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Using Proportional Hazard, MLE and GLIM For Difference Model Distributions in Survival analysis for Myocardial Infarction

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Abstract: This study offers a parametric modelling of the base-line hazard in terms of piecewise distributions method to proportional hazards analysis of survival data with covariates. It is simple to estimate maximum likelihood using generalized linear models (GLIM) and an iterative process. Applications are provided for the approach and its application to competing hazards, where a two-piece Weibull fit is clearly better than the basic Weibull model. The base-line hazard parameter can be subjected to any given monotonic rising transformation, which leads to a wide generality. Piecewise models of this type are predicted to be effective in explaining various proportional hazards survival processes including changepoints where the ruling conditions rapidly change. The data was collected in Education Erbil Hospital from 2020 to 2023 and using spss program to analysis the data.

Keywords: Proportional Hazards, Generalized Linear Models (GLIM), Maximum likelihood, Survival analysis, one and two parameters Weibull, and Myocardial Infarction.

أستخدام المخاطر النسبية، MLE وGLIM لتوزيعات نموذج الفرق في تحليل البقاء على قيد الحياة لاحتشاء عضلة القلب

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المستخلص: تمت في هذه الدراسة نموذجًا حدوديًا لمخاطر، خط الأساس من حيث طريقة التوزيعات الجزئية لتحليل المخاطر المتناسبية لبيانات البقاء على قيد الحياة مع المتغيرات المشتركة. من السهل تقدير أكبر الاحتمالية باستخدام النماذج الخطية المعممة (GLIM) والعملية التكرارية. يتم توفير التطبيقات لهذا النهج وتطبيقه على المخاطر المتنافسة، حيث يكون ملاءمة Weibull المكونة من معلمتين أفضل بشكل واضح من نموذج Weibull الأساسي. يمكن أن تخضع معلمة المخاطر خط الأساس لأي تحول صاعد رتيب، مما يؤدي إلى عمومية واسعة. من

المتوقع أن تكون النماذج متعددة التعريف من هذا النوع فعالة في شرح عمليات البقاء على قيد الحياة للمخاطر التناسبية المختلفة بما في ذلك نقاط التغيير حيث تتغير الحالة الحاكمة بسرعة. تم جمع البيانات في مستشفى اربيل التعليمي للفترة من ٢٠٢٠ الى ٢٠٢٣ وباستخدام برنامج spss لتحليل البيانات.

الكلمات المفتاحية: المخاطر التناسبية، النماذج الخطية المعممة (GLIM)، الاحتمالية كبرى، تحليل البقاء على قيد الحياة، معلمة واحدة ومعلمتين ويبل، واحتشاء عضلة القلب

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Introduction

The modeling of complex survival data containing covariates or risk factors has drawn a lot of attention since ubiquitous and sophisticated computing tools have become available. A few examples of sources that demonstrate the application of fully stated survival distributions include Raza & Broom (2016). In case take into account the log-logistic and logistic models. However, models that quantify the covariate effects relative to an otherwise unspecified null or 'base-line' hazard function may also be appropriate when the main concern is the evaluation of the covariates or the comparison of the risk groups, or if the underlying time dependence of the hazards is not well known. Numerous researchers have taken into consideration such partially defined models, including the general proportional hazards (PH) model, in which the survival function S(t) fulfils, is a good place to start Raza & Broom (2023).

$$\ln\{-\ln s(t)\} = f(t) + \alpha^t y \qquad (1)$$

A linear predictor($\alpha^t y$) represents the relative effects of the covariates y in terms of a vector of estimable parameters α, where *f(t)* is the logarithm of the integrated null (or base-line) hazard. Measuring the underlying temporal dependence should also be made easier with the use of effective covariate impact modelling in this technique Miller LD, et….(2005), examined the scenario, for instance, of a hazard that takes a constant value over a series of time intervals. But such a process may be too parameterized and is just halfway to a succinct parametric model. A concise depiction of the survival process is obtained via parsimonious modelling of the complete survivor function (as opposed to simply the cov effects) Crowder, Miller. (2012) . In situations (such as calculating the length and expense of hospital treatment for heart transplant patients, our first example) when inference on variables is not the only goal, this can offer a straightforward foundation for actuarial evaluation of survival and be of interest on its own. In this study, we establish parsimonious PH can assist point models that may be examined by GLIM analysis. We explain two parameters Weibull distribution-based applications and suggest some potential generalizations Lawless JF , et…(2003) and Raza (2008).

1- Survival analysis theory

For the sake of convenience, we present the generalisation after the theory for the piecewise Weibull base-line basis. We utilise mea change points $b_1,..., b_i$ to divide the time axis into i+ 1 intervals, and set $b_0= 0$ and $b_{i+1}=\infty$ (or the greatest probable lifetime of the persons under study) for convenience. Assuming continuous monitoring of survival times under right censoring, we establish the following indicator variables: h and d1. The kth individual for k = 1,..., n should survive to time tk with a q-dimensional covariate vector yi and a censoring indicator hk, which should be set to unity if the individual is not censored and zero otherwise. Additionally, for j = 1,..., i+1; k = 1,...,n.

Let $$d_{kj} = \begin{cases} 1 & if\ b_{j-1} < t_k \le b_j \\ 0 & otherwise \end{cases}$$

Let *f (t)* the piecewise Weibull form

$$f(t) = \beta_j \ln t + \delta_j, \qquad b_{j-1} < t \le b_j, \quad j = 2,...,i+1 \qquad (2)$$

Continuous of *f (t)* at the change points $b_1,\ldots, b_i$ requires that

$$\beta_j \ln \beta_j + \delta_j = \beta_{j+1} \ln \beta_j + \delta_{j+1} \qquad (2a)$$

Or

$$\delta_j = \delta_1 + \sum (\beta_{r-1} - \beta_r) \ln \beta_{r-1}, \qquad j = 2,...,i+1, \qquad (2b)$$

So that each changepoints adds one more parameter and

$$f(t) = \delta_1 + \beta_j \ln t + \sum_{r=2}^{j} (\beta_{r-1} - \beta_r) \ln \beta_{r-1}, \qquad \beta_{j-1} < t \le \beta_j, \ \ j = 2,..,i+1, \qquad (2c)$$

The summation over r being omitted if j=1. For the k_{th} individual we have

$$f(t_i) = \delta_j + \sum_{j=1}^{i+1} d_{ij} \left\{ \beta_j \ln t_i + \sum_{r=2}^{j} (\beta_{j-1} - \beta_r) \ln \beta_{r-1} \right\}; \qquad (2d)$$

Differentiation of the integrated hazard $H_k = \exp\{f(t_i) + \alpha^t y_k\}$

$$w_k = f'(t_k) H_k = \sum_{j=1}^{i+1} d_{ij} H_k \beta_j / t_k = \prod_{j=1}^{i+1} \beta_j^{d_{ij}} H_k / t_k. \qquad (2e)$$

Now from equation (1) and the definition of H_i we have

$$\ln s(t_k) = -H_k, \qquad (2f)$$

Or

$s(t_k)=exp(-H_k)$, and differentiation with respect to time yields the survival time density as

$$g(t_k) = h_k \exp(-H_k). \qquad (2g)$$

Utilising the censoring indictor *hi*, we can thus write the *ith* individual's contribution to the log-likelihood *L* as

$$L_i = h_i \ln w_i - H_i = h_i (\sum_{j=1}^{i+1} d_{kj} \ln \beta_j - \ln t_k) + h_i \ln H_i - H_i, \qquad (3)$$

Where

$$\ln H_k = \alpha' y_k + \delta_1 + \sum_{j=1}^{i+1} d_{kj} \{\beta_r \ln t_k + \sum_{r=2}^{j} (\beta_{r-1} - \beta_r) \ln \beta_{r-1}\}, \qquad (4)$$

The elimination of the sum over r in the case where j = 1 and M = ΣM. It is clear that the formal kernel of the log-likelihood of a Poisson *hk* with mean Mk is represented by the expression hi; ln M1- Mk in equation (3). For given values of *as* and changepoints *b1,...,bi*, the remaining right-hand side of equation (4) can be considered as a 'offset' in GLIM (i.e., a function of known parameters not including α). δ1 can be absorbed into the constant term of the linear predictor *α'y*. It is simple to obtain the first derivatives of *M* with regard to the αs and as:

$$\frac{dM}{d\alpha_j} = \sum_{k=1}^{n} (h_k - H_k) y_{kj}, \qquad j = 0,1,...,q \qquad (5)$$

$$\frac{dM}{d\beta_j} = \sum_{k=1}^{n} [\frac{h_k d_{kj}}{\beta_j} + (h_k - H_k)\{d_{kj} \ln t_k + (1-\lambda_{j,i+1}) \sum_{s=j+1}^{i+1} d_{ks} \ln \beta_j - (1-\lambda_{j1}) \sum_{s=j}^{i+1} d_{ks} \ln \beta_{j-1}\}] \quad (6a)$$

Or

$$\frac{dM}{d_{\beta j}} = \sum_{k=1}^{n} \frac{h_i d_{kj}}{\beta_j} + \sum_{k=1}^{n} (h_i - H_i) c_{kj}, \ \ j = 1,2,...,i+1, \qquad (6b)$$

Where *ckj* represents the term in curly brackets in equation (6a), and the lemda functions *λj1* and *λj,i+1* are unity and zero otherwise for *j=1* and *j=i+1*, respectively. The likelihood equations for the *βs* can be adjusted to provide updated answers, given *a* (current) solution for the βs and αs, using equations (6a) and (6b).

$$\beta_j = \frac{\sum_{k=1} h_i d_{kj}}{\sum_{k=1}^{n} (h_i - H_i) c_{kj}}, \qquad j = 1,2,...,i+1. \qquad (7)$$

The result for β when fitting a simple (single) weibull hazard without changepoints (and dropping the indicators d_{kj}) is generalised by equations (6a, 6b, and 7).

$$\frac{dM}{d\beta}=\sum_{k=1}^{n}\{\frac{h_k}{\beta}+(h_k-H_k)\ln t_k\},$$

$$\beta=\frac{\sum_{k=1}^{n}h_k}{\sum_{k=1}^{n}(h_k-H_k)\ln t_k}. \quad (8)$$

Assume, in order to generalize the argument, that g(t) = t in the piecewise Weibull equation (2), where g is any given monotonic rising transformation (the extreme value distribution, for instance, can be obtained by writing exp t for t). Next, g(t) replaces t for all k = 1,...,n; g(b,) replaces b;, j = 1,..., i; and last, g'(tk)/g(tk) replaces the component 1/tk when it is differentiated to yield wk = f'(tk)Hk. Plotting the survivor function empirically within the main risk categories Raza & Broom (2016).

2- Literature review

Myocardial infarction is most common disease in the east country affecting a large number of men at some point in their lives (who Global Burden of disease, 2022). If we could provide an appropriate model form and the quantity of changepoints (i) to provide starting values for b1,..., bi. Plotting the function g(t) against a linear timeframe should ideally result in the complementary log-transform of S(t) appearing piecewise linear. g(t) = t in g(t) represents the Weibull distribution. As long as the graph displays distinct linear segments rather of a curved, smoothly increasing gradient, the right number of changepoints (i) and accurate initial estimations should be evident. An examination of the physical conditions surrounding the survival process could provide more evidence for the value of i that was selected. Based on our personal experience and common sense, i = 1 or i = 2 should be sufficient for all but very huge data sets. An iterative technique akin to that employed for the underlying Weibull distribution can be utilised to find maximum likelihood (ML) estimates of parameters, Tahir Mahmood (2024) and Lambert PC, (2009). We may compute the offset function f(t) and estimate α using a poisson model with a log-linear link and given offset, given the initial estimates for the bs and αs and with parameters δ1 absorbed into the α/y ter. Substituting the current values of the Hks and ckjs into equation (7) yields updated estimates of the *αs*. Up to the offset-given convergence, this operation is repeated. Next, the current values for the di and Hs are substituted into the resulting equation. In order to do this, a GLIM macro that may be expanded as needed has been built for the situation of two stages and is based on the library macro weibul,Lemke. D., (016) and Ziaei J,et… (2013). ML estimates can be found by trial and error, with all other parameters being estimated conditionally on the known current changepoints. Ultimately, the entire process needs to be optimised for the choice of the changepoints a1,..., ak. The approach shouldn't take long for small i and with solid beginning estimations, as should be obtained graphically for a weibul established model.

For the cases that will follow, roughly ten trials were enough to ascertain the ML estimate b1, to the closest day. Cox., (1975) and Breslow's (1974) approach also has an issue with GLIM underestimating the standard errors for α because those are conditional on all other known parameters. While the estimation of covariate effects ought to be fairly resilient to slight variations in the base-line hazard, the standard errors for α, conditioned on all other known parameters, should be roughly orthogonal to the remaining parameters and have a negligible effect. If desired, sections of the profile likelihoods might include approximate estimates of the standard errors of the other parameters.

Because of the previously mentioned practical considerations, a lot fewer change points than the piecewise constant segments in Curado, M. P, et… (2007) and Breslow's (1972) formulation are probably going to be needed, which will lead to an economy of parameters and a simpler model.

Tests for goodness-of-fit can be performed, and conclusions drawn from the partially described study can be contrasted. As previously mentioned, this method can be expanded by permitting any monotonic time transformations in consecutive intervals and, in turn, modifying the continuity constraints on f(t). Nevertheless, the change points bj and any additional unknown parameters would need to be approximated repeatedly George., et. (2022).

3- Survival analysis data following heart transplant

Using the survival analysis of 50 transplant recipients' survival rates from the Erbil Education Hospital, we present our first illustration. instead of the degree of tissue type mismatch between the giver and recipient, the number of days from January 1, 2021, to acceptance into the Erbil Hospital Education, programme (ACC), the length of the transplant waiting period (LWT), and an indicator REJ for whether or not the death was caused by rejection (1 = yes, 0 = no). We leave out the variables ACC and LWT since earlier research, such as that of Health Grove (2017) and Bedford T, et….(2009), was unable to demonstrate their significance. We give thorough comparisons with the proportional hazards models fitted by Clark, T.G et… (2003) and Curado, M.et …(2009. With changepoints b1 at about 70 days (ln t≈4.24), Fig.1 presents a two parameter Webull model with the Kaplan-Meier survival plot of In{-In S(t)} against In t. The ML value of 70 days is confirmed by fitting this model with major effects for a range of values of b1. First, it should be noted that the piecewise exponential model is essentially a representation of the partially defined PH model proposed by Cox (1972), with the addition of a formal changepoint at each subsequent time of death. Therefore, this model offers the reference deviation that can be used to compare any fully parametric PH model's lack of fit.

Therefore, this model offers the reference deviation that can be used to compare any fully parametric PH model's lack of fit. With an excess of deviation (or deviance 2) of 577.97-504.83= 73.14 on 61-21=40 degrees of freedom (DF) (p = 0.001), the (simple) exponential model is thus ruled out. In contrast, the simple Weibull model has two parameters (2) = 560.86-504.83= 56.03 on 39 DF, 0.025<p<0.05. This is greatly outperformed by the two parameter Weibull model with *b1* = 70 days, which reduces the deviation by 14.72 on 2 DF (considering *b1* as an estimable parameter), p < 0.001; the model's lack of fit is measured by two parameters (2) = 546.14-504.83 = 41.31 on 37 DF, 0.19 <p< 0.29.

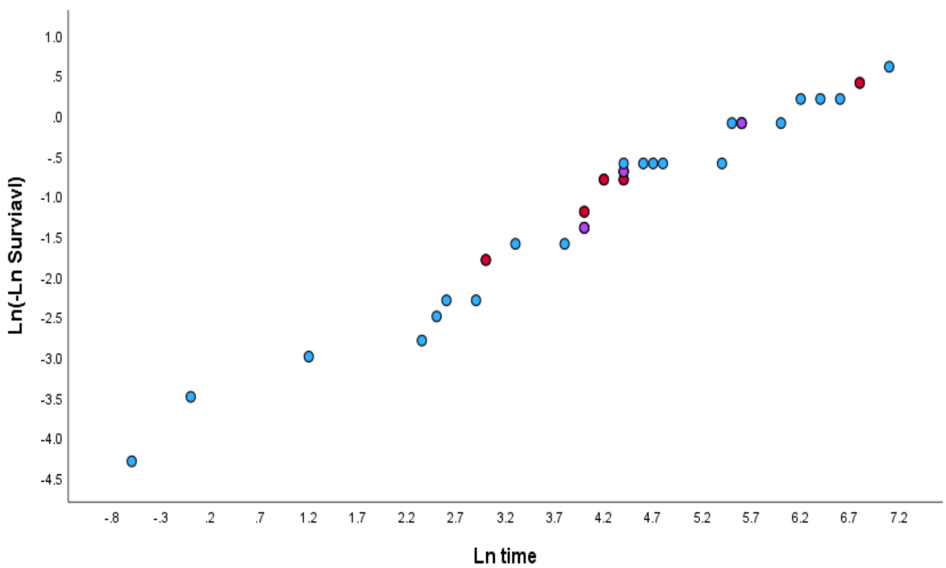

Fig. (1): *Survival plot for the Myocardial Infarction for deaths from all causes*

Figure 1 shows the Kaplan Meier survival plot for the patient deaths for all cases and of Ln time against Ln with minus Ln survival function suggested a two parameter weibull model with change points b_1 at about 70 days is equal (ln t≈4.24).

In terms of the covariates, all the models concur that AGE is significant, with the impacts of SURG and MM being somewhat more ambiguous. The estimates of corresponding parameters for all models likewise show good agreement; for the two parametere and simple Weibull models, the estimated α/y matches to within half a standard error or less.
Smaller than the standard error.

4- Survival analysis in terms of competing hazards

The Weibull models' residual plots show a little better fit, while the previous models' residual graphs exhibit curvature. According to certain theories, the abnormal plots could represent the coexistence of two or more unconnected causes of mortality, such as organ rejection following transplantation and other factors. Therefore, we take into account competing risks analysis, where deaths resulting from each cause are analysed independently. The likelihood of the complete data can be expressed as the product over the causes of the likelihood of the observed deaths owing to each cause separately, in each case treating deaths due to other cases as censored data, as is widely known, Alexander D, et… (2024) and Raza (2006).
Results for rejection-related deaths are displayed in Table 2 and Fig. 2. Trials using a main effects model validate this as the ML estimate, and the data indicate to a changepoint at roughly 68 days as previously. Around this period, also observed a sudden shift in the hazard function. Though they are hypothetical at this point in time, such causes could include modifications to the patient's environment, mobility, or medication regimen. The estimated covariate effects, as in the overall analysis, closely resemble those obtained using the basic Weibull model.
The results, however, point to rejection as a clearly distinct cause of death because AGE and MM seem to be more significant; additionally, the two parameter Weibull model's hazard shape estimates (β_1= 3.04, β_2 = 0.49) show a sharp contrast, and the residual plot's curvature practically vanishes. Deviance comparisons support the superiority of the two-parameter model (deviance χ^2 against the piecewise exponential model is 25.63 on 25 DF, $0.4<p<0.5$); deviance χ^2 versus the basic exponential model is 27.4 on 3 DF, $p < 0.005$.

Table (1): Comparison of models for the data

Model	b_1 (days)	β_1	β_2	Grand Mean	Age	Surg	MM	Deviance	DF
Two Parameters	70	1.2	0.4	-8.7 (1.05)	0.05 (0.021)	-0.83 (0.50)	0.37 (0.28)	545.58	58
One parameter	70	0.62	0.4	-7.3 (1.090)	0.06 (0.022)	-0.92 (0.50)	0.46 (0.28)	560.88	60
Exponential	70	0.62	0.4	-11.08 (1.20)	0.09 (0.024)	-1..05 (0.47)	0.214 (0.30)	577.10	61
Piecewise exponential	70	0.62	0.4	-2.95 (1.08)	0.06 (0.021)	-0.86 (0.48)	0.43 (0.28)	504.80	21

Table 1 shows, the interaction effects are globally negligible, as they have been in previous analyses. The interaction effects are globally negligible, as they have been in previous analyses.

Table (2): Modeling data because of not acceptant.

Model	b_1 (days)	β_1	β_2	Grand Mean	Age	Surg	MM	Deviance	DF
Two Parameters	70	3.04	0.49	-19.73 (1.49)	0.09 (0.03)	-1.04 (0.61)	0.84 (0.33)	385.03	58
One parameter	70	0.87	0.49	-12.21 (1.56)	0.11 (0.03)	-1.09 (0.61)	0.93 (0.32)	411.50	60
Exponential	70	0.87	0.49	-13.61 (1.60)	0.12 (0.03)	-1.13 (0.61)	1.02 (0.32)	412.48	61
Piecewise exponential	70	0.87	0.49	-5.64 (1.51)	0.09 (0.03)	-1.05 (0.61)	0.92 (0.33)	399.42	33

Table 2 shows the data suggested a changepoints at about 70 days as before, and trails with a main effect model confirm this as the ML estimate. On the other hand, also noted an abrupt change in the hazard function at about this time.

We now examine deaths that result from reasons other than rejection in a similar manner; the findings are displayed in Fig. 3. Though less definite than previously, the survival plot indicates a potential changepoint at roughly 52 days (the ML value is 50 days), as deaths not resulting from rejection do not significantly load on any of the factors during the very short observation period of this investigation. The simple exponential model is again ruled out by the deviation χ^2 versus the piecewise exponential model;

On the other hand, the two parameter model reaches χ^2 = 10.82 on 10 DF (0.3 <p<0.4) and the simple Weibull model achieves χ^2 = 15.52 on 12 DF (0.2 < p < 0.3). The two-parameter model's non-significant χ^2 versus the straightforward Weibull model is 181.07-176.37=4.7 on 2 DF (counting the change-point). The primary effects are eliminated in the second two parameter model: DF increases by only 0.98 in χ^2 .

Therefore, either Weibull model might be used for fatalities from various causes; nevertheless, the two-parameter option is preferable for a thorough study in terms of one form of model (with directly comparable estimates). For the competing risks strategy, the two parameter Weibull hazards are

$$h_{rej}(t) = 23162.86 * 0.0001314^{c} t^{2.549c-0.506} \exp(\alpha'_{rej} y)$$

$$where\, c = 1\, if\ t \le 70\, and\ c = 0\, otherwise\ and$$

$$\alpha'_{rej} y = -19.73 + 0.09956 Age - 1.042 Surg + 0.8418 MM,$$

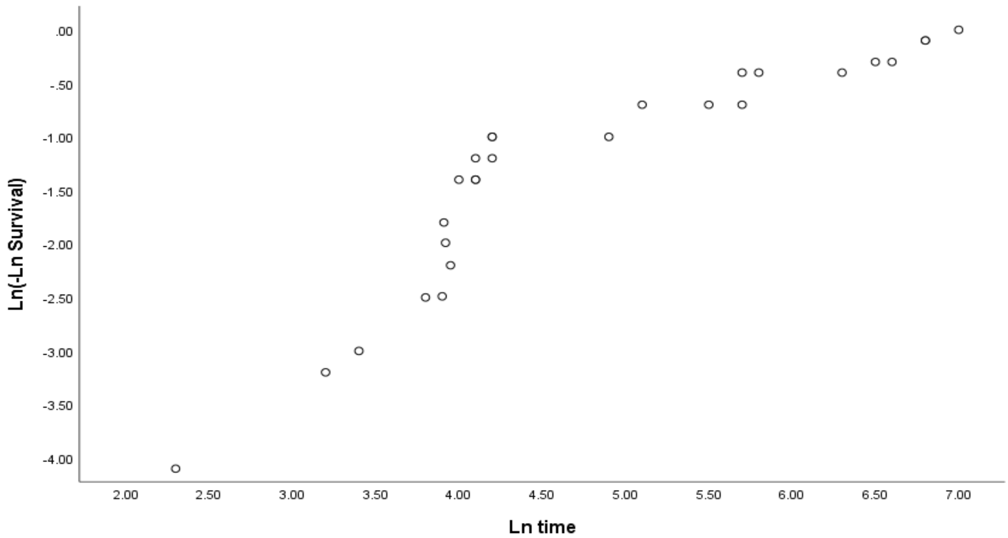

Figure (2): Survival analysis plot for deaths due to rejection.

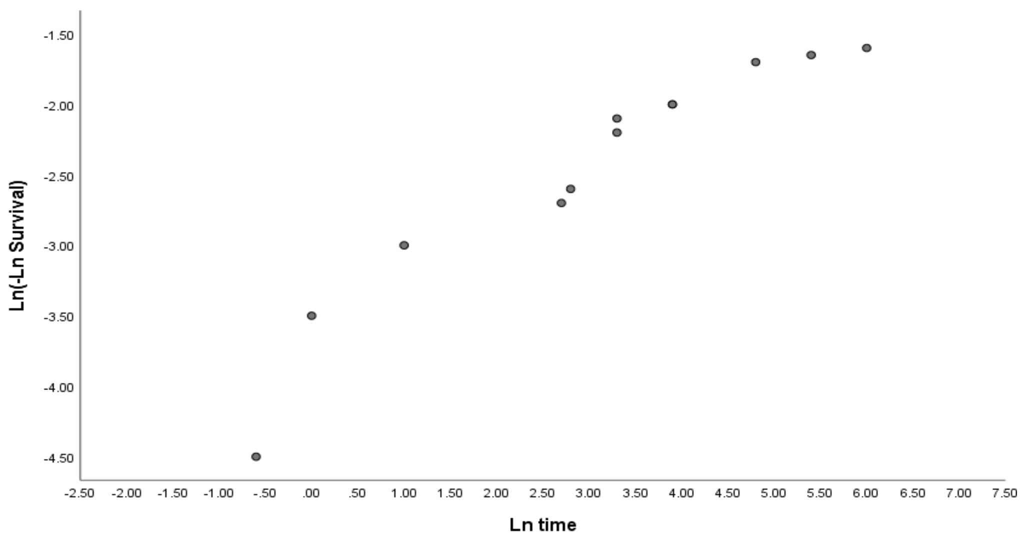

Figure (3): Survival analysis plot for deaths due to others cases.

and

$$h_{nr}(t) = 1.014 * 0.6183^{c} t^{0.448c-0.821} \exp(-4.298).$$

where c=l if t ≤ 50 and c= 0 otherwise. As noted in Section 2, the estimation of α and of the base-line hazard are approximately orthogonal, in so far as the former are but little altered by significant improvements in the latter.

5. Discussion

The model's fit is much enhanced in the examples provided by adding even a single changepoint, or a time-critical modification to the base-line hazard's parameters (but not its fundamental form). GLIM-based computation has a low burden. when discernible alterations in the risk patterns occur. Changepoints could have a physical justification as well. The heart transplant data's competing risks analysis reveals notably distinct causes of death (implant rejection as opposed to other causes), with rejection showing a distinct changepoint at roughly 9 weeks.

Physically meaningful parameters—including changepoints—are typically simpler and easier to understand. Two, three, or more changepoints can be used in the analysis, as described in Section 2, and any PH curve can be roughly represented by linear segments on, instance, the complementary logarithmic scale. There are issues with this method, too, as it returns to a partially defined model, which is harder to estimate than the Cox's model's piecewise exponential equivalent. The estimation of changepoints is likely to be laborious in the absence of strong graphical evidence or a compelling argument. The higher number of factors may make identification difficult, and standard errors may be grossly underestimated. On the other hand, the data shows how the success parsimonious changepoints model adapts to other parametric models that are mentioned without appreciably worsening the fit compared to the partially defined model.

The predictor that is linear in equation (1.4). The effects of the variables should be roughly orthogonal to the base line hazard parameters, including the scale, if they are recoded in relation to their average values. Lastly, the proportional odds model can be subjected to a similar examination. The authors plan to publish a report on this effort.

6. Conclusion

Worldwide, and particularly in developing nations, rates of Maycerdalinfraction, the most frequent cancer in men and less than one-fifth of all cancers in humans, are rising. Kurdistan-Iraq is not an exception, with an age-adjusted incidence rate of 60.3 per 100,000 per year; in fact, the Kurdistan-Iraqi Cancer Registry reports that Maycardal is the most common disease in the country, affecting approximately one-third of male patients, with particularly concerning rates among younger individuals.

A detailed assessment of the survival rate is necessary to address this issue. To that end, we utilise the Kaplan-Meier and Cox regression techniques in our work.

The primary finding is that we have created a novel technique for carrying out a survival study on a distribution system. Specifically, we have demonstrated the situations in which a two-piece Weibull fit is manifestly superior to the basic Weibull model in survival curve analysis. We have also demonstrated the process of estimating a real hazard (survivor) function from the biassed one that is derived straight from the data.

Using data from Education Erbil hospital. For some parameter estimates we get realistic survival function curves. These models are even so a significant improvement on trying to estimate survival curves.

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