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MODELLING PROGRESSION IN STAGE III COLON CANCER USING SURVIVAL ANALYSIS

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Abstract: Stage III colon cancer poses a significant challenge for the treatment and management. This study aimed to model the progression of stage III colon cancer using survival analysis and identify key predictors of survival and disease recurrence. A retrospective cohort study was conducted using data from 929 patients with stage III colon cancer. Kaplan-Meier analysis and Cox proportional hazards regression were used to estimate survival rates and identify significant predictors of overall survival. The results show that using the Kaplan Meier approach the probability of survival started with 67% in 1-36 months and increases with time to 88% in 37-72 months, then increases at its peak in 73-108 months to approximately 91%. The result further shows a typical Kaplan Meier property of stepwise decrement from state 1 to state 2 in each of the groups. Also, the log-rank test demonstrates an unadjusted comparison between the groups and reveals that the survival probabilities in each group are the same. In the overall evaluation, the result reveals that two parameters (number of positive lymph nodes and extent of local spread) considered in this study are significant and contribute immensely to the survival of patients.to

Keywords: Progressive disease, Colon cancer, Cox Regression Analysis, Kaplan Meier

1. Introduction

Progressive disease (PD) is a medical term that refers to an illness that worsens with time, either because it spreads, becomes more severe, or increasingly interferes with the body's normal function if not treated. This can happen with a variety of diseases, including cancer, HIV/AIDS, and Hepatitis B etc. and it can continue until death, severe debility, or organ failure occurs, (Iseh et al. 2025; Iseh & Matthew, 2025). Some progressive disorders can be slowed or prevented with treatment. Many progressive disorders can be slowed with medical care, but others cannot be altered by current treatments (WHO, 2018).

Progressive disorders pose a difficult challenge for healthcare practitioners and patients alike. These disorders, which develop gradually over time, have a substantial influence on quality of life and necessitate careful management and treatment measures. These diseases generally have distinct stages or phases. Progressive diseases are distinguished by their dynamic nature, with patients moving through multiple health states over time, such as diagnosis to remission, relapse, or death (Siegel et al., 2020; Ekong et al. 2021; Iseh et al. 2022). Colon cancer is a major public health concern around the world, and stage III disease marks a vital point in the illness's evolution. Stage III colon cancer, defined by the spread of disease to adjacent lymph nodes, presents a significant barrier for therapy and management. Survival analysis, a statistical approach for analyzing time-to-event data, offers a powerful tool for understanding the factors influencing disease progression and patient outcomes. This study aims

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to model the progression of stage III colon cancer using survival analysis, with a focus on identifying key predictors of survival and disease recurrence.

Despite breakthroughs in treatment and care, stage III colon cancer is still a leading source of morbidity and mortality, with a 5-year survival rate of 60-70%. Patient demographics, tumor features, and treatment modalities all have an impact on the course of the disease. However, the proportional importance of these characteristics and their interactions is unclear, making it difficult to establish effective treatment methods and properly predict patient outcomes. This study aims to close the information gap by using survival analytic approaches to model the evolution of stage III colon cancer and identify critical indicators of survival and disease recurrence. The primary goal of this research is to model and assess the progression of the survival time distribution of people with stage III colon cancer, as well as to identify factors impacting survival of people with stage III colon cancer utilizing some survival modeling methodologies.

2. Literature Review

Survival analysis is a statistical method for analyzing data in which the outcome variable of interest is the time until an event occurs (Hosmer et al., 2008). It is the analysis of the duration of the occurrence or non-occurrence of an event within the risk period, and an individual is only eligible to experience an event if there was a period during which they were at 'risk' of experiencing the event. According to Wooldridge (2001), survival analysis is concerned with how various therapies or demographic variables affect survival times.

As a result, in medical research, time to event might refer to the time until a cancer recurrence, a change in medication regimens, mortality, or infection. However, some respondents may not notice a transition until the end of the observation time. These responses are classified as right-censored observations. A truncated observation is incomplete because of the study's inherent selection procedure (Hosmer et al., 2008). Survival analysis refers to a set of statistical approaches used to describe and quantify time-to-event data, with the term 'failure' defining the occurrence of the event of interest. According to Stevenson (2007), the term 'survival time' refers to how long it takes for failure to occur.

A survival rate is a statistical metric that describes the likelihood of distinct outcomes for a group of patients at a given moment in time. The higher the survival rate, the lesser the danger for this group of patients. Survival analysis is not as straightforward as it may seem. If one were to measure the time between diagnosis and death or record the vital status when last observed for each patient in a chosen patient group, one might be tempted to describe the group's survival as the proportion alive at the end of the investigation period (Torey and Broom, 2007).

This simple measure is informative only if all of the patients were observed for the same length of time. In most real situations, not all members of the group are observed for the same amount of time. Patients diagnosed near the end of the study period are more likely to be alive at last contact and will have been followed for less time than those diagnosed earlier. Even though it was not possible to follow these persons as long as the others, their survival might eventually prove to be just as long or longer. Although we do not know the complete survival time for these individuals, we do know a minimum survival time (time from diagnosis to last known contact date), and this information is still valuable in estimating survival rates (Woolson, 1981; Iseh & Udoh, 2022).

Similarly, it is frequently impossible to ascertain the outcome status of all patients who were initially included in the group (Iseh et al. 2025; Iseh & Matthew, 2025). People may be lost to follow-up for a variety of reasons, including moving, changing names, changing providers, or death. Thus, if a survival rate is to adequately depict the outcomes for a whole group, it must account for the fact that various members in the group are watched for varying durations of time and that others' vital state is unknown at the time of analysis.

Subjects who are monitored until they achieve the endpoint of interest (such as death or recurrence) are referred to as uncensored cases in the terminology of survival analysis, while those who survive until the conclusion of the follow-up or who are occasionally lost to follow-up are referred to as censored cases. The life table method and the Kaplan-Meier method are two fundamental survival techniques

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that allow one to calculate total group survival while accounting for both censored and uncensored observations. The first approach that was widely utilized to describe cancer survival outcomes was the life table method. When data are only accessible in grouped categories, it is most helpful (Leung et al., 1997).

The first step after gathering time-to-event data is to define it; often, a survival curve is used to do this. Non-parametric (or semi-parametric) approaches are more common than parametric approaches in epidemiology. The Kaplan-Meier approach, the life table method, and the Nelson-Aalen method are three non-parametric techniques for characterizing time-to-event data. There are times when our study subjects' survivability patterns are predicted. In this case, time to event can be described using parametric distributions. We can accurately anticipate time to event for our observed data well after the period during which events happened, which is an advantage of adopting a parametric distribution (Stevenson, 2007).

Nonparametric models

These models don't assume anything about the hazard function's shape or how the covariates impact it. Instead, the empirical data is used to estimate the hazard function, which displays changes over time. Only by stratifying the data into groups (by gender) and plotting and contrasting distinct hazard functions for each group can the impact of covariate variables be demonstrated. Continuous data, multivariate analysis, and controlling for additional explanatory variables are all beyond the capabilities of nonparametric models. The main illustration of the nonparametric method of event history analysis is Kaplan-Meier survival analysis.

Semi-parametric models

These models likewise make substantial assumptions about how covariates impact the hazard function, but they do not make any assumptions regarding the shape of the hazard function with respect to time. In particular, they make the assumption that over time, hazard rates are proportionate amongst groups.

These models can facilitate multivariate analysis, both non-parametric analysis and semi-parametric analysis like Cox regression yield the same estimates when no covariates are taken into account. As a result, in event history analysis, semi-parametric models are frequently the preferred approach. However, in parametric and semi-parametric analysis, such intervals are regarded as informative and non-informative, respectively, if no failures occur during that time. The main illustration of the semi-parametric method of event history.

Analysis of cancer survival data and related outcomes is necessary to assess cancer treatment programs and to monitor the progress of regional and national cancer control programs. In the progression, this study seeks to avail researchers, biostatisticians and epidemiologists a better insight of the alternative methods that can be used in waiting time (survival) data analysis. These methods can be used either by themselves or as complementary tools to gain more insight into the risk factor dynamics at any given point of the patients' survival time.

3. Methodology

The scope of this study under theoretical pining is categorized into proper data collection, modelling and comparison techniques to ensure acceptable result. This is presented as follows:

i. **Data collection:** Data is collected from R data sets on Stage III colon cancer patients.

ii. **Modelling and Comparison Techniques:** The survival analysis techniques are used as the statistical tool to develop the progression of model.

3.1 Data Collection and Data Analysis

This section considers the source of data collection and cleaning and preprocessing of data to handle missing values, outliers, and inconsistencies, exploratory analysis using descriptive statistics before application of the model and model validation to ensure accuracy and generalizability.

Source: Data is collected on 929 stage III colon cancer patients from R data sets with the following codes in extracting the data;

```
install.packages("survival")
install.packages("gems")
library("survival")
```

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```
library("gems")
data("cancer",package="survival")
data1<-subset(colon,etype==1)
```

Progression of Stage III colon cancer

The different stages of stage III colon cancer which is used as the states in the Survival analysis are classified as:

Stage 1 (Stage III colon cancer): Alive and Disease free (S_1)

Stage 2 (Stage III colon cancer): Alive and Recurrence (S_2)

Stage 3 (Stage III colon cancer): Death (S_3)

Survival analysis

i. **Cohort definition:** The observation of patients based on stage III colon cancer stages over time to assess the relationship between the exposures and the development of the health outcome.

ii. **Time-to-event data:** Time-to-event data is used to analyze the duration patients spend in each stage III colon cancer stage and the factors influencing progression.

Survival models

Survival models are used to calculate survival probability and find predictors of progression and survival. It is frequently used in medical research to determine the percentage of patients who survive a given period of time after therapy. It is crucial to highlight that the Kaplan-Meier curve can account for certain types of censored data, specifically right-censoring, which occurs when a patient withdraws from a study, is lost to follow-up, or is alive but has no events at the last follow-up. Individual patients with right-censored survival periods are indicated by little vertical tick marks on the plot. When there is no truncation or censoring, the Kaplan-Meier curve complements the empirical distribution function. The survival function estimator is as follows:

$$S(k) = p_1 \times p_2 \times p_3 \times \ldots \times p_k$$

In the above equation p_1 constitutes surviving proportion in the first period, p_2 is the proportion survived over the second period, and so on. The proportion of surviving for period i where they survived up to period j is given as:

$$\boldsymbol{p_{ij} = 1 - \frac{d_{ij}}{r_{ij}}}$$

where, r_i is the number of patients living at start of the period i, and d_i is the number of deaths.

Cox proportional hazards (PH)

The Cox Proportional Hazard model is given by;

$$h(t, \boldsymbol{X}, \boldsymbol{\beta}) = h_0(t)\, exp\left[\sum_{i=1}^{p} \beta_i x_i\right] = h_0(t)\, exp[\boldsymbol{\beta}' x_i]$$

where $h(t, \boldsymbol{X}, \boldsymbol{\beta})$ is the hazard function at time t for a subject with covariate values $x_1, x_2, \ldots, x_p$ and the estimated coefficients of the covariates of $\beta_1, \beta_2, \ldots, \beta_p$. $h_0(t)$ is the baseline hazard function, which is the hazard function for an individual for whom all the variables included in the model are zero, $\boldsymbol{X} = (x_1, x_2, \ldots, x_p)$ is the value of the vectors of the explanatory/predictor variables for a particular individual, $\boldsymbol{\beta} = (\beta_1, \beta_2, \ldots, \beta_p)$ is a vector of the estimated coefficients of explanatory/predictor variables and exp is the exponential function. Cox PH model is therefore preferred over parametric event history analysis models when there is no clear theoretical reason for positing a particular baseline hazard ratio.

4. Empirical Studies

Survival models analysis

Kaplan Meier estimates (K-M)

The Kaplan Meier Survival Probability is given in Table 1 to display the survival rate with time while the log-rank test is given in Table 2 to compare if there is no difference in the survival probability of an event at any time point in each of the groups.

Table 1: K-M Survival Probability Estimates

State	Group	Start (n_{ij})	Living (r_{ij})	Deaths (d_{ij})	Survival Prob. $p_{ij} = 1 - \frac{d_{ij}}{r_{ij}}$	Cum. Survival $S_{ij} = p_{ij} \times p_{(ij)-1}$
1	1-[0-36 months]	100	75	25	0.6667	0.6667

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2	1-[0-36 months]	330	254	76	0.7008	0.4672
3	1-[0-36 months]	0	0	0	0	0
1	2-[37-72 months]	167	149	18	0.8792	0.8792
2	2-[37-72 months]	56	45	11	0.7556	0.6643
3	2-[37-72 months]	0	0	0	0	0
1	3-[73-108 months]	156	143	13	0.9091	0.9091
2	3-[73-108 months]	120	107	13	0.8785	0.7986
3	3-[73-108 months]	0	0	0	0	0

Log rank

The log-rank test is non-parametric hypothesis test to compare two or more survival or time-to-event functions which tests the null hypothesis that there is no difference in the probability of an event at any time point in each of the groups.

$$\chi^2(log\ rank) = \sum_{i=1}^{3}\sum_{j=1}^{3}\frac{(O_{ij}-E_{ij})^2}{E_{ij}} \sim \chi^2_{\propto,(3-1)(3-1)}$$

Where;

O_{ij} is the observed number of deaths in state i, group j.

E_{ij} is the expected number of deaths in state i, group j.

H_0: *The Survival Probability for all groups are the same*

H_1: *The Survival Probability for all groups are not the same*

Table 2: Log-Rank Estimate Tableau

State	Group	Start (n_{ij})	Living (r_{ij})	Deaths $(d_{ij}) = O_{ij}$	$E_{ij} = \frac{d_{ij} * r_{ij}}{n_{ij}}$	$\frac{(O_{ij}-E_{ij})^2}{E_{ij}}$
1	1-[0-36 months]	100	75	25	18.75	2.0833
2	1-[0-36 months]	330	254	76	58.497	5.2371
3	1-[0-36 months]	0	0	0	0	0
1	2-[37-72 months]	167	149	18	16.0599	0.2344
2	2-[37-72 months]	56	45	11	8.8393	0.5282
3	2-[37-72 months]	0	0	0	0	0
1	3-[73-108 months]	156	143	13	11.9167	0.0985
2	3-[73-108 months]	120	107	13	11.5917	0.1711
3	3-[73-108 months]	0	0	0	0	0

$$\chi^2(log\ rank) = \sum_{i=1}^{3}\sum_{j=1}^{3}\frac{(O_{ij}-E_{ij})^2}{E_{ij}} = 8.3526$$

$\chi^2_{crit} = \chi^2_{0.05,4} = 9.49$

Since chi-square critical value is less than the log rank, therefore, the null hypothesis is accepted. Hence, the survival probability of all groups is the same.

The cox regression model is given as;

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$$h(t, y_i) = h_0(t)\, exp \sum_{i=1}^{8} [\beta_i x_i]$$

Where the independent variables are;

Table 3: Variable Description

Variables	Description	Coding
y_i	Stage III Colon Cancer Status	1 = Alive and Disease Free 2 = Alive and Recurrence 3 = Death
x_1	Sex	0 = Female 1 = Male
x_2	Age	
x_3	Presence of Obstruction	0 = No 1 = Yes
x_4	Perforation of the Colon	0 = No 1 = Yes
x_5	Adherence to Nearby Organs	0 = No 1 = Yes
x_6	Number of Positive Lymph Nodes	
x_7	Tumour Differentiation	1 = Well 1= Moderate 1= Poor
x_8	Extent of Local Spread	

The hazard rate is obtained as follows;

Table 4: Hazard Rate Estimate

State	Group	Start (n_{ij})	Living (r_{ij})	Deaths (d_{ij})	Hazard Rate $\frac{d_{ij}}{r_{ij}}$	Cum. Hazard
1	1-[0-36 months]	100	75	25	0.3333	0.3333
2	1-[0-36 months]	330	254	76	0.2992	0.6326
3	1-[0-36 months]	0	0	0	0	0.6326
1	2-[37-72 months]	167	149	18	0.1208	0.1208
2	2-[37-72 months]	56	45	11	0.2444	0.3652
3	2-[37-72 months]	0	0	0	0	0.3652
1	3-[73-108 months]	156	143	13	0.0909	0.0909
2	3-[73-108 months]	120	107	13	0.1215	0.2124
3	3-[73-108 months]	0	0	0	0	0.2124

The Hazard function is given as;

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$$H_o = \sum_{i:t_j \le t} \frac{d_{ij}}{r_{ij}}$$

Table 5: Hazard Function for Each Group

Group	Hazard Function (H_0)	$exp(H_0)$
1-[0-36 months]	0.6326	1.8825
2-[37-72 months]	0.3652	1.4408
3-[73-108 months]	0.2124	1.2366

The parameter estimates for the cox regression model for all groups;

Table 6: Parameter Estimates for Group 1

Variables	Group 1 (β_{1i})	p-value
x_1	-0.029	0.434
x_2	-0.001	0.446
x_3	0.056	0.279
x_4	-0.001	0.992
x_5	0.206	0.000
x_6	0.120	0.000
x_7	0.132	0.000
x_8	0.184	0.000

$$h(t, y_1) = 1.8825\,[exp\{-0.029x_1 - 0.001x_2 + 0.056x_3 - 0.001x_4 + 0.206x_5 + 0.120x_6 + 0.132x_7 + 0.184x_8\}]$$

From the parameter estimates in Table 6, the significant parameters were, $\beta_5, \beta_6, \beta_7$, and β_8. Therefore, the variable (Adherence to nearby organs, Number of positive lymph nodes, Tumour differentiation, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients.

Table 7: Parameter Estimates for Group 2

Variables	Group 2 (β_{2i})	p-value
x_1	0.012	0.788
x_2	-0.004	0.046
x_3	0.064	0.333
x_4	-0.038	0.752
x_5	0.108	0.167
x_6	0.134	0.000
x_7	0.129	0.010
x_8	0.159	0.000

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$$h(t, y_2) = 1.4408\,[\exp\{0.012x_1 - 0.004x_2 + 0.064x_3 - 0.038x_4 + 0.108x_5 + 0.134x_6 + 0.129x_7 + 0.159x_8\}]$$

From the parameter estimates in Table 7, the significant parameters were, $\beta_2, \beta_6, \beta_7$, and β_8. Therefore, the variable (Age, Number of positive lymph nodes, Tumour differentiation, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients.

Table 8: Parameter Estimates for Group 3

Variables	Group 3 (β_{3i})	p-value
x_1	-0.067	0.041
x_2	0.001	0.413
x_3	0.009	0.735
x_4	-0.225	0.022
x_5	-0.375	0.000
x_6	0.210	0.000
x_7	0.029	0.386
x_8	0.065	0.023

$$h(t, y_3) = 1.2366\,[\exp\{-0.067x_1 + 0.001x_2 + 0.009x_3 - 0.225x_4 - 0.375x_5 + 0.210x_6 + 0.029x_7 + 0.065x_8\}]$$

From the parameter estimates in Table 8, the significant parameters were, $\beta_1, \beta_4, \beta_5, \beta_6$, and β_8. Therefore, the variables (Sex, Perforation of the colon, Adherence to nearby organs, Number of positive lymph nodes, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients.

5. Discussion of results

This section considers a comprehensive discussion of the step-by-step results of analysis carried out using the survival analysis.

From Table 1, the Kaplan Meier approach is used to estimate the unadjusted survival probability beyond a certain time point. It is clearly seen that, the probability of survival started with 67% in 1-36 months and increases with time to 88% in 37-72 months then increases at its peak in 73-108 months to about 91%. The result shows a typical Kaplan Meier property of stepwise decrement from state 1 to state 2 in each of the groups. Also, the log-rank test shown in Table 2 demonstrates an unadjusted comparison between the groups and reveals that the survival probabilities in each group are the same.

The contributions of each of the factors were obtained for each of the groups. The results shown, for group 1 (1-36 months) the parameter estimates in Table 6, the significant parameters were, $\beta_5, \beta_6, \beta_7$, and β_8. Therefore, the variable (Adherence to nearby organs, Number of positive lymph nodes, Tumour differentiation, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients. From the parameter estimates in Table 7 for group 2 (37-72 months), the significant parameters were, $\beta_2, \beta_6, \beta_7$, and β_8. Therefore, the variable (Age, Number of positive lymph nodes, Tumour differentiation, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients. Also, from the parameter estimates in Table 8, the significant parameters were, $\beta_1, \beta_4, \beta_5, \beta_6$, and β_8. Therefore, the variables (Sex, Perforation of the colon, Adherence to nearby organs, Number of positive lymph nodes, and Extent of local spread) contributes significantly in the variation of the stage 3 colon cancer status of patients.

6. Conclusion

Using Survival Analysis, this study successfully and effectively predicted the course of stage III colon cancer patients as they progressed through the various stages of treatment. This methodology provides a strong framework

for understanding and improving the results of stage III colon cancer treatment. This investigation has provided vital insights that will be used to improve treatment strategies and educate public health policies. The overall goal is to improve patient care and health outcomes. Again, the use of survival analysis to investigate the pattern of survival with right and left censored data has been extremely revealing. The Kaplan Meier survival approach demonstrates an incremental stepwise likelihood of survival as treatment time for stage III colon cancer increases. Furthermore, the Cox regression analysis assessed the relationship between numerous variables and patient survival outcomes. Overall, the results show that two factors (number of positive lymph nodes and extent of local dissemination) addressed in this study are relevant and have a considerable impact on patient survival.

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