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Statistical Evaluation of Different Prostate Cancer Treatments

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Abstract: The three commonly used treatments for prostate cancer are: radiation therapy, surgery, or combination of radiation and surgery. Our present study is using real prostate cancer data from Surveillance Epidemiology and End Results program (SEER Database) to evaluate and rank the effectiveness of these treatments using survival and basic parametric analyses. In addition, the evaluation of the subject treatment is based on the stage the prostate cancer has been classified.

1. Introduction

Prostate cancer is believed to usually occur in older men. A study by Chan, Y. M. et al. (2012) revealed that prostate cancer usually begins at age 37 but is very predominant in men at age 67. The early stage of prostate cancer usually has no symptoms. However, based on the patient's level of risk, most physicians recommend going through the screening test. The first case of prostate cancer was described by J. Adams, a surgeon at The London Hospital, in 1853. He discovered this by histological examination and noted that this was a rare disease [3]. One hundred and fifty-nine years down the line, prostate cancer has become a significant health issue partly because it is the most commonly diagnosed cancer in men with a high percentage of recorded deaths annually. In the United States, prostate cancer is the second leading cause of death in American men, behind only lung cancer. It is estimated that approximately one in six men will be diagnosed with prostate cancer in his lifetime. This year alone (2012), the estimated new cases of prostate cancer in the United States are approximately 241,740 with an estimated 28,170 deaths representing about 12% of estimated deaths by prostate cancer diagnosis [31], [32].

The increase in the incidence of prostate cancer diagnosis has led to several remarkable changes in treatment over the past century. Androgen-ablation therapy which involves medical castration with oral oestrogens was one of the first effective treatments for any cancer. This therapy dates back to the eighteenth century. Initially, several patients responded to the androgen-ablation treatment but over time developed fatal androgen-independent disease [16]. This realization led to the introduction of hormone treatment and chemotherapy. The hormone treatment was either to block the production of adrenal androgen or prevent androgen interaction within the target tissue. Chemotherapy treatment was mainly used for hormone refractory prostate cancer. Different clinical trials involving some agents of chemotherapy (mitoxantrone and corticosteroid, estramustine, vincristine, etoposide, doxorubicin, and the taxanes paclitaxel and docetaxel) emerged from 1950-1975 [17]-[20]. Results indicate survival advantage in patients treated with these chemotherapy combinations [3].

In the twentieth century, prostatectomy and radiation therapy emerged. Prostatectomy involves the use of surgical and radiological techniques to treat prostate cancer. The first systematic technique for removal of the prostate was by Hugh Hampton Young in 1904 at the Johns Hopkins Hospital [9] and the next surgical advancement was introduced by Terrence Millin in 1945 [10]. This treatment was not very common because most patients were left impotent by the procedure. However, in 1983, Patrick Walsh developed a modified technique to control bleeding allowing erectile function and sexual potency to be maintained [11]. The first report on the use of radiation to treat prostate cancer involved the introduction of radium sources as an alternative to surgery [3], [12]. This technique was initially difficult to perform and uncomfortable for patients. It lost popularity as a treatment for prostate cancer in the 1940s but returned in the 1950s after the introduction of higher-energy cobalt machines that could penetrate to deeper levels. Over the years, other radioisotopes have been developed.

Currently, there are several treatments recommended by physicians for prostate cancer. The most common types are surgery, radiation therapy, combination of surgery and radiation therapy, and hormone therapy. However, in this analysis, we will focus on the evaluation of the treatment types: surgery, radiation therapy, combination of surgery and radiation therapy, and no treatment. No treatment involves the group of patients who did not receive any form of treatment during the period under study.

2. Data Description

Data on prostate cancer patients collected from 1973 to 2008 was obtained from the Surveillance Epidemiology and End Result (SEER) program. This database has approximately 500,788 records of prostate cancer patients with several variables. However, due to page limitation, we will consider only White patients with Adenocarcinoma histology type for this analysis. A total of 21,955 records representing White patients with Adenocarcinoma histology type were obtained from the database. This number represents reported cases from 1988 to 2003. Disease characteristics such as age of patient, geographic region from which the case was reported, stage of the cancer, tumor grade, survival time, and treatment type among others were reported for each patient.

Treatment is categorized as radiation therapy, surgery, combination of radiation and surgery, and no treatment. The stage of the prostate cancer and the grade of the tumor are categorized as stage I, stage II, stage III, stage IV and grade I (well differentiated), grade II (moderately differentiated), grade III (poorly differentiated), and grade IV (undifferentiated) respectively. The 21,955 records originated from four geographic regions as follows: Northeast (Connecticut), South (Metropolitan Atlanta), Midwest (Iowa and Metropolitan Detroit), and West (San Francisco-Oakland, Hawaii, New Mexico, Seattle-Puget Sound, and Utah). The survival times are measured in years and all recorded deaths are due to prostate cancer.

2.1 Distribution of Stage of Cancer by Treatment, Region, Age, and Tumor Grade

The distribution of the stage of the prostate cancer by the type of treatment, region of cancer classification, age of the patient, and grade of the tumor are given in Table 1.

Table 1: Distribution of Stage of Cancer by Treatment, Region of Classification, Age, and Tumor Grade

	Stage I		Stage II		Stage III		Stage IV		
	n	%	n	%	n	%	n	%	Total
Overall	8265	37.7	6083	27.7	5798	26.4	1809	8.2	21955
Treatment									
Radiation	2018	55.3	1120	30.7	384	10.5	126	3.5	3648
Surgery	4736	31.9	4238	28.5	4723	31.8	1159	7.8	14856
Radiation & Surgery	440	25.8	385	22.6	585	34.4	292	17.2	1702
No Treatment	1071	61.2	340	19.4	106	6.1	232	13.3	1749
Region									
Northeast	1260	60.2	407	19.5	302	14.4	123	5.9	2092
South	259	25.6	274	27.0	420	41.5	60	5.9	1013
Midwest	2931	38.2	2111	27.5	1966	25.7	659	8.6	7667
West	3815	34.1	3291	29.4	3110	27.8	967	8.7	11183
Age (years)									
40-49	115	28.6	117	29.1	128	31.8	42	10.5	402
50-59	993	28.5	1052	30.1	1134	32.5	310	8.9	3489
60-69	2741	31.0	2487	28.1	2845	32.1	776	8.8	8849
70-79	3363	45.0	1984	26.6	1578	21.1	545	7.3	7470
80+	1053	60.3	443	25.4	113	6.5	136	7.8	1745
Tumor Grade									
I	0	0	971	69.9	342	24.6	77	5.5	1390
II	7349	44.8	4241	25.9	3890	23.7	922	5.6	16402
III	898	23.1	760	19.6	1469	37.8	756	19.5	3883
IV	18	22.2	17	21.0	35	43.2	11	13.6	81
Unknown	0	0	94	47.2	62	31.2	43	21.6	199

Overall, 37.7% of the cases were classified in stage I, 27.7% in stage II, 26.4% in stage III, and 8.2% in stage IV. The pattern of prostate cancer disease varies by treatment, region, age, and tumor grade. Variation in treatment patterns shows that of all the White patients, 67.7% had surgery, 16.6% received radiation therapy, 8.0% had no form of treatment, and 7.7% had combination of surgery and radiation therapy. Of all the patients who received radiation therapy or no treatment, more than half were classified in stage I (55.3% & 61.2%). Surgery was more typical among patients classified in stage I (31.9%), stage II (28.5%), or stage III (31.8%). Of all the patients classified under each treatment option, the proportion of patients who had combination of surgery and radiation therapy treatment was comparatively higher in stage IV (17.2% vs. 13.3, 7.8, & 3.5).

In regards to regional classification, more than half of the reported cases (51.0%) were from West region, 34.9% from Midwest region, 9.5% from Northeast region, and 4.6% from South region. Of all the reported cases from the Northeast region, 60.2% were classified in stage I. The distribution of the disease by age show that 40.3% of the patients were in their 60s, 34.0% were in their 70s, 15.9% were in their 50s, 8.0% were 80+ years, and 1.8% were in their 40s. More than half of the patients aged 80+ years

(60.3%) were classified in stage I and nearly half of the patients in their 70s were also classified in stage I (45.0%).

The overall distribution of the tumor grade revealed that approximately 74.7% of the tumors were moderately differentiated, 17.7% were poorly differentiated, 6.3% were well differentiated, 0.4% was undifferentiated and 0.9% was unknown. More than half of the well differentiated tumors were classified in stage II and nearly half of the unknown tumor grade were also classified in stage II. Among the moderately differentiated tumors, approximately 44.8% were from stage I.

2.2 Distribution of Prostate Cancer Treatment by Age and Region

Table 2 relates the pattern of treatment by age of the patient and the region of cancer classification. The data shows variation in treatment selection by age of the patient. Of all the age groups, patients are frequently treated by surgical procedure. Older patients age 80+ years frequently receive no form of cancer treatment compared to radiation therapy or combination of surgery and radiation therapy (22.3% vs. 15.6% & 3.8%). However, patients in their 70s frequently receive radiation therapy compared to no treatment or combination of surgery and radiation therapy (26.4% vs. 11.0% & 8.6%). Patients in these two age groups were less treated with combination of surgery and radiation therapy.

In regards to regional classification, patients are more frequently treated by surgical procedure in all the regions. However, in the northeast region, a reasonable proportion of the patients also received radiation therapy or no cancer related treatment. In the south region, a small number of patients had no form of cancer treatment.

Table 2: Distribution of Prostate Cancer Treatment by Age of Patient and Region of Classification

	Radiation		Surgery		Radiation & Surgery		No Treatment		
	n	%	n	%	n	%	n	%	Total
Age									
40-49	20	5.0	337	83.8	32	8.0	13	3.2	402
50-59	236	6.8	2887	82.7	249	7.1	117	3.4	3489
60-69	1145	12.9	6581	74.4	713	8.1	410	4.6	8849
70-79	1975	26.4	4034	54.0	642	8.6	819	11.0	7470
80+	272	15.6	1017	58.3	66	3.8	390	22.3	1745
Region									
Northeast	614	29.4	919	43.9	113	5.4	446	21.3	2092
South	86	8.4	812	80.2	97	9.6	18	1.8	1013
Midwest	1214	15.8	5258	68.6	653	8.5	542	7.1	7667
West	1734	15.5	7867	70.4	839	7.5	743	6.6	11183

3. Evaluation of the Types of Treatment by Stage of the Cancer

In this study, we compared the types of treatment using survival and basic parametric analyses. Classical distributions were fitted to the observed survival times of the different types of treatment in each stage to identify the probability distribution function that characterizes the behavior of the survival times. A P-P plot and a Kolmogorov-Smirnov test were examined to verify the goodness-of-fit. Based on the identified probability distribution function, the corresponding maximum likelihood estimates of the parameters are obtained together with the analytical structure of the estimated survival function and the expected survival time estimated under the appropriate probability distribution function. Of all the groups studied, we identified three different probability distribution functions; Weibull, Lognormal and Gamma.

3.1 Stage I

The appropriate probability distribution function (PDF) that characterize the behavior of the survival times in this stage of prostate cancer patients who received radiation therapy treatment was three-parameter Weibull probability distribution function with maximum likelihood estimates given by shape parameter $\hat{\alpha} = 2.1178$, scale parameter $\hat{\beta} = 9.559$, and location parameter $\hat{\gamma} = -0.5541$. By way of illustration, fitted graphical display of the identified Weibull density function with the inherent maximum likelihood estimates and corresponding P-P plot are given by Figure 1. The P-P plot follows a reasonable straight line pattern indicating that the 3P-Weibull density function is a good fit for the observed data. This visual observation was consistent with the results of Kolmogorov-Smirnov goodness-of-fit test.

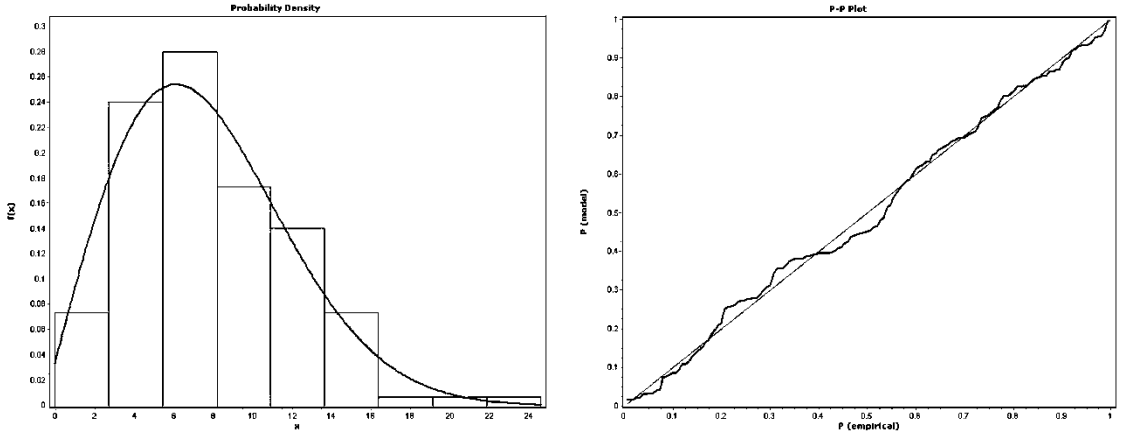

Figure 1: Fitted 3P-Weibull probability density function and P-P plot

Following the above process, we have identified the probability distribution functions that characterize the behavior of the survival times under the treatment options surgery, combination of surgery and radiation, and no form of cancer treatment. Three-parameter Weibull was again identified for surgery treatment, two-parameter Weibull for combination of surgery and radiation therapy, and three-parameter lognormal for no treatment. Their corresponding maximum likelihood estimates (MLE), expected survival times, and estimated survival functions are given in Table 3.

The expected survival time for patients receiving combination of surgery and radiation therapy treatment is approximately 8.6 years with a 44.3% chance of survival, radiation therapy is 7.9 years with a likelihood of 46.3%, surgery is 7.0 years with a likelihood of 41.7%, and no treatment is 6.2 years with a likelihood of 42.7%. The variation in the expected survival times is partly due to differences in the level of survivorship. A graphical display of the estimated survival functions is given by Figure 2.

Table 3: PDFs of the survival times by treatment, MLEs, expected survival times and estimated survival functions for Stage I.

Treatment	PDF	MLE	E(t)	$\hat{S}(t)$
Radiation	3P-Weibull	shape $= 2.1178$ scale $= 9.559$ location $= -0.5541$	7.9118	$\exp\left[-\left(\frac{t-(-0.5541)}{9.559}\right)^{2.1178}\right]$
Surgery	3P-Weibull	shape $= 1.4468$ scale $= 7.7954$ location $= -0.1095$	6.9609	$\exp\left[-\left(\frac{t-(-0.1095)}{7.7954}\right)^{1.4468}\right]$
Radiation & Surgery	2P-Weibull	shape $= 1.8212$ scale $= 9.6219$	8.5520	$\exp\left[-\left(\frac{t}{9.6219}\right)^{1.8212}\right]$
No Treatment	3P-Lognormal	shape $= 2.3855$ scale $= 0.3651$ location $= -5.4163$	6.1970	$1-\Phi\left[\frac{\ln(t-(-5.4163))-2.3855}{0.3651}\right]$

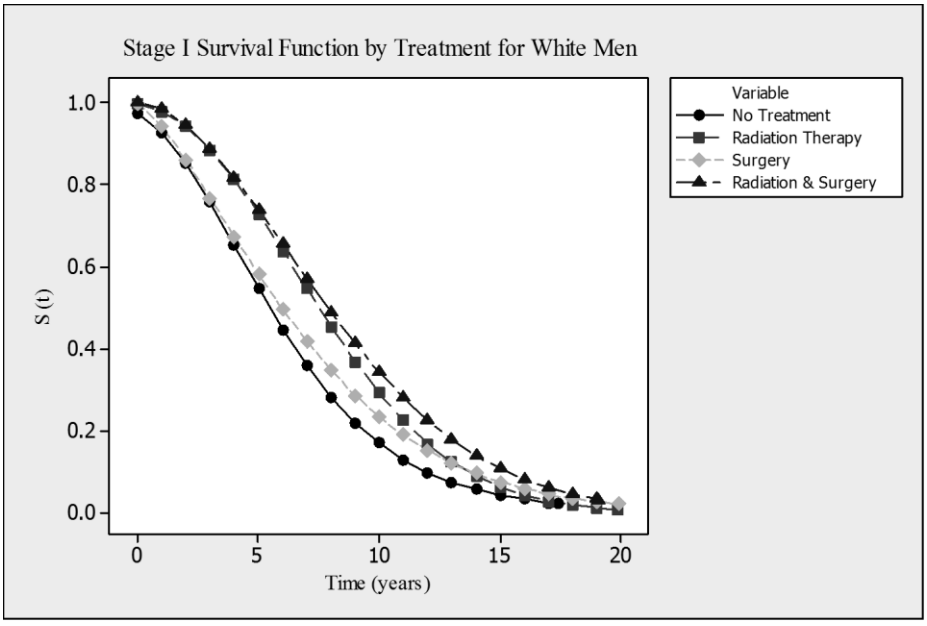

Figure 2: Survival Function for Stage I Prostate Cancer Patients by Treatment

Visually, there are differences in the survivorships. Based on this knowledge, a pair-wise comparison test of the survivorships was performed to establish all possible differences and the results given in Table 4. From the table, all the p-values indicate differences between the survivorships. Thus, combination of surgery and radiation therapy shows a

better survivorship than surgery, radiation therapy, or no treatment. Radiation therapy on average shows a better survivorship than surgery or no treatment, and surgery also shows a better survivorship than no treatment. However, between radiation therapy and surgery, radiation therapy shows a better survivorship than surgery within 13 years and after 13 years, surgery tends to show a better survivorship than radiation therapy. These differences in survivorships in conjunction with the expected survival times reveal that combination of surgery and radiation is more effective followed by radiation therapy, surgery, and no form of cancer treatment.

Table 4: Pair-wise Comparison of Stage I Prostate Cancer Survivorship by Treatment

Test	Average Difference in S(t)	$p-value$
$S_{Rad}(t) > S_{Surg}(t)$	0.0505	0.001
$S_{RadSurg}(t) > S_{Rad}(t)$	0.0292	< 0.0001
$S_{Rad}(t) > S_{NoTreat}(t)$	0.0965	< 0.0001
$S_{RadSurg}(t) > S_{Surg}(t)$	0.0796	< 0.0001
$S_{Surg}(t) > S_{NoTreat}(t)$	0.0386	< 0.0001
$S_{RadSurg}(t) > S_{NoTreat}(t)$	0.1262	< 0.0001
$S_{Rad}(t \leq 13) > S_{Surg}(t \leq 13)$	0.0783	< 0.0001
$S_{Surg}(t > 13) > S_{Rad}(t > 13)$	0.0144	< 0.0001

3.2 Stage II

In this stage, the Weibull distribution was identified as the appropriate probability distribution function that characterizes the behavior of the survival times under the different types of treatment. More specifically, the three-parameter Weibull was identified for radiation therapy, surgery, and no treatment whereas two-parameter Weibull was appropriate for combination of surgery and radiation therapy. Details of the identified probability distribution functions, maximum likelihood estimates, expected survival times, and estimated survival functions are given in Table 5.

The approximate expected survival time for combination of surgery and radiation therapy treatment is 9.0 years with 46.0% likelihood to survive this number of years, surgery is 8.2 years with a likelihood of 44.9%, radiation therapy is 7.9 years with a likelihood of 45.4%, and no treatment is 5.8 years with a likelihood of 43.5%. Graphs of the estimated survival functions as a function of time are given by Figure 3.

A visual inspection of the survival curves suggests differences in the survivorships. Thus, a formal statistical test was performed to establish all possible differences and the results given in Table 6. The test results indicate that on average combination of surgery and radiation shows a better survivorship than surgery, radiation therapy, or no treatment. Furthermore, surgery on average shows a better survivorship than radiation therapy or no treatment, and radiation therapy shows a better survivorship than no treatment. However, it is important to mention that combination of surgery and radiation showed a better survivorship than surgery within 14 years. After 14 years, surgery began to show a better survivorship than combination of surgery and radiation. Also, surgery showed a better

survivorship than radiation therapy after 6 years, but within 6 years, radiation therapy showed a better survivorship than surgery. Based on the observed differences in survivorship and taking into consideration the expected survival times, combination of surgery and radiation therapy is more effective in this stage followed by radiation therapy, surgery, and no form of cancer treatment.

Table 5: PDFs of the survival times by treatment, MLEs, expected survival times and estimated survival functions for Stage II

Treatment	PDF	MLE	E(t)	$\hat{S}(t)$
Radiation	3P-Weibull	shape $= 1.9969$ scale $= 9.2834$ location $= -0.3509$	7.8765	$\exp\left[-\left(\frac{t-(-0.3509)}{9.2834}\right)^{1.9969}\right]$
Surgery	3P-Weibull	shape $= 1.8585$ scale $= 10.194$ location $= -0.8517$	8.2011	$\exp\left[-\left(\frac{t-(-0.8517)}{10.194}\right)^{1.8585}\right]$
Radiation & Surgery	2P-Weibull	shape $= 2.1379$ scale $= 10.127$	8.9687	$\exp\left[-\left(\frac{t}{10.127}\right)^{2.1379}\right]$
No Treatment	3P-Weibull	shape $= 1.6363$ scale $= 6.7436$ location $= -0.2296$	5.8047	$\exp\left[-\left(\frac{t-(-0.2296)}{6.7436}\right)^{1.6363}\right]$

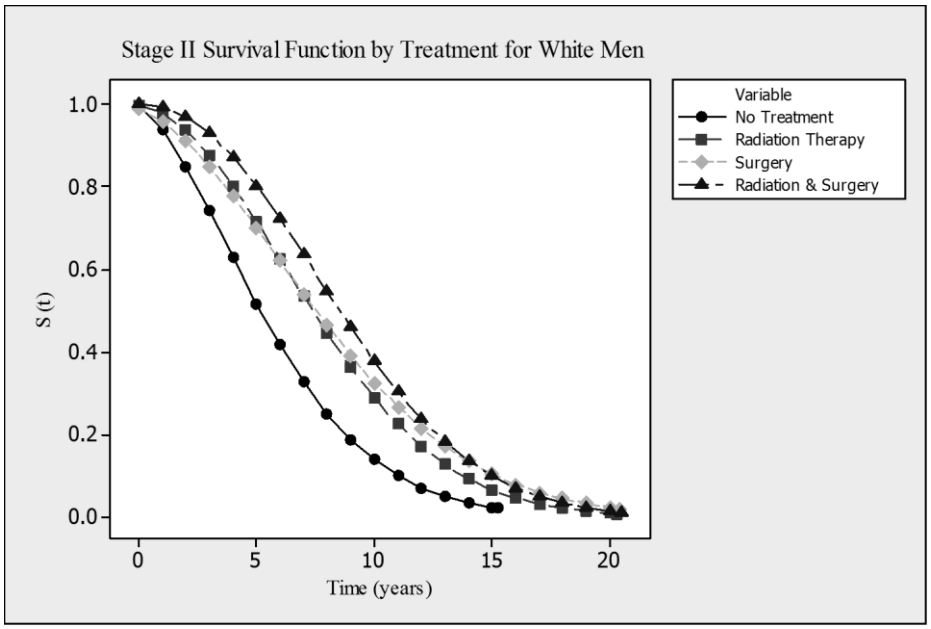

Figure 3: Survival Function for Stage II Prostate Cancer Patients by Treatment

Table 6: Pair-wise Comparison of Stage II Prostate Cancer Survivorship by Treatment

Test	Average Difference in S(t)	p − value

$S_{Surg}(t) > S_{Rad}(t)$	0.0136	0.013
$S_{RadSurg}(t) > S_{Rad}(t)$	0.0516	< 0.0001
$S_{Rad}(t) > S_{NoTreat}(t)$	0.1239	< 0.0001
$S_{RadSurg}(t) > S_{Surg}(t)$	0.0380	0.0005
$S_{Surg}(t) > S_{NoTreat}(t)$	0.1344	< 0.0001
$S_{RadSurg}(t) > S_{NoTreat}(t)$	0.1873	< 0.0001
$S_{Rad}(t \leq 6) > S_{Surg}(t \leq 6)$	0.0188	0.0005
$S_{Surg}(t > 6) > S_{Rad}(t > 6)$	0.0298	< 0.0001
$S_{RadSurg}(t \leq 14) > S_{Surg}(t \leq 14)$	0.0567	< 0.0001
$S_{Surg}(t > 14) > S_{RadSurg}(t > 14)$	0.0089	< 0.0001

3.3 Stage III

The Weibull distribution was again identified as the appropriate probability distribution function that characterizes the behavior of the survival times under the different types of treatment. More specifically, the three-parameter Weibull was identified for surgery and combination of radiation therapy and surgery whereas two-parameter Weibull was appropriate for radiation therapy, and no treatment. Table 7 shows the identified probability distribution functions, maximum likelihood estimates, expected survival times, and estimated survival functions.

Table 7: PDFs of the survival times by treatment, MLEs, expected survival times and estimated survival functions for Stage III

Treatment	PDF	MLE	E(t)	$\hat{S}(t)$
Radiation	2P-Weibull	shape $= 1.591$ scale $= 8.2707$	7.4192	$\exp\left[-\left(\frac{t}{8.2707}\right)^{1.591}\right]$
Surgery	3P-Weibull	shape $= 3.0006$ scale $= 13.929$ location $= -3.1911$	9.2473	$\exp\left[-\left(\frac{t-(-3.1911)}{13.929}\right)^{3.0006}\right]$
Radiation & Surgery	3P-Weibull	shape $= 2.4313$ scale $= 11.0$ location $= -0.6831$	9.0707	$\exp\left[-\left(\frac{t-(-0.6831)}{11.0}\right)^{2.4313}\right]$
No Treatment	2P-Weibull	shape $= 1.2674$ scale $= 5.9282$	5.5044	$\exp\left[-\left(\frac{t}{5.9282}\right)^{1.2674}\right]$

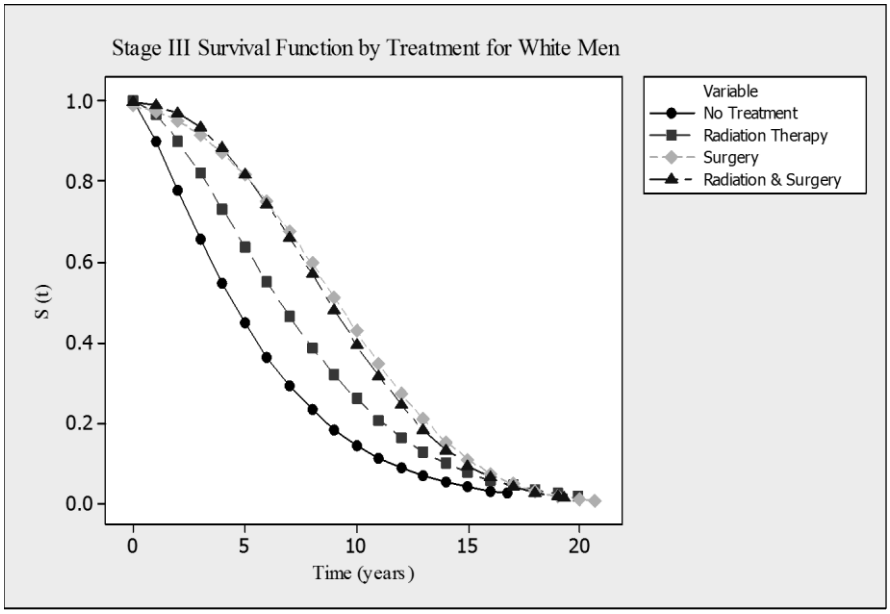

Figure 4: Survival Function for Stage III Prostate Cancer Patients by Treatment

The expected survival time for surgery treatment is approximately 9.2 years with 49.5% chance of survival, combination of surgery and radiation is approximately 9.1 years with a likelihood of 47.1%, radiation therapy is approximately 7.4 years with a likelihood of 43.3%, and no treatment is approximately 5.5 years with a likelihood of 40.3%. A graphical display of the estimated survival functions is given by Figure 4. The graphs reveal possible differences between the survivorships and this observation was supported by a statistical test. The results of the tests are given in Table 8.

Table 8: Pair-wise Comparison of Stage III Prostate Cancer Survivorship by Treatment

Test	Average Difference in S(t)	$p-value$
$S_{Surg}(t) > S_{Rad}(t)$	0.0935	< 0.0001
$S_{RadSurg}(t) > S_{Rad}(t)$	0.0844	< 0.0001
$S_{Rad}(t) > S_{NoTreat}(t)$	0.1083	< 0.0001
$S_{Surg}(t) > S_{RadSurg}(t)$	0.0091	0.0165
$S_{Surg}(t) > S_{NoTreat}(t)$	0.2185	< 0.0001
$S_{RadSurg}(t) > S_{NoTreat}(t)$	0.2084	< 0.0001
$S_{Surg}(t \leq 17) > S_{Rad}(t \leq 17)$	0.1043	< 0.0001
$S_{Rad}(t > 17) > S_{Surg}(t > 17)$	0.0041	0.1295
$S_{RadSurg}(t \leq 16) > S_{Rad}(t \leq 16)$	0.1000	< 0.0001
$S_{Rad}(t > 16) > S_{RadSurg}(t > 16)$	0.0045	0.0645
$S_{RadSurg}(t \leq 5) > S_{Surg}(t \leq 5)$	0.0125	0.002
$S_{Surg}(t > 5) > S_{RadSurg}(t > 5)$	0.0184	< 0.0001

From the test results, surgery on average shows a better survivorship than combination of surgery and radiation, radiation therapy, or no treatment. Combination of surgery and

radiation on average also shows a better survivorship than radiation therapy or no treatment, and radiation therapy shows a better survivorship than no treatment. However, a detailed test revealed that surgery shows a better survivorship than combination of surgery and radiation after 5 years. Also, surgery shows a better survivorship than radiation therapy within 17 years. Combination of surgery and radiation also shows a better survivorship than radiation therapy within 16 years. The differences in survivorships together with the expected survival times suggest surgery is more effective in this stage followed by combination of radiation therapy and surgery, radiation therapy, and no treatment. In this ranking process, there was a trade-off between the level of survivorship and the expected survival time.

3.4 Stage IV

Here, the Gamma and Weibull distributions were identified to characterize the behavior of the survival times under the different types of treatment. The three-parameter gamma probability distribution was identified for radiation therapy, two-parameter Weibull for combination of radiation and surgery, and three-parameter Weibull for both surgery and no treatment. The estimated maximum likelihoods, expected survival times, and estimated survival functions are given in Table 9.

Table 9: PDF of the survival times by treatment, MLEs, expected survival times and estimated survival functions for Stage IV

Treatment	PDF	MLE	E(t)	$\hat{S}(t)$
Radiation	3P-Gamma	shape = 1.3068 scale = 4.3562 location = 0.1269	5.8196	$1-\frac{\Gamma_{\frac{t-0.1269}{4.3562}}(1.3068)}{\Gamma(1.3068)}$
Surgery	3P-Weibull	shape = 1.3482 scale = 7.0367 location = −0.0578	6.3963	$\exp\left[-\left(\frac{t-(-0.0578)}{7.0367}\right)^{1.3482}\right]$
Radiation & Surgery	2P-Weibull	shape = 1.3244 scale = 7.7222	7.1062	$\exp\left[-\left(\frac{t}{7.7222}\right)^{1.3244}\right]$
No Treatment	3P-Weibull	shape = 0.9462 scale = 3.9693 location = 0.08	4.1501	$\exp\left[-\left(\frac{t-0.08}{3.9693}\right)^{0.9462}\right]$

The expected survival time for combination of surgery and radiation is approximately 7.1 years with a survival probability of 40.9%, surgery is 6.4 years with a likelihood of 41.0%, radiation therapy is 5.8 years with a likelihood of 38.6%, and no treatment is 4.2 years with a likelihood of 35.5%.

A display of the survival functions as a function of time is given by Figure 5. There are differences in the survivorships and thus we proceeded to perform a pair-wise comparison test to establish all possible differences. All the tests are statistically significant at the 5% level. This indicates that undergoing combination of surgery and radiation shows a better survivorship than surgery, radiation therapy, or no treatment.

Furthermore, surgery showed a better survivorship than radiation therapy and no treatment, and radiation therapy also showed a better survivorship than no treatment.

Based on the observed differences in survivorship and taking into account the expected survival times, combination of surgery and radiation therapy is a more effective form of treatment in this stage followed by surgery, radiation therapy, and no cancer treatment.

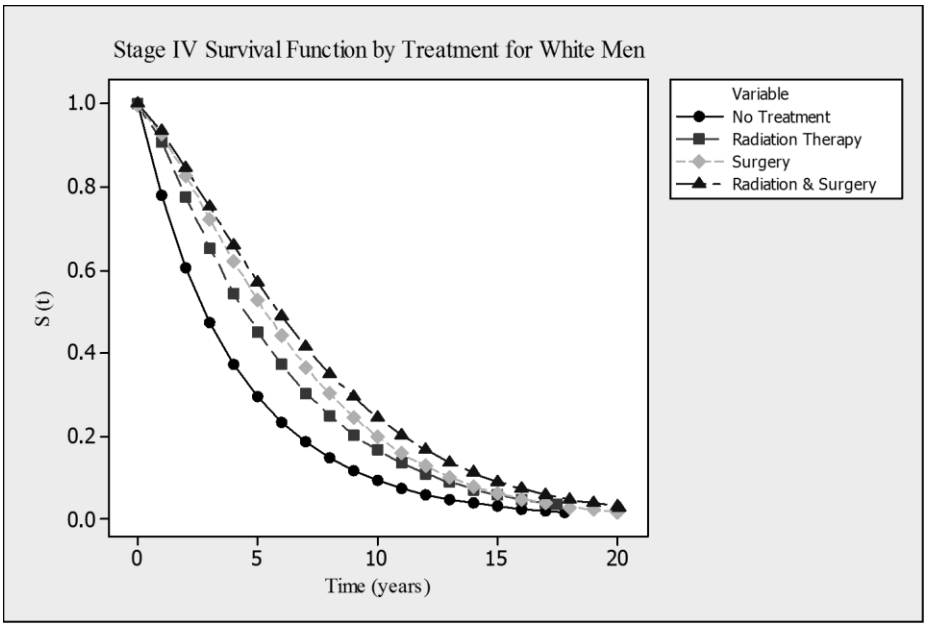

Figure 5: Survival Function for Stage IV Prostate Cancer Patients by Treatment

Table 10: Pair-wise Comparison of Stage IV Prostate Cancer Survivorship by Treatment

Test	Average Difference in S(t)	$p-value$
$S_{Surg}(t) > S_{Rad}(t)$	0.0344	< 0.0001
$S_{RadSurg}(t) > S_{Rad}(t)$	0.0681	< 0.0001
$S_{Rad}(t) > S_{NoTreat}(t)$	0.0878	< 0.0001
$S_{RadSurg}(t) > S_{Surg}(t)$	0.0311	< 0.0001
$S_{Surg}(t) > S_{NoTreat}(t)$	0.1221	< 0.0001
$S_{RadSurg}(t) > S_{NoTreat}(t)$	0.1559	< 0.0001

4. Conclusion

The relationship of prostate cancer survival with treatment has been identified for some time. A result of this study reinforces the idea while taking into consideration the stage of the cancer and other prognostic factors.

The age of the patient, the geographic region from where the case was reported, and the grade of the tumor were independently associated with treatment. However, for patients below the age of 45 years, there was no statistical association between the stage of the prostate cancer and treatment. Evidence from the analysis revealed that regardless

of the clinical or pathological stage of the cancer, patients diagnosed with prostate cancer that did not undergo any form of cancer related treatment had a poor survivorship and a relatively less survival time.

In the evaluation of the prostate cancer treatments considered in this study, there were variations in the efficacy of the treatments. Combination of surgery and radiation therapy was ranked 1 in stage I, II, & IV and 2 in stage III. Surgery was ranked 1 in stage III, 2 in stage IV, and 3 in stage I & II. Radiation therapy was ranked 2 in stage I & II and 3 in stage III & IV. No form of cancer treatment was ranked 4 in all the stages. In the evaluation process, some treatments showed better survivorship than others for a period of time and changed its effect or show no statistical difference. This was evident in stage I, II, & III.

5. References

[1] Hosain, G. M. M., Sanderson, M., Du, X. L., Chan, W. & Strom, S. S. *Racial/Ethnic differences in treatment discussed, preferred, and received for prostate cancer in a tri-ethnic population*. American Journal of Men's Health, 2012; 6(3): 249-257.

[2] Pulte, D., Redaniel, M. T., Brenner, H. & Jeffreys, M. *Changes in survival by ethnicity of patients with cancer between 1992-1996 and 2002-2006: is the discrepancy decreasing?* Annals of Oncology, 2012.

[3] Denmeade, S. R. & Isaacs, J. T. *A history of prostate cancer treatment*. Nature Reviews Cancer, 2002; 2: 389-396.

[4] Palmer, J. F. (editor). *The works of John Hunter, F. R. S. with notes*. Longman, London 1835

[5] Lytton, B. *Prostate cancer: a brief history and the discovery of hormonal ablation treatment*. The Journal of Urology, 2001; 165(6 pt 1): 1859-1862

[6] White, W. J. *Surgical removal of the hypertrophied prostate*. Annals of Surgery, 1893; 152

[7] Deming, C. L., Jenkins, R. H. & Van Wagenen, G. *Further studies in the endocrinological relationship of prostatic hypertrophy*. The Journal of Urology, 1935; 34: 678

[8] Moore, R. A. & McClellan, A. M. *Histological study of the effect of the sex hormones on the human prostate*. The Journal of Urology, 1938; 40: 641

[9] Young, H. H. *Four cases of radical prostatectomy*. Johns Hopkins Bull, 1905; 16: 315

[10] Millin, T. *Retropubic prostatectomy, a new extravesical technique*. The Lancet, 1945; 2: 693-696

[11] Walsh, P. C., Lepor, H. & Eggleston, J. C. *Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations*. The Prostate, 1983; 4: 473-485

[12] Young, H. H. *Use of radium in cancer of the prostate and bladder*. The Journal of the American Medical Association, 1917; 68(16): 1174-1177

[13] Pilepich, M. V. et al. *Androgen deprivation with radiation therapy compared with radiation therapy alone for locally advanced prostatic carcinoma: a randomized comparative trial of the Radiation Therapy Oncology Group*. Urology, 1995; 45: 616-623

[14] Pilepich, M. V. et al. *Phase III trial of androgen suppression using goserelin in unfavorable-prognosis carcinoma of the prostate treated with definitive radiotherapy: Report of Radiation Therapy Oncology Group Protocol 85-31*. The Journal of Clinical Oncology, 1997; 15: 1013-1021

[15] Bolla, M. et al. *Improved survival in patients with locally advanced prostate cancer treated with radiotherapy and goserelin*. The New England Journal of Medicine, 1997; 337(5): 295-300

[16] Feldman, B. J. & Feldman, D. *The development of androgen-independent prostate cancer*. Nature Reviews Cancer, 2001; 1(1): 34-45

[17] Sella, A. et al. *Phase II study of ketoconazole combined with weekly doxorubicin in patients with androgen-independent prostate cancer*. Journal of Clinical Oncology, 1994; 12: 683-688

[18] Hudes, G. R. et al. *Phase II trial of 96-hour paclitaxel plus oral estramustine phosphate in metastatic hormone-refractory prostate cancer*. Journal of Clinical Oncology, 1997; 15: 3156-3163

[19] Pienta, K. J. et al. *Phase II evaluation of oral estramustine and oral etoposide in hormone-refractory adenocarcinoma of the prostate*. Journal of Clinical Oncology, 1994; 12: 2005-2012

[20] Savarese, D. M. et al. *Phase II study of docetaxel, estramustine, and low-dose hydrocortisone in men with hormone-refractory prostate cancer: a final report of CALGB 9780. Cancer and Leukemia Group B*. Journal of Clinical Oncology, 2001; 19: 2509-2516

[21] Fleming, C. et al. *A decision analysis of alternative treatment strategies for clinically localized prostate cancer*. The Journal of the American Medical Association, 1993; 269(20): 2650-2658

[22] Chan, Y. M., Bonsu, N. O. M. & Tsokos, C. P. *Parametric analysis of prostate cancer*. Proceedings of Dynamic Systems and Applications, 2012; 6: 85-90

[23] Mettlin, C. J. et al. *The national cancer data base report on race, age, and region variations in prostate cancer treatment*. Cancer, 1997; 80(7): 1261-1266

[24] Lu-Yao, G. L. et al. *Follow up prostate cancer treatments after radical prostatectomy: a population-based study*. Journal of National Cancer Institute, 1996; 88: 166-173

[25] Mettlin, C., Murphy G. P. & Menck, H. *Trends in treatment of localized prostate cancer by radical prostatectomy: observations from the Commission on Cancer National Cancer Database 1985-1990*. Urology, 1994; 43: 488-492

[26] Murphy, G. P. et al. *National patterns of prostate cancer treatment by radical prostatectomy: results of a survey by the America College of Surgeons Commission on Cancer*. The Journal of Urology, 1994; 152: 1817-1819

[27] Zincke, H. et al. *Radical prostatectomy for clinically localized prostate cancer: long term results of 1,143 patients from a single institution*. Journal of Clinical Oncology, 1994; 12: 2254-2263

[28] Mettlin, C. J., Menck, H. R., Winchester, D. P. & Murphy, G. P. *Comparison of breast, colorectal, lung and prostate cancers reported in the National Cancer Database to the Surveillance, Epidemiology and End Results data*. Cancer, 1997; 79: 2052-2061

[29] Severson R. K., Montie, J. E., Porter, A. T. & Demers, R. Y. *Recent trends in incidence and treatment of prostate cancer among elderly men*. Journal of the National Cancer Institute, 1995; 87(7): 532-534

[30] Imperato, P. J., Nenner, R. P. & Will, T. O. *Radical prostatectomy: lower rates among African-American men*. Journal of the National Medical Association, 1996; 88(9): 589-594

[31] National Center for Biotechnology Information (NCBI), a division of the National Library of Medicine (NLM) at the National Institute of Health (NIH).

[32] National Cancer Institute at the National Institutes of Health.

[33] Surveillance Epidemiology and End Results (SEER) Program.

[34] Plackett, R. L. *Karl Pearson and the chi-squared test*. International Statistical Review, 1983; 51(1): 59-72

[35] Chernoff, H. & Lehmann, E. L. *The use of maximum likelihood estimates in chi-squared tests for goodness of fit*. The Annals of Mathematical Statistics, 1954; 25(3): 579-586