

ROLE OF AGEING METRICS TO ANALYSE THE SURVIVAL DATA OF TONGUE CANCER PATIENTS

B. ELINA^{1*}, PULAK SWAIN^{2†}, SATYA KR. MISRA³, SUBARNA BHATTACHARJEE⁴

^{1,4} Department of Mathematics, Ravenshaw University, Cuttack-753003, Odisha, India

² Department of Mathematics, ITER (SOA University), Bhubaneswar-751030, Odisha, India

³ Department of Mathematics, KIIT University, Bhubaneswar-751024, Odisha, India

¹elina.2294@gmail.com, ²pulakswain1994@gmail.com,

³satyamisra05@gmail.com, ⁴subarna.bhatt@gmail.com

Abstract

The paper vividly describes the non-parametric estimation of basic quantities for right censored data of times to death for patients with tongue cancer. Here we compare patients with two different sets of DNA profile using several parameters like reliability function, cumulative hazard rate function, smoothed hazard rate function and ageing intensity function. With the help of graphical representations of these functions, we analyse which DNA profile patients have better prognosis.

Keywords: survival function, hazard rate, cumulative hazard rate, ageing intensity function.

AMS 2020 Subject Classification: Primary 60E15, Secondary 62N05, 60E05.

1. INTRODUCTION

A quantitative analysis of failure data through various reliability functions such as, survival function, hazard (failure) rate, reversed hazard rate is known to researchers since a long time. These failure data are usually related to mechanical or a biological systems. In recent literature [4], [11], [5], [7], we also find the use of ageing intensity function along with other ageing metrics as discussed above to know about the ageing phenomena underlying a given failure data.

In many biomedical applications the primary endpoint of interest is time to a certain event. Example include: time of deaths, time it takes for a patient to respond to a therapy, time from response until disease relapse (that is, disease returns), etc.

Two important issues arise when studying time-to-event data (we will assume the "event" to be death):

(i) Some individuals are still alive till the end of the study or at the time of analysis. So the event of interest, namely death, has not occurred. Therefore we have right censored data.

(ii) Length of follow-up varies due to staggered entry. So we cannot observe the event for those individuals with insufficient times.

Suppose the events occur at D distinct times $t_1 < t_2 < \dots < t_D$, and at time t_i there are d_i events. Let Y_i be the number of individuals who are at risk at time t_i . Y_i is a count of the number of individuals with a time on study of t_i or more. The quantity $\frac{d_i}{Y_i}$ provides an estimate of the conditional probability that an individual who survives to just prior to time t_i experiences the

*The work was jointly done with the first author when she was in Ravenshaw University, Cuttack-753003, Odisha, India.

†Corresponding author : E-mail: pulakswain1994@gmail.com

event at time t_i .

The ageing intensity function $L(t)$ of any system at time $t > 0$, with probability density function $f(t)$, survival function $\bar{F}(t)$, hazard rate $h(t) = \frac{f(t)}{\bar{F}(t)}$, and cumulative hazard rate

$$H(t) = \frac{\int_0^t h(u)du}{t}$$

is given by [8]

$$\begin{aligned} L(t) &= \frac{-tf(t)}{\bar{F}(t) \ln \bar{F}(t)}, \text{ where defined,} \\ &= \frac{th(t)}{\int_0^t h(u)du} \\ &= \frac{h(t)}{H(t)}. \end{aligned}$$

Works on aforementioned functions can be found in [8], [17], [2], [6], [16], [12, 13], [14], [18], [5], [19].

In the present work, we first make a review on the notion of commonly known Kaplan-Meier and Nelson-Aalen Estimator used in survival analysis. Further, we take up a right censored data of times to death for patients with tongue cancer to illustrate the significance of the ageing metrics. In particular, we examine through different ageing metrics for drawing an inference about the distribution of the time to some event X , based on sample of right censored survival data of "Times to Death for Patients with Tongue Cancer".

The rest of the paper is organized as follows. A brief literature on Kaplan-Meier and Nelson-Aalen estimation is given in Section 2. Consequently, Section 3 presents the kernel based estimation for the ageing intensity function. Further, the survival analysis of the tongue cancer patients is done in Section 4 with the help of several ageing metrics. Finally, the concluding remarks are provided in Section 5.

2. VARIANCE OF KAPLAN-MEIER AND NELSON-AALEN ESTIMATORS

The standard estimator of the survival function proposed by [9] called Product limit estimators defined as

$$\hat{S}(t) = \begin{cases} 1 & \text{if } t < t_1 \\ \prod_{t_i \leq t} \frac{d_i}{Y_i} & \text{if } t > t_1 \end{cases} \quad (1)$$

The variance of the Product-Limit estimator is estimated by Greenwood's formula

$$\hat{V}[\hat{S}(t)] = (\hat{S}(t))^2 \sum_{t_i \leq t} \frac{d_i}{Y_i(Y_i - d_i)}. \quad (2)$$

The standard error of the product-Limit estimator is given by $\{\hat{V}[\hat{S}(t)]\}^{\frac{1}{2}}$. An estimator of the cumulative hazard rate, was first suggested by [15] and then rediscovered by [1] which is referred as Nelson-Aalen estimator of the cumulative hazard, defined as

$$\tilde{H}(t) = \begin{cases} 0 & \text{if } t \leq t_1 \\ \sum_{t_i \leq t} \frac{d_i}{Y_i} & \text{if } t \geq t_1 \end{cases} \quad (3)$$

The estimated variance of the Nelson-Aalen estimator is given by

$$\sigma_H^2(t) = \sum_{t_i < t} \frac{d_i}{(Y_i)^2}. \quad (4)$$

The standard error of the Nelson-Aalen estimator is given by $(\sigma_H^2(t))^{\frac{1}{2}}$.

3. KERNEL BASED ESTIMATION OF THE AGEING INTENSITY

Kernel-smoothed estimators of $h(t)$ are based on the Nelson-Aalen estimator $\tilde{H}(t)$ and its variance $\hat{V}[\tilde{H}(t)]$.

Let $\Delta\tilde{H}(t_i) = \tilde{H}(t_i) - \tilde{H}(t_{i-1})$ and $\Delta\hat{V}[\tilde{H}(t)] = \hat{V}[\tilde{H}(t_i)] - \hat{V}[\tilde{H}(t_{i-1})]$ denote the magnitude of the jumps in $\tilde{H}(t_i)$ and $\hat{V}[\tilde{H}(t_{i-1})]$ at time t_i . $\Delta\tilde{H}(t_i)$ provides a crude estimator of $h(t)$ at the death times. The Kernel smoothed estimator of $h(t)$ is a weighted average of these crude estimates over event times close to t . Closeness is determined by a bandwidth b , so that event times in the range $t - b$ to $t + b$ are included in the weighted average which estimate $h(t)$. The weights are controlled by the choice of a kernel function $K(\cdot)$, defined on the interval $[-1, 1]$, which determines how much weight is given to points at a distance from t .

The kernel used in following estimation of hazard rate is uniform kernel with

$$K(x) = \frac{1}{2} \text{ for } -1 \leq x \leq 1, \quad \text{if } b \leq t \leq t_D - b \quad (5)$$

$$K_q(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3} \text{ for } -1 \leq x \leq q, \quad \text{if } t \leq b \text{ given } q = \frac{t}{b} \quad (6)$$

$$K_q(x) = \frac{4(1+q^3)}{(1+q)^4} - \frac{6(1-q)}{(1+q)^3} \text{ for } -1 \leq x \leq q, \quad \text{if } t_D - b \leq t \leq t_D \text{ given } q = \frac{(t_D - t)}{b} \quad (7)$$

The kernel smoothed estimator of $h(t)$ based on the kernel $K(\cdot)$ is given by

$$\hat{h}(t) = b^{-1} \sum_{i=1}^D K\left(\frac{t - t_i}{b}\right) \Delta\tilde{H}(t_i). \quad (8)$$

The variance of $\hat{h}(t)$ is estimated by the quantity

$$\sigma^2[\hat{h}(t)] = b^{-2} \sum_{i=1}^D K\left(\frac{t - t_i}{b}\right)^2 \Delta\hat{V}[\tilde{H}(t_i)]. \quad (9)$$

Section 4 is based on the study of ageing phenomenon on the patients with cancer of the tongue.

4. STUDY ON THE EFFECTS OF PLOIDY ON THE PROGNOSIS OF PATIENTS WITH MOUTH CANCER

4.1. Background

Patients were selected who had a paraffin-embedded sample of the cancerous tissue taken at the time of surgery. The tissue samples were examined using a flow cytometer to determine if the tumor had an aneuploid or diploid DNA profile. The data in the Table 1 is on the patients with tongue cancer (c.f. [10]).

Data on 79 Patients with Cancer of the Tongue:

g : Tumor DNA profile – 1: Aneuploid, 2: Diploid

T : Time (in weeks) to death or on study time

δ : Death indicator – 1: Dead, 0: Alive

4.2. Results

From the survival function graph given in Figure 1, it can be observed that the curve end at different points as the times on study are different for two DNA group patients (i.e., 400 weeks for aneuploid patients and 231 weeks for diploid patients). Secondly the figure suggests the aneuploid patients have the best and diploid patients the least favourable prognosis. The disease free survival probability are 0.2286 ($SE = 0.0954$) for aneuploid patients and 0.0833 ($SE = 0.0716$)

Table 1: Data on 79 patients with cancer of the tongue

g	T	δ	g	T	δ
1	1	1	1	93	0
1	3	1	1	93	0
1	3	1	1	101	0
1	4	1	1	104	0
1	10	1	1	108	0
1	13	1	1	109	0
1	16	1	1	131	0
1	16	1	1	150	0
1	24	1	1	231	0
1	26	1	1	240	0
1	27	1	1	400	0
1	28	1	2	1	1
1	30	1	2	3	1
1	30	1	2	4	1
1	32	1	2	5	1
1	41	1	2	5	1
1	51	1	2	8	1
1	65	1	2	12	1
1	67	1	2	13	1
1	70	1	2	18	1
1	73	1	2	26	1
1	77	1	2	27	1
1	91	1	2	30	1
1	93	1	2	42	1
1	96	1	2	56	1
1	100	1	2	62	1
1	104	1	2	69	1
1	157	1	2	104	1
1	167	1	2	104	1
1	61	0	2	112	1
1	74	0	2	129	1
1	79	0	2	181	1
1	80	0	2	8	0
1	81	0	2	67	0
1	87	0	2	76	0
1	87	0	2	104	0
1	88	0	2	176	0
1	89	0	2	231	0

for diploid patients.

We also observe from Table 2 and Table 3 that the estimated survival function at 12 months after the transplant for aneuploid group is 0.6731 and diploid group is 0.4863 (that is, at 1 year (12 months), 67.31% of aneuploid patients were alive, whereas 48.63% of diploid patients were alive). The extended final plateau of the graph indicates that people are being cured.

From the cumulative hazard rate graph (Figure 2), we interpreted that the estimate of the cumulative hazard rate function is steeper for first 100-110 weeks (i.e., in first 110 weeks the hazard rate is approximately constant). And the plot shows that the aneuploid group patients

Table 2: Product limit estimator and its estimated variance for aneuploid group patients

t_i	d_i	Y_i	$\hat{S}(t)$	$\hat{V}[\hat{S}(t)]$	$\{\hat{V}[\hat{S}(t)]\}^{\frac{1}{2}}$
1	1	52	0.980769	0.000362711	0.01904496
3	2	51	0.942308	0.00104546	0.03233357
4	1	49	0.923077	0.001365498	0.03695265
10	1	48	0.903846	0.001671313	0.0408817
13	2	47	0.865385	0.002240271	0.0473315
16	2	45	0.826923	0.002752333	0.05246268
24	1	43	0.807692	0.002987028	0.05465371
26	1	42	0.788462	0.003207499	0.05663478
27	1	41	0.769231	0.003413746	0.05842727
28	1	40	0.75	0.003605769	0.06004806
30	2	39	0.711538	0.003947144	0.0628263
32	1	37	0.692308	0.004096495	0.06400387
41	1	36	0.673077	0.004231623	0.06505092
51	1	35	0.653846	0.004352526	0.06597368
65	1	33	0.634033	0.004473413	0.06688358
67	1	32	0.614219	0.004578501	0.06766462
70	1	31	0.594406	0.00466779	0.00466779
72	1	30	0.574592	0.00474128	0.06885695
73	1	29	0.554779	0.004798971	0.06927461
77	1	27	0.534231	0.004856632	0.06968954
91	1	19	0.506114	0.005107841	0.07146916
93	1	18	0.477996	0.005302736	0.07281989
96	1	16	0.448122	0.005497328	0.07414397
100	1	14	0.416113	0.005691417	0.07544148
104	1	12	0.381437	0.005884598	0.07671114
157	1	5	0.305149	0.008421952	0.0917712
167	1	4	0.228862	0.009102169	0.09540529

have the smallest death rate and the diploid group patients have the highest death rate. We also observe from Table 4a and Table 4b respectively that the estimated cumulative hazard function at 12 months after the transplant for aneuploid group is 0.3892 and diploid group is 0.6999 (i.e., at 1 year (12 months), 38.92% of aneuploid patients were dead whereas 69.99% of diploid patients were dead). Table 5a, Table 6a give a record of hazard rate and ageing intensity of aneuploid and diploid patients respectively. One can note that Table 5b to Table 5d depict the method to calculate hazard rate of aneuploid group at $t = 4, 30, 167$ respectively. On a similar line, the values of $\hat{h}(t_i)$ at different t_i s for aneuploid group are obtained in Table 5a. Table 6b to Table 6d reflect the computation of hazard rate of diploid group at $t = 8, 27, 181$ respectively. The required values of $\hat{h}(t_i)$ at other t_i 's for diploid group are shown in Table 6a. Thus we get a crude estimate of hazard function.

Since Figure 2 shows a crude estimate of the hazard rate so as to provide a smoothed estimated hazard rate we used uniform kernel estimation which is shown in Figure 3. The figure indicates the risk of death or hazard rate decreases slowly but the initial peak is high for diploid group patients.

From the smoothed hazard rate graphs of two DNA group patients, we compare the hazard rate of two graphs on various subintervals. These comparisons are given in Table 7.

Let $h_1(t)$ be the hazard rate function of the aneuploid patients and $h_2(t)$ be the hazard rate

Table 3: Product limit estimator and its estimated variance for diploid group patients

t_i	d_i	Y_i	$\hat{S}(t)$	$\hat{V}[\hat{S}(t)]$	$\{\hat{V}[\hat{S}(t)]\}^{\frac{1}{2}}$
1	1	28	0.964286	0.001229956	0.035070732
3	1	27	0.928571	0.002368805	0.048670367
4	1	26	0.892857	0.003416545	0.058451221
5	2	25	0.821429	0.005238703	0.072378882
8	1	23	0.785714	0.00601312	0.077544307
12	1	21	0.748299	0.006787295	0.082385044
13	1	20	0.710884	0.00745542	0.086344773
18	1	19	0.673469	0.008017493	0.089540453
23	1	18	0.636054	0.008473514	0.092051693
26	1	17	0.598639	0.008823484	0.093933402
27	1	16	0.561224	0.009067402	0.095222909
30	1	15	0.52381	0.009205269	0.095944095
42	1	14	0.486395	0.009237085	0.096109754
56	1	13	0.44898	0.009162849	0.095722771
62	1	12	0.411565	0.008982561	0.094776375
69	1	10	0.370408	0.008800344	0.093810147
104	2	8	0.277806	0.00816587	0.090365204
112	1	5	0.222245	0.007695797	0.087725689
129	1	4	0.166684	0.006644173	0.081511795
181	1	2	0.083342	0.005133974	0.071651756

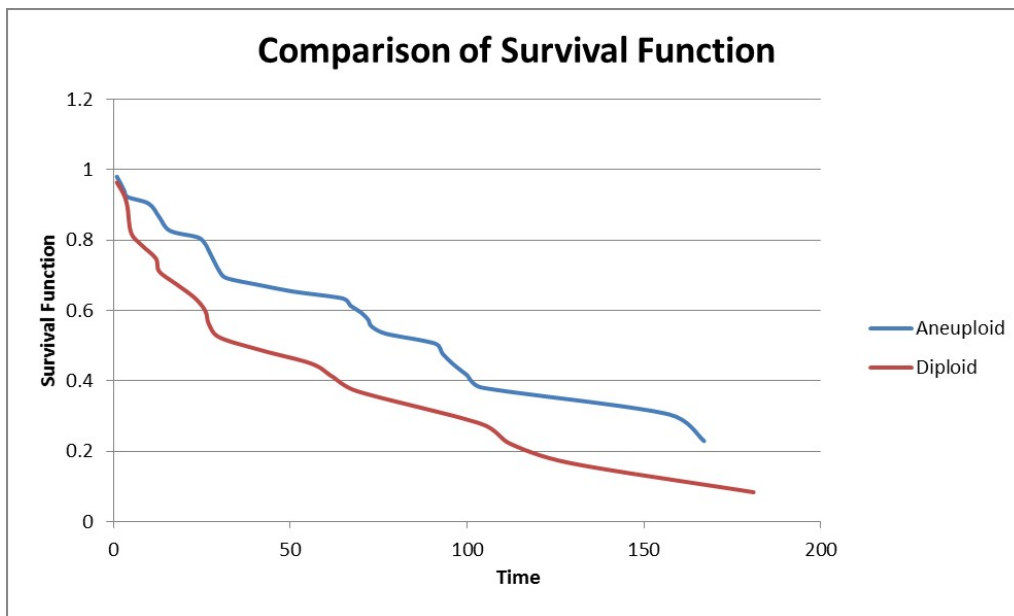


Figure 1: Comparison of survival function between aneuploid and diploid patients.

function of diploid patients.

On the basis of the above analysis we can clearly observe at interval $[1, 5)$, $[5, 13)$, $[13, 23)$, $[23, 41)$ and $[41, 42)$, the hazard rate for aneuploid patients is less than the diploid patients where as at the subintervals $[42, 51)$, the hazard rate for diploid patients is less than the aneuploid patients. Similarly we can compare the hazard rates on remaining subintervals and on an overall we

Table 4: Construction of the Nelson-Aalen estimator and its estimated variance for aneuploid and diploid tumor

t_i	$\tilde{H}(t_i)$	$\sigma_{\tilde{H}}^2(t)$	Standard Error
1	0.019230769	0.00036982	0.01923077
3	0.058446456	0.00113876	0.03374548
4	0.078854619	0.00155525	0.03943667
10	0.099687952	0.00198928	0.04460133
13	0.142241144	0.00289467	0.0538021
16	0.186685588	0.00388232	0.06230826
24	0.209941402	0.00442315	0.06650679
26	0.233750926	0.00499005	0.07064026
27	0.25814117	0.00558493	0.07473239
28	0.28314117	0.00620993	0.07880311
30	0.334423221	0.00752485	0.08674592
32	0.361450248	0.00825531	0.09085876
41	0.389228026	0.00902692	0.0950101
51	0.417799454	0.00984325	0.09921313
65	0.448102485	0.01076152	0.10373775
67	0.479352485	0.01173808	0.10834243
70	0.511610549	0.01277867	0.11304276
72	0.544943883	0.01388978	0.11785489
73	0.579426641	0.01507884	0.12279592
77	0.616463678	0.01645058	0.12825981
91	0.669095257	0.01922066	0.1386386
93	0.724650813	0.02230708	0.14935555
96	0.787150813	0.02621333	0.16190532
100	0.858579384	0.03131537	0.1769615
104	0.941912717	0.03825982	0.19560117
157	1.141912717	0.07825982	0.27974956
167	1.391912717	0.14075982	0.37517971

(a) Aneuploid

t_i	$\tilde{H}(t_i)$	$\sigma_{\tilde{H}}^2(t)$	Standard Error
1	0.035714286	0.00127551	0.03571429
3	0.072751323	0.002647252	0.05145146
4	0.111212861	0.004126542	0.06423817
5	0.191212861	0.007326542	0.08559522
8	0.234691122	0.009216901	0.09600469
12	0.28231017	0.011484475	0.10716564
13	0.33231017	0.013984475	0.11825597
18	0.384941749	0.016754558	0.1294394
23	0.440497304	0.019840978	0.14085801
26	0.499320834	0.023301186	0.15264726
27	0.561820834	0.027207436	0.16494677
30	0.6284875	0.03165188	0.17790975
42	0.699916072	0.036753921	0.19171312
56	0.776839149	0.042671081	0.20656698
62	0.860172482	0.049615525	0.22274543
69	0.960172482	0.059615525	0.24416291
104	1.210172482	0.090865525	0.30143909
112	1.410172482	0.130865525	0.3617534
129	1.660172482	0.193365525	0.43973347
181	2.160172482	0.443365525	0.66585699

(b) Diploid

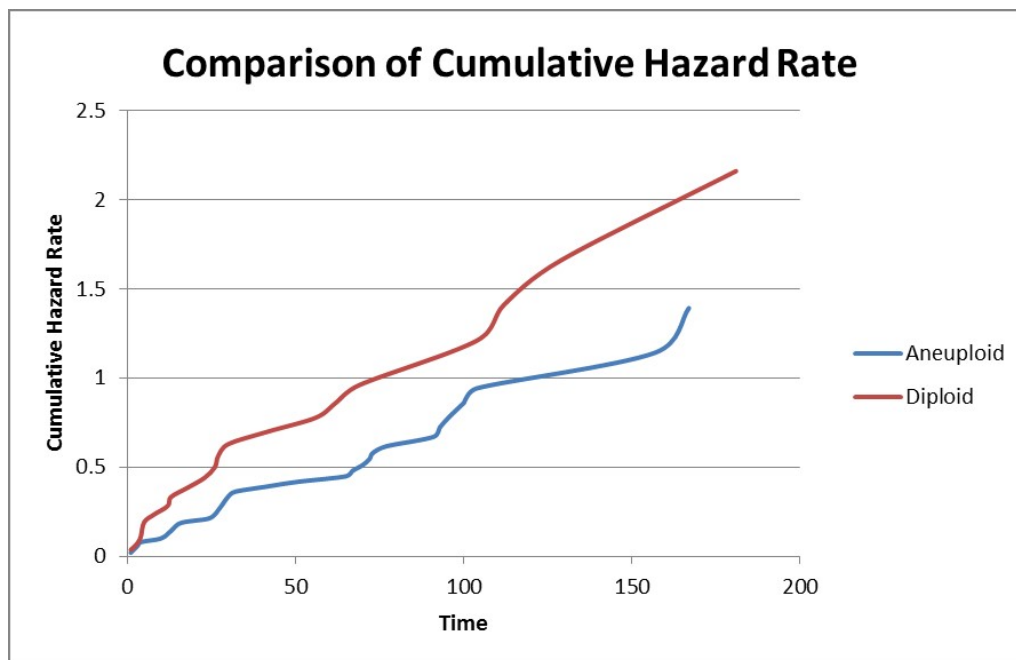


Figure 2: Comparison of cumulative hazard rate between aneuploid and diploid patients.

can again confirm the impression that aneuploid group patients have the lowest rate of death. From the ageing intensity graphs of two DNA group patients Figure 4, we compare the ageing intensities of two graphs at different intervals of time. These comparisons are given in Table 8.

Table 5: Analysis of uniform smoothed hazard rate for aneuploid group patients

t_i	d_i	Y_i	$\tilde{H}(t_i)$	$\hat{h}(t_i)$	$\hat{L}(t_i)$
1	1	52	0.019230769	0.013989484	0.727453187
3	2	51	0.058446456	0.009881253	0.169065048
4	1	49	0.078854619	0.010365443	0.131450046
10	1	48	0.099687952	0.009334279	0.093634980
13	2	47	0.142241144	0.008372741	0.058863004
16	2	45	0.186685588	0.007744815	0.041485877
24	1	43	0.209941402	0.010960455	0.052207212
26	1	42	0.233750926	0.010960455	0.046889462
27	1	41	0.258141170	0.008738233	0.033850598
28	1	40	0.283141170	0.008738233	0.030861754
30	2	39	0.334423221	0.008738233	0.026129265
32	1	37	0.361450248	0.010127122	0.028018024
41	1	36	0.389228026	0.004168812	0.010710461
51	1	35	0.417799454	0.002817460	0.006743571
65	1	33	0.448102485	0.008081359	0.018034623
67	1	32	0.479352485	0.009933211	0.020722144
70	1	31	0.511610549	0.009933211	0.019415571
72	1	30	0.544943883	0.009933211	0.018227952
73	1	29	0.579426641	0.009933211	0.017143173
77	1	27	0.616463678	0.009933211	0.016113214
91	1	19	0.669095257	0.012105785	0.018092768
93	1	18	0.724650813	0.012105785	0.016705681
96	1	16	0.787150813	0.016272452	0.020672598
100	1	14	0.858579384	0.085857938	0.100000000
104	1	12	0.941912717	0.010863095	0.011533017
157	1	5	1.141912717	0.022500000	0.019703783
167	1	4	1.391912717	0.100000000	0.071843585

(a)

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.019231	0.3	1.501458	0.02887419
3	0.039216	0.1	1.239067	0.048590875
4	0.020408	0	1.107872	0.022609633
10	0.020833	-0.6	0.3207	0.006681254
13	0.042553	-0.9	-0.07289	-0.003101519
16	0.044444	-1.2	0	0
24	0.023256	-2	0	0
26	0.02381	-2.2	0	0
27	0.02439	-2.3	0	0
28	0.025	-2.4	0	0
30	0.051282	-2.6	0	0
32	0.027027	-2.8	0	0
41	0.027778	-3.7	0	0
51	0.028571	-4.7	0	0
65	0.030303	-6.1	0	0
67	0.03125	-6.3	0	0
70	0.032258	-6.6	0	0
72	0.033333	-6.8	0	0
73	0.034483	-6.9	0	0
77	0.037037	-7.3	0	0
91	0.052632	-8.7	0	0
93	0.055556	-8.9	0	0
96	0.0625	-9.2	0	0
100	0.071429	-9.6	0	0
104	0.083333	-10	0	0
157	0.2	-15.3	0	0
167	0.25	-16.3	0	0
				$h(4) = 0.010365443$

(b) At $t = 4 < b (= 10)$, $K_q(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3}$

$$x = \frac{4-t_i}{10}, \hat{h}(8) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i)$$

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.019231	2.9	0	0
3	0.039216	2.7	0	0
4	0.020408	2.6	0	0
10	0.020833	2	0	0
13	0.042553	1.7	0	0
16	0.044444	1.4	0	0
24	0.023256	0.6	0.5	0.011627907
26	0.02381	0.4	0.5	0.011904762
27	0.02439	0.3	0.5	0.012195122
28	0.025	0.2	0.5	0.0125
30	0.051282	0	0.5	0.025641026
32	0.027027	-0.2	0.5	0.013513514
41	0.027778	-1.1	0	0
51	0.028571	-2.1	0	0
65	0.030303	-3.5	0	0
67	0.03125	-3.7	0	0
70	0.032258	-4	0	0
72	0.033333	-4.2	0	0
73	0.034483	-4.3	0	0
77	0.037037	-4.7	0	0
91	0.052632	-6.1	0	0
93	0.055556	-6.3	0	0
96	0.0625	-6.6	0	0
100	0.071429	-7	0	0
104	0.083333	-7.4	0	0
157	0.2	-12.7	0	0
167	0.25	-13.7	0	0
				$h(30) = 0.008738233$

(c) At $t = 30, (10 =) b < t < t_D - b (= 157)$, $K_q(x) = \frac{1}{2}$

$$x = \frac{30-t_i}{10}, \hat{h}(27) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i)$$

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.019231	16.6	0	0
3	0.039216	16.4	0	0
4	0.020408	16.3	0	0
10	0.020833	15.7	0	0
13	0.042553	15.4	0	0
16	0.044444	15.1	0	0
24	0.023256	14.3	0	0
26	0.02381	14.1	0	0
27	0.02439	14	0	0
28	0.025	13.9	0	0
30	0.051282	13.7	0	0
32	0.027027	13.5	0	0
41	0.027778	12.6	0	0
51	0.028571	11.6	0	0
65	0.030303	10.2	0	0
67	0.03125	10	0	0
70	0.032258	9.7	0	0
72	0.033333	9.5	0	0
73	0.034483	9.4	0	0
77	0.037037	9	0	0
91	0.052632	7.6	0	0
93	0.055556	7.4	0	0
96	0.0625	7.1	0	0
100	0.071429	6.7	0	0
104	0.083333	6.3	0	0
157	0.2	1	0	0
167	0.25	0	4	1
				$h(167) = 0.1$

(d) At $t = 167, (157 =) t_D - b < t < t_D (= 167)$, $K_q(x) = \frac{4(1+q^3)}{(1+q)^4} - \frac{6(1-q)}{(1+q)^3}$

$$x = \frac{167-t_i}{10}, \hat{h}(167) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i)$$

Table 6: Analysis of uniform smoothed hazard rate for diploid group patients

t_i	d_i	Y_i	$\tilde{H}(t_i)$	$\hat{h}(t_i)$	$\hat{L}(t_i)$
1	1	28	0.035714286	0.031166063	0.872649778
3	1	27	0.072751323	0.023461182	0.322484609
4	1	26	0.111212861	0.024474361	0.220067724
5	2	25	0.191212861	0.024130904	0.126199167
8	1	23	0.234691122	0.021894230	0.093289553
12	1	21	0.282310170	0.017461373	0.061851733
13	1	20	0.332310170	0.020239151	0.060904398
18	1	19	0.384941749	0.018530399	0.048138189
23	1	18	0.440497304	0.017308867	0.039293922
26	1	17	0.499320834	0.014808867	0.029658019
27	1	16	0.561820834	0.014808867	0.026358700
30	1	15	0.628487500	0.012177288	0.019375545
42	1	14	0.699916072	0.003571429	0.005102653
56	1	13	0.776839149	0.008012821	0.010314646
62	1	12	0.860172482	0.008012821	0.009315365
69	1	10	0.960172482	0.009166667	0.009546896
104	2	8	1.210172482	0.022500000	0.018592391
112	1	5	1.410172482	0.022500000	0.015955495
129	1	4	1.660172482	0.012500000	0.007529338
181	1	2	2.160172482	0.200000000	0.092585199

(a)

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.03571429	0.7	0.720164	0.025720132
3	0.03703704	0.5	0.679012	0.025148574
4	0.03846154	0.4	0.658435	0.025324438
5	0.08000000	0.3	0.637859	0.051028744
8	0.04347826	0	0.576131	0.025049174
12	0.04761905	-0.4	0.493827	0.023515552
13	0.05000000	-0.5	0.473251	0.023662525
18	0.05263158	-1	0.37037	0.019493158
23	0.05555556	-1.5	0	0
26	0.05882353	-1.8	0	0
27	0.06250000	-1.9	0	0
30	0.06666667	-2.2	0	0
42	0.07142857	-3.4	0	0
56	0.07692308	-4.8	0	0
62	0.08333333	-5.4	0	0
69	0.10000000	-6.1	0	0
104	0.25000000	-9.6	0	0
112	0.20000000	-10.4	0	0
129	0.25000000	-12.1	0	0
181	0.50000000	-17.3	0	0
				$h(8) = 0.02189423$

(b) At $t = 8 < b (= 10)$, $K_q(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3}$,

$$x = \frac{8-t_i}{10}, \hat{h}(8) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i)$$

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.03571429	2.6	0	0
3	0.03703704	2.4	0	0
4	0.03846154	2.3	0	0
5	0.08000000	2.2	0	0
8	0.04347826	1.9	0	0
12	0.04761905	1.5	0	0
13	0.05000000	1.4	0	0
18	0.05263158	0.9	0.5	0.026315789
23	0.05555556	0.4	0.5	0.027777778
26	0.05882353	0.1	0.5	0.029411765
27	0.06250000	0	0.5	0.03125
30	0.06666667	-0.3	0.5	0.033333333
42	0.07142857	-1.5	0	0
56	0.07692308	-2.9	0	0
62	0.08333333	-3.5	0	0
69	0.10000000	-4.2	0	0
104	0.25000000	-7.7	0	0
112	0.20000000	-8.5	0	0
129	0.25000000	-10.2	0	0
181	0.50000000	-15.4	0	0
				$h(27) = 0.014808867$

(c) At $t = 27, (10 =) b < t < t_D - b (= 171)$, $K_q(x) = \frac{1}{2}$,

$$x = \frac{27-t_i}{10}, \hat{h}(27) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i)$$

t_i	$\Delta H(t_i)$	x	$K_q(x)$	$K_q(x)\Delta H(t_i)$
1	0.03571429	1.8	0	0
3	0.03703704	1.78	0	0
4	0.03846154	1.77	0	0
5	0.08000000	1.76	0	0
8	0.04347826	1.73	0	0
12	0.04761905	1.69	0	0
13	0.05000000	1.68	0	0
18	0.05263158	1.63	0	0
23	0.05555556	1.58	0	0
26	0.05882353	1.55	0	0
27	0.06250000	1.54	0	0
30	0.06666667	1.51	0	0
42	0.07142857	1.39	0	0
56	0.07692308	1.25	0	0
62	0.08333333	1.19	0	0
69	0.10000000	1.12	0	0
104	0.25000000	-7.7	0.77	0
112	0.20000000	0.69	0	0
129	0.25000000	0.52	0	0
181	0.50000000	0	4	2
				$h(181) = 0.2$

(d) At $t = 181, (171 =) t_D - b < t < t_D (= 181)$, $K_q(x) = \frac{4(1+q^3)}{(1+q)^4} - \frac{6(1-q)}{(1+q)^3}$,

$$x = \frac{181-t_i}{10}, \hat{h}(181) = (10)^{-1} \sum_i K_q(x) \Delta \tilde{H}(t_i) = 0.2$$

Let $L_1(t)$ be the ageing intensity of the aneuploid patients and $L_2(t)$ be the ageing intensity of diploid patients.

From the Table 8 we get, at interval $[1, 5)$, the ageing intensity for aneuploid patients is less than the diploid patients where as at the subintervals $[5, 13)$, the ageing intensity for aneuploid patients is more than the diploid patients. But as we proceed, we observe that there is an alternate sign for the rest of the subintervals. Thus we cannot get a concluding remark. To obtain the desired result, we now calculate the total time for which aneuploid patients have less ageing intensity than diploid patients and vice versa.

After calculations, we get to know that the aneuploid patients have low ageing intensity than the diploid patients for a time of 101 weeks, whereas the diploid patients have less ageing intensity than aneuploid patients for a time of 79 weeks.

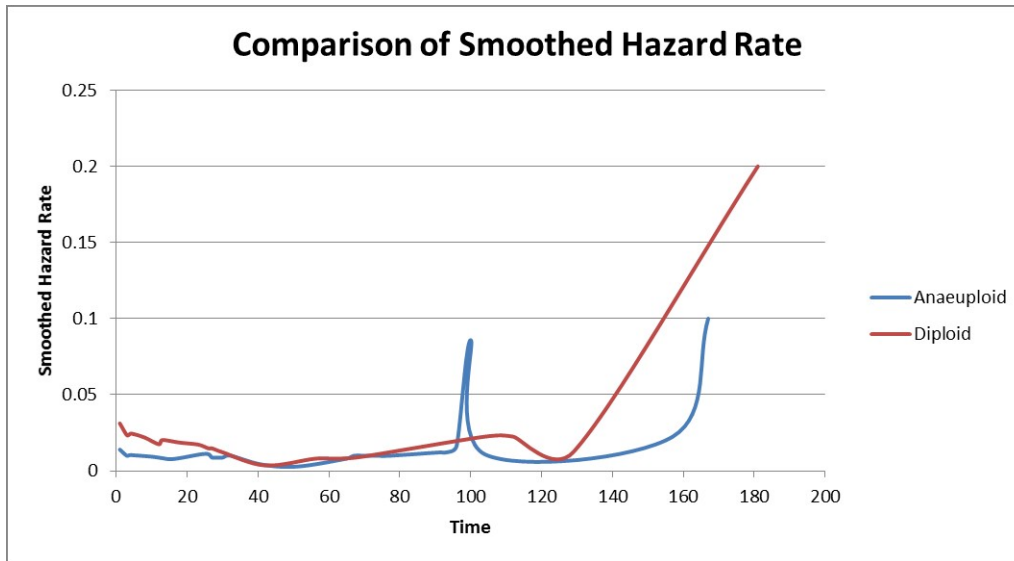


Figure 3: Comparison of smoothed hazard rate between aneuploid and diploid patients.

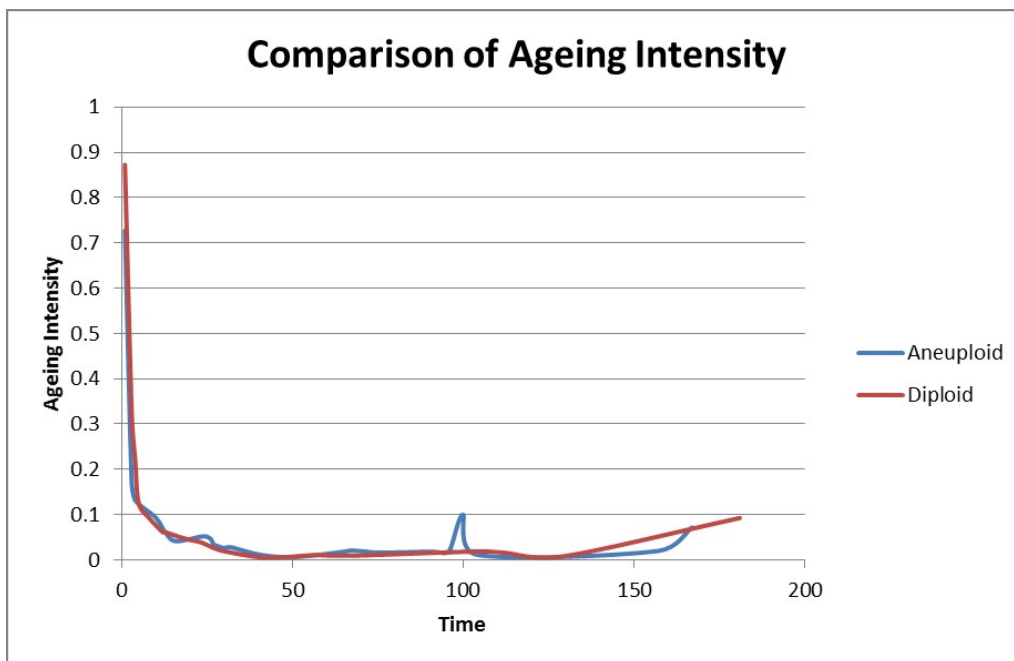


Figure 4: Comparison of ageing intensity between aneuploid and diploid patients.

On the basis of the above analysis we can clearly observe that the cancer patients with aneuploid DNA have less ageing intensity than the patients with diploid DNA profile.

5. CONCLUSION

There are several factors which are the majors of prognosis for the death (failure) of a man in case of the transplant among the patients with tongue cancer. Nonetheless, the study is confined to the effect of ploidy on the survival of patients with tongue cancer. Based on the failure data available for the patients with tongue cancer with aneuploid and diploid DNA profile, statistical analyses were made and graphical interpretation was studied from the curves obtained with several parameters like reliability function cumulative hazard rate function, smoothed hazard

Table 7: Interval-wise comparison of hazard rates between aneuploid and diploid patients

Interval	Comparison of $h(t)$
[1, 5)	$h_1(t) < h_2(t)$
[5, 13)	$h_1(t) < h_2(t)$
[13, 23)	$h_1(t) < h_2(t)$
[23, 41)	$h_1(t) < h_2(t)$
[41, 42)	$h_1(t) < h_2(t)$
[42, 51)	$h_1(t) > h_2(t)$
[51, 65)	$h_1(t) < h_2(t)$
[65, 104)	$h_1(t) > h_2(t)$
[104, 157)	$h_1(t) < h_2(t)$
[157, 181)	$h_1(t) > h_2(t)$

Table 8: Interval-wise comparison of ageing intensities between aneuploid and diploid patients

Interval	Comparison of $L(t)$
[1, 5)	$L_1(t) < L_2(t)$
[5, 13)	$L_1(t) > L_2(t)$
[13, 23)	$L_1(t) < L_2(t)$
[23, 41)	$L_1(t) > L_2(t)$
[41, 42)	$L_1(t) < L_2(t)$
[42, 51)	$L_1(t) > L_2(t)$
[51, 65)	$L_1(t) < L_2(t)$
[65, 104)	$L_1(t) > L_2(t)$
[104, 157)	$L_1(t) < L_2(t)$
[157, 181)	$L_1(t) < L_2(t)$

rate function and ageing intensity. It is analysed from the graph in all the cases that patients with aneuploid DNA profile ought to be one of the basis for prognosis for the patients with tongue cancer. Hence it is inferred that patients with aneuploid tumors may get benefit significantly from a prolonged tumor free period. Here we discuss about the analysis of the censored and uncensored failure data through various measures of ageing phenomenon. Moreover, we summarize various ageing concepts of the lifetimes that have been widely studied in the field of reliability.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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