aim is to measure each of these modalities in their entirety, regardless of their approach or variables in implementation.

Radical prostatectomy was most often compared to EBRT, since these are the two leading treatments for localized prostate cancer. A study assessing 10-year survival rates of men with localized prostate cancer that underwent RP and EBRT found the 10-year survival probability was 75.3% after RP and 36.7% after EBRT. In a multivariate Cox regression model, EBRT was associated with a 3.9-fold higher chance of mortality in the entire study group.⁵ This study was limited by the inclusion of all levels of Gleason scores, including the poorly differentiated. The

study also included individuals who were already at lower probability for 10-year survival, due to comorbidities. This study demonstrated a wide difference in survival rates between EBRT and RP, but other population-based studies did not yield similar results.

A study was performed with the goal to assess the survival among men with localized prostate cancer who received RP or EBRT, but also included patients treated with brachytherapy. Patients with localized prostate cancer were included in the study and were treated with RP, EBRT and brachytherapy. The results of this study demonstrated a 10-year overall survival of 88.9% (RP), 82.6% (EBRT) and 81.7% (BT).⁶ The prostate cancer specific mortality was found to be lowest amongst patients who received RP. In conclusion, this study found that EBRT was associated with a significantly increased risk of prostate cancer specific mortality compared to radical prostatectomy. BT was also associated with a significantly decreased overall survival compared to RP. The difference in 10-year survival probability in this paper did not vary as much as the findings from the prior study,⁵ but still demonstrated that RP was associated with a statistically significant improvement in overall and cancer specific mortality.

The findings that RP has improved mortality outcomes compared to other modalities was echoed in a similar article. In a population based analysis, 68,665 patients with localized prostate cancer were treated with RP or EBRT and their cancer caused mortality was assessed. The results of this analysis demonstrated that the 10-year cancer specific mortality rates of EBRT was over 2-fold higher than RP. In patients aged 65-69 years old the 10-year cancer specific mortality rate for EBRT was 2.7% higher than RP.⁷ The results showed radiotherapy was associated with statistically significant less favorable cancer-specific mortality amongst all age ranges and prostate cancer grades. The author concluded that patients undergoing prostatectomy fare

substantially better than those treated with radiation therapy, especially for patients with high-risk prostate cancer. The benefit of this study, is the sample group was divided into age ranges; cancer risks; and adjusted for comorbidities, which could influence the overall survival rates. These findings again state that radical prostatectomy was associated with better mortality outcomes compared to radiation therapy.

The tumor risk of metastasis or local spread is a variable that some studies addressed and could potentially have an impact on the survival rates of patients who underwent different treatment modalities. Even if the prostate cancer is localized, there is still potential for spread, which can change the recommendation for treatment. A study was performed to analyze the long-term survival of high-risk prostate cancer patients who were treated with RP vs EBRT. Their population-based analysis identified 1,238 patients who were treated with RP, and 609 treated with EBRT between 1988-2004. The inclusion criteria was a PSA \geq 20ng/mL; Gleason score 8-10; and tumor stage of \geq T3.⁸ At this tumor stage the cancer is still localized, but has potentially spread to the surrounding tissue. The results of this study demonstrated that the 10-year cancer specific survival was 92% for the RP group and 88% for the EBRT group.⁸ The risk of all-cause mortality was found to be statistically significantly greater in the EBRT group compared to the RP group.⁸ The author felt continued investigation into the variable impact of prostate cancer therapies on quality-of-life and non-cancer mortality was important to aid in identifying the optimal treatment for these patients.

The population-based studies, above all, demonstrated that radical prostatectomy was associated with high 10-year cancer specific survival outcomes, or lower cancer specific mortality rates compared to external beam radiation. These results were consistent with the findings of

eight other population-based studies and retrospective analyses studies, which were identified throughout the literature review. However, the impact on quality-of-life is a major deciding factor for patients undergoing prostate cancer treatment and is the second variable this article will attempt to identify.

Treatment Impact on Quality-of-Life

Patients undergoing treatment for prostate cancer are most often concerned with the impact each treatment modality has on their quality of life. There are several symptoms that are associated with each type of treatment, and some symptoms are shared by multiple treatments. There is an importance of educating patients on these side effects of treatment, as this may guide their selection, but the aim is to identify the treatment with least impact on quality of life. However, analyzing the symptoms is difficult, as well as predicting which patients may become symptomatic. The most common and most irritating symptoms were identified in hopes of determining a treatment plan associated with the least impact on quality of life.

A study performed to evaluate the quality of life outcomes used data obtained for 4 years after treatment for local prostate cancer in 475 patients. This was performed by interviewing patients and administering a questionnaire where they identified their most concerning symptoms. Urinary incontinence was the most commonly reported symptom and occurred in 307 patients receiving RP and 78 patients receiving EBRT.⁹ Sexual dysfunction affected all treatment groups in the study, but radical prostatectomy demonstrated a higher chance of regaining baseline function compared to EBRT.⁹ Bowel dysfunction was observed to occur with more frequency in patients receiving EBRT than RP. The strengths of this study were the documentation of the patient's pre-treatment baseline, so they could assess any subsequent

decline in function or new symptoms and their possible return to baseline. This analysis was limited, because there were no statistical analytical tools that could be performed to qualify the effects on quality of life. Patients who had cancer recurrence were not separated from the study, and this recurrence can negatively impact the patients' well-being.

In an attempt to mitigate some of the common side effects patients experience after treatment, there have been new developments in how these procedures are performed, specifically radical prostatectomy. Nerve sparing radical prostatectomy procedures have increased in prevalence in recent years, creating a decrease in urinary symptoms after treatment. In a prospective study, 1201 patients and 625 spouses were evaluated to measure treatment outcomes and patient satisfaction. Five hundred sixty-one of these patients underwent nerve sparing radical prostatectomy; 41 underwent non-nerve sparing procedures; and 202 patients received EBRT. Health-related quality of life was evaluated before, during, and after treatments in domains of sexual function, urinary incontinence, urinary irritation or obstruction, urinary function, bowel or rectal function and vitality of hormonal control.¹⁰ It was found that all groups reported their sexual quality of life was affected, but patients in the nerve-sparing RP group had better recovery of sexual quality of life compared to non-nerve sparing RP. However, 44% of men in the RP group reported erectile dysfunction compared to 22% in the EBRT group. Urinary incontinence peaked at two months after surgery and then gradually returned to baseline for most patients, and their baseline scores of urinary irritation and obstruction improved after RP. The EBRT groups' post-surgical urinary symptoms had resolved after 12 months and were improved over baseline after 24 months.¹⁰ Comparing urinary symptoms between RP and EBRT groups, shows 7% and 11% of patients reported worse urinary symptoms from baseline after 2

years, respectively. The bowel dysfunction was the next most significant domain and indicated that 9% of EBRT patients reported rectal urgency, pain, fecal incontinence, or hematochezia, while there were no substantive change in bowel function reported in the RP group.¹⁰ The limitations of this study is the number of coexisting illnesses and severity of cancer was highest in patients in the radiotherapy group and smallest in the RP group, which could potentially increase the negative perception on satisfaction of EBRT compared to RP. This study demonstrates that barring its limitations, RP is associated with less urinary, sexual dysfunction, and bowel symptoms compared to EBRT groups, as well as decreased recovery time of symptoms.

Decisional regret, after prostate cancer treatment, is directly correlated to post-treatment urinary symptoms and overall patient satisfaction.¹¹ In a retrospective study, a self-administered questionnaire was sent to prostate cancer patients in France. Of the completed questionnaires, 110 patients had received RP and 28 received EBRT. The results of the questionnaire found urinary incontinence was reported by 34.5% of patients treated with RP and 17.8% of patients treated with radiotherapy only. Questions regarding decisional regret were also asked, and it was found that the main reason for decisional regret was due to incomplete information about prostate cancer. Thirty-four percent of patients contributed the regret to urinary symptoms from treatment that they were not warned about.¹¹ This study demonstrates the importance of appropriate patient education, when deciding their preferred course of treatment, especially in the era of patient-centered care.

Conclusion

In analyzing the effects of radical prostatectomy and external beam radiation therapy on prostate cancer specific mortality, almost all literature reviewed demonstrated that RP had higher probabilities of survival and lower probabilities of cancer specific mortality compared to EBRT. Quality of life outcomes were difficult to statistically evaluate, but the studies that were reviewed demonstrated a higher percentage of post-treatment symptomatic complaints with EBRT compared to RP. These two treatment modalities did share complaints of urinary incontinence and urinary irritation, but these symptoms improved and/or returned to baseline significantly sooner in the RP group compared to the EBRT group. Rectal symptoms including pain, fecal incontinence, and hematochezia were only experienced by the EBRT group. Due to the improved mortality rates and decreased severity and duration of post-treatment symptoms, radical prostatectomy is seemingly a better first-line treatment modality compared to external beam radiation therapy. Given that prostate cancer is the most prevalent cancer amongst US men, there is sufficient data to suggest that radical prostatectomy should be considered for first line treatment in individuals with localized prostate cancer. However, current studies are underway assessing the use of improved radiation therapy techniques in treatment of localized prostate cancer but this data is still not fully collected. The goal of a health care provider is to help patients make a proper decision, but that is based on the most current information, and that information is dynamic, fluid, evolving and requires further research.

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