

A Modern Analytical Approach for Assessing the Treatment Effectiveness of Pancreatic Adenocarcinoma Patients Belonging to Different Demographics and Cancer Stages

Aditya Chakraborty^{1,*}, Chris P. Tsokos²

¹Assistant Professor Eastern Virginia Medical School

²Distinguished University Professor University of South Florida

*Corresponding author: chakraa@evms.edu

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Abstract Purpose: The purpose of the study is to detect the treatment effectiveness for different patient groups (belonging to different demographics and cancer stages, taking different treatments) at early stages. **Method:** In this study, we introduced an analytical method to monitor the behavior of survival times of pancreatic adenocarcinoma patients by introducing two new concepts: Survival Index (SI), and Stochastic Growth Intensity Function (SGIF), $\zeta(t)$. A total of 108 patient groups receiving three different treatments; only chemotherapy (C), only radiation (R), and a combination of chemotherapy and radiation (C + R) were constructed using the SEER Cancer Database.

Results: Our analytical method is helpful to predict the survival pattern based on the (SI) as a function of time t ; which necessarily provides information if the specific treatment has been useful for the particular patient group. That is if $(SI) > 1$ implies the treatment has an adverse effect on the patient's survival. $(SI) \approx 1$ implies the survival rate is approximately constant by the implementation of the treatment, and $(SI) < 1$ implies the treatment has been effective on the patient's survival. **Conclusion:** The adaptability of our technique stems from the fact that our algorithm may be used for any number of patient groups of any age, of any race, at any specific cancer stage, and receiving any unique treatment or combination.

Keywords: pancreatic cancer, survival index, Stochastic Growth Intensity Factor (SGIF), SEER Cancer Database

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1. Introduction

Given the destructive nature of pancreatic cancer, it remains one of the major threats devastating human existence. However, there are various treatment options (chemotherapy, radiation, surgery, immunotherapy, targeted therapy) to cure the lethal carcinogenic disease [1-3]; very few studies have been conducted to understand at which stage a particular treatment option is the most effective. Also, it is crucial to understand how the treatment options are affecting the mortality of patients from a specific race belonging to a particular age group, at different cancer stages; which essentially means applying a particular treatment of interest or a combination of both if the mortality of a patient from a specific race at a specific stage is increasing, decreasing, or staying the same. There are several data-driven research in the literature to understand the nature of pancreatic cancer at different stages and what risk factors are the major cause

of this type of cancer, [4-6]. In our study, we have introduced a new analytical approach by defining the Survival Indicator (SI) to monitor the behavior of cancer survivorship for patients from different age groups, different cancer stages, and different races, as a stochastic realization of time. The present study uses data from the Surveillance, Epidemiology, and End Results (SEER) database [7,8], which contains information on patients who were deceased due to pancreatic adenocarcinoma. The analytical method we propose is based on the survival times (in months) and cause-specific death (deaths due to pancreatic cancer) for each patient. The survival times of patients are one of the most pivotal factors used in all cancer research. It is necessary to evaluate the severity of cancer, which helps to determine the prognosis and help identify the correct treatment options [9,10]. We have extracted a sufficiently large random sample of patients diagnosed with pancreatic adenocarcinoma from different races (Caucasian, African American, Others), and four cancer stages which contain the information of different treatment options (chemotherapy (C), radiation (R),

combination of both (C+R)). The information for the age variable was categorized in three different groups; 40 to 59, 60 to 79, and 80 and above. The schematic structure of

the data used in this study for different races, cancer stages, and age groups are shown in [Table 1](#), [Table 2](#), and [Table 3](#) below.

Table 1. Showing the Number of Patients for White Population in Different Cancer Stages, Categorized by Age Groups

Caucasian			
Age: [40 - 59)			
Stages	C	R	C+R
I	148	12	123
II	1206	52	1351
III	514	33	663
IV	5070	123	556
Age: [60 - 79)			
Stages	C	R	C+R
I	568	75	490
II	3406	249	3268
III	1286	117	1358
IV	11263	305	869
Age: [80 - Above)			
Stages	C	R	C+R
I	237	118	162
II	704	144	478
III	281	451	210
IV	1783	132	120

Table 2. Showing the Number of Patients for Black Population in Different Cancer Stages, Categorized by Age Groups

African American			
Age: [40 - 59)			
Stages	C	R	C+R
I	34	3	29
II	211	14	249
III	104	13	126
IV	1000	45	101
Age: [60 - 79)			
Stages	C	R	C+R
I	88	15	82
II	394	45	391
III	212	15	203
V	1476	68	113
Age: [80 - Above)			
Stages	C	R	C+R
I	18	18	5
II	61	15	33
III	17	4	11
IV	157	15	10

Table 3. Showing the Number of Patients for Other (American Indian/AK Native, Asian/Pacific Islander) Race Groups in Different Cancer Stages, Categorized by Age Groups

Others			
Age: [40 - 59)			
Stages	C	R	C+R
I	16	1	12
II	118	10	104
III	44	6	65
IV	461	16	62
Age: [60 - 79)			
Stages	C	R	C+R
I	50	9	37
II	263	22	244
III	149	18	147
IV	918	34	101
Age: [80 - Above)			
Stages	C	R	C+R

I	25	14	6
II	63	16	43
III	27	6	21
IV	134	16	20

2. Methodology

2.1. Analytical Method for Developing the Survival Indicator (SI)

In the context of pancreatic cancer, researchers are often interested to investigate the survival rate patterns as a function of time for patients belonging to a specific race, age group, cancer stages, and specific treatments they received. For example, it would be interesting to monitor if the time to death of a patient belonging to the Caucasian race receiving chemotherapy from the age group [60-79] at Stage IV shows an increasing or decreasing trend. As a result, it is critical to track how the survival rate changes over time as a result of the application of a certain treatment. It will also be useful to identify any patient group, for which any specific treatment has been beneficial (increased survival). In this regard, we define *Stochastic Growth Intensity Factor (SGIF)* that measures the rate of change of a survival time as a stochastic realization of time. The analytical structure of the *SGIF* function is:

$$\zeta(t; SI; \phi) = \frac{SI}{\phi} \left(\frac{t}{\phi} \right)^{SI-1}, \quad SI > 0, \phi > 0, t > 0, \quad (1)$$

Where SI and ϕ are the shape and scale parameters of Weibull distribution, respectively, and t denotes the time behavior of the incident under investigation. The *SGIF* is based on a non-homogeneous Poisson process [11,12] which is used extensively in the field of reliability theory [13], and pancreatic cancer survival modeling [14]. In the context of cancer survivorship, we formally define the *Survival Indicator (SI)* from Equation 1 as follows:

Definition 2.1. The *Survival Indicator (SI)* for a patient group belonging to a particular race, from a specific age group is an index based on the survival time, that determines the improvement or deterioration of survival of that particular group at a specified cancer stage when any definite treatment or a combination of more than one treatment is administered to the patient group.

Mathematically, it can be expressed as follows:

$$SI_{jk}^{lm} = \frac{n_{jk}^{lm}}{\sum_{i=1}^n \log \left(\frac{(t_n)_{jk}^{lm}}{(t_i)_{jk}^{lm}} \right)} \quad (2)$$

where SI_{jk}^{lm} is the Survival Indicator value SI of the j^{th} , ($j = 1 = C, 2 = R, 3 = C + R$) treatment group, at Stage k , $k = 1, 2, 3, 4$, for age group l , ($l = 1 = [40 - 59], 2 = [60 - 79], 3 = [80 - \text{above}]$) belonging to race m , ($m = 1 \equiv \text{white}, 2 \equiv \text{black}, \text{and } 3 \equiv \text{others}$).

The term $(t_n)_{jk}^{lm}$ is the largest time to death, and n_{jk}^{lm} is the number of patients.

For example, SI_{32}^{12} represents the index indicator value for the **African American** patient group, under age group [40 - 59] at **Stage II** who received **chemotherapy + radiation**. Now, we can express the Stochastic Growth Intensity Function (*SGIF*), as a function of SI , for any specific group in the following way:

$$\zeta(t; SI_{jk}^{lm}; \phi) = \frac{SI_{jk}^{lm}}{\phi} \left(\frac{t}{\phi} \right)^{SI_{jk}^{lm}-1}, \quad SI_{jk}^{lm} > 0, \phi > 0, t > 0. \quad (3)$$

We will show how SI_{jk}^{lm} depends on the interpretation of the *SGIF* ζ .

- Case 1: $\zeta(t)$ is decreasing with time, that is, the patient survival rate is improving as a function of time $t \Rightarrow SI_{jk}^{lm} < 1$
- Case 2: $\zeta(t)$ is increasing with time, that is, the patient survival rate is deteriorating as a function of time $t \Rightarrow SI_{jk}^{lm} > 1$
- Case 3: $\zeta(t)$ is neither increasing nor decreasing; that is, the patient survival rate is constant as a function of $t \Rightarrow SI_{jk}^{lm} \approx 1$

Now, provided the values of SI_{jk}^{lm} and ϕ , we can calculate the value of the *SGIF*, $\zeta(\cdot)$ (given in (3)), which can be utilized in modeling the stochastic characterization of a specific patient group, receiving any specific treatment or combination of treatments at any given time t . $\zeta(t)$ measures if the patient survival rate increases, remains approximately the same, or decreases by the implementation of radiation, chemotherapy, or the combination of both. A decrease in $\zeta(t)$ implies that values of *SGIF* are decreasing or an improvement in the survival time of a specific patient group diagnosed with pancreatic cancer as a function of time. This means that $SI < 1$. A rise in $\zeta(t)$ suggests that values of *SGIF* are increasing, implying that $SI > 1$. This means that the survival time is decreasing with respect to time. When there is no change in $\zeta(t)$, it implies that $SI \approx 1$; thus, the survival time is approximately constant by the implementation of any treatment/drug for a specific patient group. Therefore, the behavior of the change in the cancer survival growth model is dependent on SI of the *SGIF*. That is, we can use SI to monitor the survival times of patients as a function of time.

3. Results

The following tables (Table 4. A, Table 4. B, and Table 4. C) shows the SI values for Caucasian race group at the four cancer Stages, categorized by three age groups ([40-59], [60-79], and [80-above]), who receive three treatment options (only chemotherapy (C), only radiation (R), and the combination of both (C+R)).

Table 4.A. Showing the SI and ϕ Values for the Caucasian Race Groups in Different Cancer Stages, for Age Group [40-59]

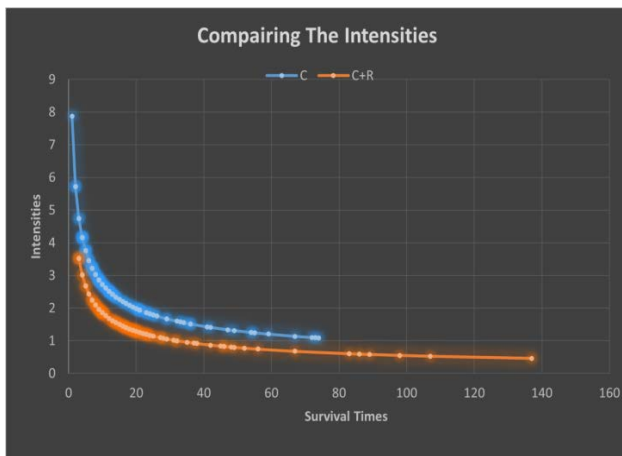
Caucasian						
Age: [40 - 59]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.54	.007	1.09	1.94	.47	.004
Stage II	.45	1.5×10^{-5}	.41	.008	.36	2.4×10^{-7}
Stage III	.39	1.4×10^{-5}	.48	.03	.42	.001
Stage IV	.33	7.2×10^{-10}	.29	5.28×10^{-6}	.37	4.19×10^{-6}

Table 4.B. Showing the SI and ϕ Values for the Caucasian Race Groups in Different Cancer Stages, for Age Group [50-79]

Caucasian						
Age: [60 - 79]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.4	1.74×10^{-5}	.52	.01	.41	4.2×10^{-5}
Stage II	.4	2.15×10^{-7}	.37	4.2×10^{-5}	.46	2.8×10^{-6}
Stage III	.37	4.8×10^{-7}	.33	7.8×10^{-5}	.42	2.8×10^{-6}
Stage IV	.3	4.3×10^{-12}	.32	9.6×10^{-7}	.43	9.65×10^{-6}

Table 4.C. Showing the SI and ϕ Values for the Caucasian Race Groups in Different Cancer Stages, for Age Group [80-above]

Caucasian						
Age: [80 - Above]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.37	4.39×10^{-5}	.41	.0008	.4	.0004
Stage II	.4	8.2×10^{-6}	.43	.0007	.46	.0001
Stage III	.4	6.4×10^{-4}	.5	.02	.53	.002
Stage IV	.33	2.2×10^{-8}	.32	1.5×10^{-5}	.4	.0004

**Figure 1. Showing the Failure Intensities for Caucasian Race at Stage I, Under Age Group [40-59], Who Received Only Chemotherapy, and the group who received Chemotherapy & Radiation**

From Table 4. A, we see that at Stage I, for age group [40-59], the SI is .47 for the patient who received chemotherapy and radiation (C+R) together, which is less than the SI (.54) of the patient group who received only chemotherapy (C). We can infer that the $SGIF \zeta(t)$, for group C+R at Stage I, age group [40-59] is less than the group who receive only C for the Caucasian race, which implies that chemotherapy together with radiation has been more effective at Stage I for the particular age group which is also evident from Figure 1. It is also important to

note that, the $SI = 1.09 (> 1)$ for only the radiation (R) group at Stage I implying that the $SGIF$ is decreasing with time for the particular age group receiving radiation therapy only which is not effective with respect to the survival. The importance of our analytical method is, it can be implemented for any chosen group at any given cancer stage, from any particular age group receiving any specific treatment. The following tables (Table 5. A, Table 5. B, and Table 5. C) shows the SI values for Black race group at the four cancer Stages, categorized by three age groups ([40-59], [60-79], and [80-above]), who receive three treatment options (only chemotherapy (C), only radiation (R), and the combination of both (C+R)).

Table 5.A. Showing the SI and ϕ Values for the African American Race Groups in Different Cancer Stages, for Age Group [40 - 59]

African American						
Age: [40 - 59]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.12	.6	4.52	12.01	.56	.19
Stage II	.54	.004	.91	1.15	.48	.001
Stage III	.4	.001	.83	1.18	.5	.005
Stage IV	.36	4.45×10^{-7}	.41	.005	.38	.0004

Table 5.B. Showing the SI and ϕ Values for the African American Race Groups in Different Cancer Stages, for Age Groups [60-79]

African American						
Age: [60 - 79]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.4	.0016	1.08	1.19	.43	.005
Stage II	.42	.00005	.38	.0046	.53	.001
Stage III	.42	.00024	1.19	1.03	.65	.014
Stage IV	.35	7.67×10^{-8}	.32	.0001	.64	.02

Table 5.C. Showing the SI and ϕ Values for the African American Race Groups in Different Cancer Stages, for Age Groups [80-above]

African American						
Age: [80 - Above]						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.78	.69	.65	.36	1.21	8.19
Stage II	.65	.06	.73	.61	.48	.05
Stage III	1.31	1.95	1.39	6.31	.74	1.49
Stage IV	.43	.0005	.81	.35	1.2	2.05

From the above Table 5. A, we notice that the survival index (SI) is greater than 1 for African- American patients from age group [40-59], at Stage I receiving only radiation therapy ($SI = 4.52$), patients from age group [60-79], at Stage I receiving only radiation therapy ($SI = 1.08$), patients from age group [80-above], at Stage I receiving both chemotherapy and radiation ($SI = 1.21$), patients from age group [80-above], at Stage III receiving only chemotherapy ($SI = 1.31$) and, only radiation therapy ($SI = 1.39$). We also note that at Stage IV, under the age group [80-above], for patients who received both chemotherapy and radiation (C+R), the SI is 1.2. These results raise red flags regarding implementing the specific

treatments to the specific patient groups of African-American race for which SI is more than 1, implying that the survival rate is deteriorating for these patients.

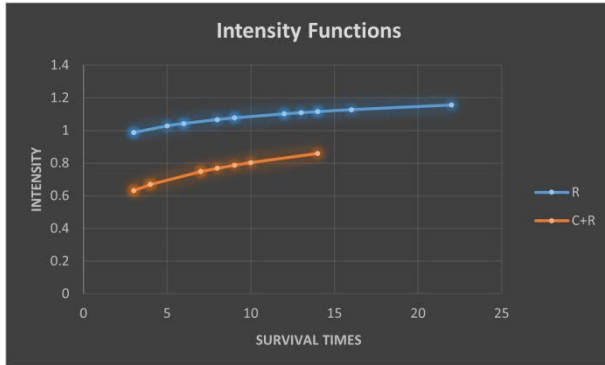


Figure 2. Showing the Comparison between the Failure Intensities for African-American Race at Stage I, Under Age Group [60-79), Who Received Only Radiation, and the group who received Chemotherapy & Radiation at Stage IV, under age group [80-above)

The following tables (Table 6. A, Table 6. B, and Table 6. C) shows the SI values for Other (American Indian/AK Native, Asian/Pacific Islander) race group at the four cancer Stages, categorized by three age groups ([40-59), [60-79), and [80-above)), who receive three treatment options (only chemotherapy (C), only radiation (R), and the combination of both (C+R)).

In Table 6. A, the "-" in Stage I, for the age group [40-59) implies that there are insufficient data points to calculate the SI and ϕ values. From Table 3 in Section 1, we see that there is only a *single* observation that falls under the category. Since any inference based on a single observation is misleading, we did not calculate the SI and ϕ values for the specific group of patients. We see that under the age group [40-59) at Stage III, the patients who received only radiation therapy the SI is 1.44, an indication that the failure intensity ($SGIF$) is increasing. Also, we see the same scenario for the patients belonging to the age group [80-above) at Stage III who received only radiation ($SI = 1.75$), for the patients who received chemotherapy and radiation together ($SI = 1.26$), and for the patients at Stage IV who received chemotherapy and radiation together ($SI = 1.41$).

Table 6.A. Showing the SI and ϕ Values for Other (American Indian/AK Native, Asian/Pacific Islanders) Race Groups in Different Cancer Stages, for Age Group [40-59)

Others						
Age: [40 - 59)						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.55	.74	-	-	.5	.98
Stage II	.59	.02	.96	2.6	.66	.07
Stage III	.63	.14	1.44	5.76	.7	.12
Stage IV	.35	2.62×10^{-6}	.33	.02	.54	.02

Table 6.B. Showing the SI and ϕ Values for Other (American Indian/AK Native, Asian/Pacific Islanders) Race Groups in Different Cancer Stages for Age Group [60-79)

Others						
Age: [60 - 79)						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.65	.13	.57	.93	.58	.15
Stage II	.52	.002	.5	.17	.5	.002
Stage III	.51	.003	.5	.13	.61	.01
Stage IV	.31	3.4×10^{-8}	.67	.06	.41	.004

Table 6.C. Showing the SI and ϕ Values for Other (American Indian/AK Native, Asian/Pacific Islanders) Race Groups for Age Group [80-above)

Others						
Age: [80 - Above)						
Treatment	C		R		C+R	
Parameter	SI	ϕ	SI	ϕ	SI	ϕ
Stage I	.7	.42	.69	.67	.84	3.19
Stage II	.5	.02	.72	.49	.72	.18
Stage III	.6	.18	1.75	1.1	1.26	1.96
Stage IV	.42	.0003	.77	.3	1.41	1.31

4. Conclusion

In this study, we focused on two main aspects.

- Analytical Development in the subject area.
- Data Analysis and Monitoring the Survival Time of a *specific* group of patients.

In Section 2.1, we have defined the Survival Indicator SI and explained how it could be implemented in the pancreatic cancer survival data. Survival Indicators (SI) were computed for all the cancer stages, categorized by race and age three age groups. These SI values play a vital role in deciding the treatment effectiveness of patients belonging to specific groups as a function of time. Figure 3 illustrates the analytical process. However, no specific risk factors were considered due to the limitation of the data set, the process can be performed in the presence of any additional risk factors. The following Figure 3 illustrates the schematic procedure explaining how the procedures can be implemented to access the treatment effectiveness in the presence of different risk factors.

If a doctor/medical professional knows beforehand that a treatment has been effective for a specific patient group (out of 108 patient groups that we considered), that information can be utilized to treat any future patient from that particular group. This analytical procedure can be useful in clinical decision-making related to any time-to-event cancer data.

A data-driven analytical process to monitor pancreatic cancer survival time

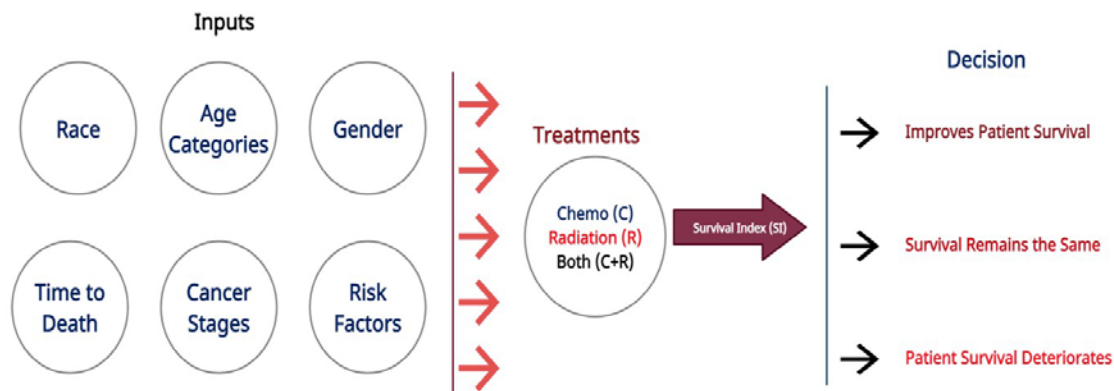


Figure 3. Analytical Process to Evaluate the Treatment Effectiveness

5. Declarations

5.1. Funding

None

5.2. Competing Interest

The authors declare no conflict of interest related to this study

5.3. Ethics Approval

Not Applicable

5.4. Consent to participate

Not Applicable

5.5. Declarations

The manuscript is taken from Chapter 4 of the doctoral dissertation of the corresponding author (<https://www.proquest.com/docview/2696879982?pq-origsite=gscholar&fromopenview=true>)

5.6. Availability of Data Availability

The data can be requested from SEER. (<https://seer.cancer.gov/seerstat/>)

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