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Weighted Estimation in Cox Regression: An Application to Breast Cancer Data

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ABSTRACT

Cox regression is a well-known approach for modeling censored survival data. However, the model has an assumption of proportional hazards which requires an attention. In this study, we examine weighted estimation in Cox regression model under nonproportional hazards. Our aim is to propose various weighting functions that are more appropriate than existing ones. The proposed and existing weighting functions are applied to a data set in breast cancer in order to analyze their effects on the analysis results. In order to analyze the performance and effect of proposed and existing weighting functions, a wide simulation study, covering different censoring rates and tied observations, is carried out.

Key Words: *Cox regression model, Log-rank tests, Nonproportional hazards, Weighted estimation.*

Mathematics Subject Classification: 62N01, 62N02

1. INTRODUCTION

Survival analysis is a class of statistical methods for studying the occurrence and timing of events. This analysis has many areas of application in a broad field of different subjects e.g. in biostatistics, in engineering as

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reliability analysis or in sociology as event-history analysis. Survival data is a term used for describing data that measure the survival time, which is defined as the time to the occurrence of a given event. This event can be the death, development of a disease, response to a treatment, equipment failures, births, marriages, divorces, promotions, earthquakes and so forth.

Survival data have some features that are difficult to handle with traditional statistical methods: censoring and time-dependent covariates. Regression models for survival data are particularly interested in studying the effect of the variables on survival. The most common model for such an effect is the so-called Cox [7] regression model or the proportional hazards model which is used widely in medical and epidemiological studies. For this model, the exact form of the underlying survival distribution does not need to be known; nevertheless the adequacy of this model includes the assumption of proportional hazards (PH). We assume that the hazard functions of different individuals are proportional and hazard ratio is independent of time with the PH assumption. In short follow-up studies, assumption of a constant hazard ratio is reasonable. However, especially in long follow-up studies it is common for the hazard ratios vary with time and thus the assumption of PH is not justified and nonproportional hazards occur.

When the PH assumption is violated, results from a Cox regression model are unreliable [15] and modeling the data by the extensions of Cox regression such as stratified Cox regression model or Cox regression model with time dependent covariates is more appropriate. An alternative approach for modeling nonproportional hazards is Cox regression model with weighted estimation. Weighted estimation in Cox regression model is suggested by Schemper [20, 21] and has advantages over the other suggested models in case of nonproportional hazards. This model has no limitation for the distribution of survival time, it can be analyzed without additional parameters and it does not need to determine a strata variable.

In this study, we propose new weighting functions by considering available survival function estimates in the literature. We consider weighted estimation in Cox regression model with the proposed and available weights over a breast cancer data set. A simulation study is achieved to compare weighting functions including tied and censored observations for different sample sizes.

This paper is organized as follows. In Section 2, Cox regression model and its key properties are introduced. Weighted estimation in Cox regression model is reviewed, proposed weighting functions and model selection criteria are mentioned. In Section 3, sample data of the breast cancer is given to illustrate the models discussed in Section 2 and results are reported. The simulation study is carried out and the results are evaluated in Section 4. A discussion is given in Section 5.

2. COX REGRESSION MODEL AND ITS EXTENTIONS UNDER NONPROPORTIONAL HAZARDS

2.1. Cox Regression Model

The most common approach to model covariate effects on survival time is the Cox regression model [7] which takes into account the effect of censored observations. When subjects have not experienced the event of interest at the end of the study, the exact survival times of these subjects are unknown and these are called censored observations. The Cox regression model is defined as:

$$h(t) = h_0(t)\exp(\beta' x), \tag{2.1}$$

where t denote time until the event of interest, **x** is a row vector of covariates of dimension p and **β** is a p-vector of covariate coefficients and $h(t)$ is the hazard at time t for individual with covariate vector $\mathbf{x} = (x_1, x_2, ..., x_p)$. $h_0(t)$ is a function describing the dependence of the hazard on time t. This function is completely unspecified. Coefficient vectors of the covariates are estimated using a maximum likelihood (ML) procedure and ML estimates are obtained by maximizing a (partial) likelihood function (L). A likelihood function, which considers tied observations, suggested by Breslow [5] is given by

$$L(\beta) = \prod_{j=1}^{k} \frac{\exp(\boldsymbol{\beta}'\mathbf{s}_j)}{\left[\sum_{\ell \in R(t_j)} \exp(\boldsymbol{\beta}'\mathbf{x}_\ell)\right]^{d_j}}, \tag{2.2}$$

where the ordered death times are denoted by $t_1 < ... < t_k$ and the set of individuals who are at risk at time t_j are denoted by $R(t_j)$. In Eq. (2.2), the $\mathbf{s}_j$ is the vector of sums of each of the p covariates for those individuals who die at the j^{th} death time, $t_{(j)}, j = 1, 2, ..., r$. If there are d_j deaths at $t_{(j)}$, the h^{th} element of s_j is $s_{hj} = \sum_{r=1}^{d_j} x_{hjr}$, where x_{hjr} is the value of the h^{th} covariate, $h = 1, 2, ..., p$, for the r^{th} of d_j individuals, $r = 1, 2, ..., d_j$ who die at the j^{th} death time, $j = 1, 2, ..., k$ [5].

Since the Cox regression model relies on the PH assumption, it is very important to verify that covariates satisfy the assumption of proportionality. The assessment of PH assumption can be done by many numerical or graphical approaches. None of these approaches is known to be superior in finding out nonproportionality. Interpreting graphical plots can be arbitrary. The conclusions are highly dependent on the subjectivity of the researcher. Some of these graphical approaches are log-minus-log survival plots of survival functions, a plot of survival curves based on the Cox regression model and Kaplan-Meier estimates for each group, a plot of cumulative baseline hazards in different groups [2], a plot of difference of the log cumulative baseline hazard versus time, a smoothed plot of the ratio of log-cumulative hazard rates time, a smoothed plot of scaled Schoenfeld residuals versus time and a plot of estimated cumulative hazard versus number of failures [3]. There are various numerical approaches such as a test of including a time dependent covariate in the model [7], a test based on the Schoenfeld partial residuals [22], which is a measure of the difference between the observed and expected value of the covariate at each time [23], a test based on a comparison of different generalized rank estimators of the hazard ratio [10], a test based on a semiparametric generalization of the Cox regression model [16,20].

If the PH assumption is violated, the Cox regression model is invalid and extensions of the Cox regression model should be used.

2.2. Cox Regression Model with Weighted Estimation

Weighted estimation in Cox regression model is proposed by Schemper [20] in case of nonproportional hazards. The model is an extension of Cox regression model, but unlike Cox regression model, the weighting function is defined for the covariates that do not satisfy the PH assumption in the first derivatives of log likelihood function given by Eq. (2.2). Estimates of β_j are obtained by setting the first derivatives of log L given by Eq. (2.3) to zero,

$$\frac{\partial \log L}{\partial \beta_k} = \sum_{j=1}^{r} f_k(t_j) \left[s_{jk} - \frac{d_j \sum_{\ell \in R(t_j)} x_{\ell k} \exp(\beta' \mathbf{x}_\ell)}{\sum_{\ell \in R(t_j)} \exp(\beta' \mathbf{x}_\ell)} \right], \quad 1 \le k \le p \qquad (2.3)$$

where $f_k(t_j)$ is the weighting function. The maximum likelihood estimates (MLE) of the β-parameters in the Cox regression model can be found by maximizing log-likelihood function using numerical methods such as Newton-Raphson procedure. The corresponding information matrix $I(\hat{\beta})$ is given by,

$$I_{ks} = -\frac{\partial^2 \log L}{\partial \beta_k \beta_s}$$

$$= \sum f_k(t_j) f_s(t_j) d_j \left\{ \sum_{\ell \in R(t_i)} \frac{x_{\ell k} x_{\ell s} \exp(\beta' \mathbf{x}_\ell)}{\sum_{\ell \in R(t_j)} \exp(\beta' \mathbf{x}_\ell)} \right. \qquad (2.4)$$

$$\left. - \frac{\left[\sum_{\ell \in R(t_j)} x_{\ell k} \exp(\beta' \mathbf{x}_\ell) \right] \left[\sum_{\ell \in R(t_j)} x_{\ell s} \exp(\beta' \mathbf{x}_\ell) \right]}{\left[\sum_{\ell \in R(t_{ji})} \exp(\beta' \mathbf{x}_\ell) \right]^2} \right\}, \quad 1 \le k, s \le p$$

In Eq. (2.3) and (2.4), weighting function ($f_k(t_j)$) is taken as 1 for proportional hazards whereas different weighting functions can be taken for nonproportional hazards. The suggested weighting functions by Schemper 820] are given as follows;

$$f_k(t_j) = \Re(t_j) \qquad (2.5)$$

and

$$f_k(t_j) = n\tilde{S} \qquad (2.6)$$

where $\Re(t_j)$ is the size of the risk set R(t_j), $\tilde{S}$ is the (Kaplan-Meier) estimated survival function and n is the total sample size (Gehan [9]; Prentice [18]).

There is a close connection between Cox regression model and log rank test. Cox regression model with weighted estimation is obtained by using the weighting functions of log rank tests. In Table 1, weighting functions numbered by (1)-(7) are the functions used for weighted log rank tests in the literature and weighting functions numbered by (1) and (2) are the functions used by Schemper [20]. The existing weighting functions numbered (3) to (7) have not been used in the studies of Schemper [20,21]. Also, the weighting functions numbered (8) to (12) have been used as weights neither in the log rank tests nor in the Cox regression. In this study, we propose weighting functions numbered (13) to (20). They are formulated from existing survival function estimates. And we suggest that the use of the weighting functions numbered (3) to (20) in the weighted estimation in Cox regression can be beneficial [4].

In Table 1, n_j denotes the individuals at risk and d_j denotes the individuals died within the interval [t_j, t_{j+1}). S_j^{ALT}, is the survival function estimate of Altshuler [1], S_j^* is the survival function estimate of Prentice-Marek [19], S_j^{**} is the survival function estimate of Harris

Albert [11], S_j^{KM} is the survival function estimate of Kaplan-Meier [12], S_j^{*PREN} is the survival function estimate of Prentice [18], S_j^{PREN} is the survival function estimate of Moreau et al.[14] (see Leton and Zuluaga [13] for details). These estimates are used in proposed weighting functions.

Table 1. Weighting functions.

	Weighting function	
	Gehan	n_j
	N-KM	NS_j^{KM}
	Moreau	$S_j^{PREN} = \prod_{i=1}^{j} \frac{n_i}{n_i + d_i}$
	Tarone-Ware (TW)	$\sqrt{n_j}$
	Weighted Peto-Peto	S_{j-1}^{KM}
	Andersen (Weighted Prentice-Marek)	$S_j^* n_j / (n_j + 1)$
	Modified Peto-Peto	$S_j^{KM} n_j / (n_j + 1)$
	Altshuler	$S_j^{ALT} = \prod_{i=1}^{j} \exp\left(-\frac{d_i}{n_i}\right)$
	Harris-Albert	$S_j^{**} = \prod_{i=1}^{j} \frac{n_i + d_i - 1}{n_i + d_i}$
0	Peto-Peto (KM)	$S_j^{KM} = \prod_{i=1}^{j} \frac{n_i - d_i}{n_i}$
1	Prentice	$S_j^{*PREN} = \prod_{i=1}^{j} \frac{n_i}{n_i + 1}$
2	Prentice-Marek	$S_j^* = \prod_{i=1}^{j} \frac{n_i - d_i + 1}{n_i + 1}$
3	N-Altshuler	NS_j^{ALT}
4	N-Harris-Albert	NS_j^{**}
5	N-Moreau	NS_j^{PREN}
6	N-Prentice	NS_j^{*PREN}
7	N-Prentice-Marek	NS_j^*

8	Modified Altshuler	$S_j^{ALT} n_j / (n_j + 1)$
9	Modified Harris-Albert	$S_j^{**} n_j / (n_j + 1)$
0	Modified Moreau	$S_j^{PREN} n_j / (n_j + 1)$

3. EMPIRICAL STUDY : AN APPLICATION TO BREAST CANCER DATA

3.1. Data Set

In the analysis, breast cancer data of 42 patients [8] are chosen to illustrate the use of weighting functions. Patients, who are diagnosed with breast cancer, are taken into the study. In the following analysis, recurrence of the illness after the operation time is the endpoint of interest (failure). This variable is measured in months and there is 146-month-follow-up period. Patients, who are still alive at the end of the follow-up period, are treated as censored observations. The complete data set consists of 42 observations, of which 61.90% are censored.

Prognostic factors, which affect the survival time of breast cancer patients, are tried to be determined. Since our main aim is to analyze the behavior of the suggested weighting functions, we take into consideration only two qualitative covariates: medical treatment type (X_1) and radiotherapy (X_2) in the following study. Medical treatment type indicates which treatment type: TMX or L-PAM, the patient attended. Radiotherapy indicates whether the patient receive radiotherapy or not. Table 2 shows summary of the covariates.

Table 2. Summary of data.

Variable		Number of total event (n)	%	Number of failed events	Number of censored events
Medical treatment type	TMX	20	47.6	10	10
	L-PAM	22	52.4	6	16
Radiotherapy	Not received	16	38.1	6	10
	Received	26	61.9	10	16

Of the 42 patients in the sample, 16 patients failed and 26 survived. During the period, the average duration of the whole sample is 45.95 months, while the average duration is 51 months for the patients that failed and 42.85 months for the patients that censored.

3.2. The Results

Before modeling the data, the PH assumption is assessed by a statistical test. This test is accomplished by finding the correlation between the Schoenfeld residuals for a particular covariate and the ranking of individual failure times. It is shown by a correlation analysis of partial residuals with time: p value obtained for treatment type is 0.0157 whereas 0.7022 for radiotherapy. Hence, it is found that medical treatment type does not hold the PH assumption. Although a statistical test is just more objective, a graphical approach is also more informative. For instance, parallelism of the log-minus-log plots for different levels of covariates shows the satisfaction of the PH assumption. The same conclusion for the PH assumption of covariates is derived from the log-minus-log plots given by Figure 1 and 2.

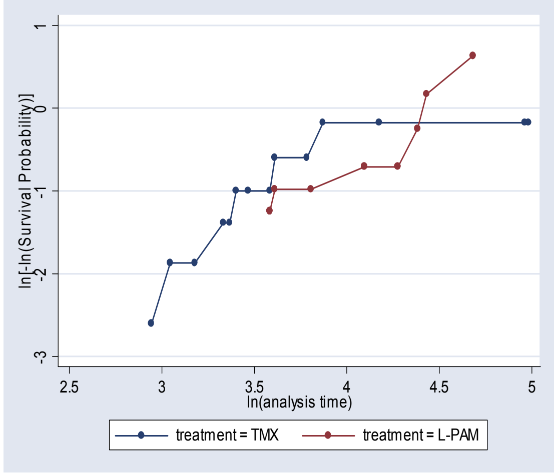

Figure 1. Estimated survival function for treatment.

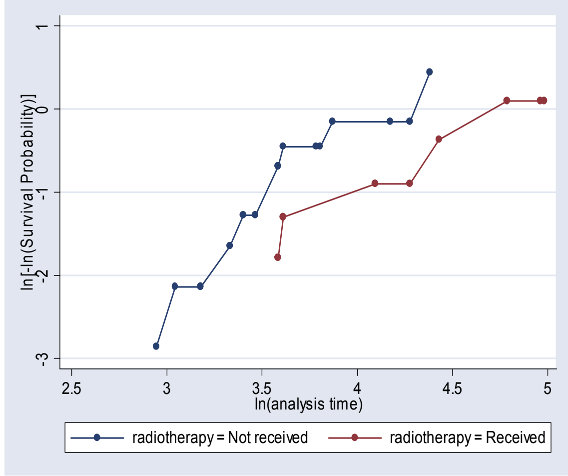

Figure 2. Estimated survival function for radiotherapy.

Thus, the example of real data permits a focused comparison of competitive techniques related to the Cox regression model which are useful in the presence of nonproportional hazards.

If the PH assumption is not satisfied, another strategy is to run a Cox regression model with weighted estimation. In this study, we carry on weighted estimation in Cox regression model. All computations are carried out on a computer code prepared in MATLAB. The parameter estimates and standard errors are given by Table 3.

Table 3. Results of parameter estimates.

Models			$\hat{\beta}_1$	$\hat{\beta}_2$	$SE(\hat{\beta}_1)$	$SE(\hat{\beta}_2)$
Cox regression model			-0.1008	-1.1259	0.5299	0.5607
Weighting function	**1**	Gehan	-0.2068	-1.1343	0.0141	0.5617
	2	N-KM	0.0499	-1.1149	0.0137	0.5590
	3	Moreau	-0.1170	-1.1271	0.5404	0.5607
	4	Tarone-Ware	-0.1546	-1.1301	0.0866	0.5612
	5	Weighted Peto-Peto	-0.1241	-1.1277	0.5373	0.5608
	6	Andersen	-0.1199	-1.1274	0.5548	0.5608
	7	Modified Peto-Peto	-0.1204	-1.1274	0.5551	0.5608
	8	Altshuler	-0.1172	-1.1272	0.5405	0.5607
	9	Harris-Albert	-0.2093	-1.1345	0.6083	0.5617
	10	Peto-Peto (KM)	-0.1175	-1.1272	0.5406	0.5607
	11	Prentice	-0.1923	-1.1331	0.6009	0.5616
	12	Prentice-Marek	-0.1170	-1.1271	0.5404	0.5607
	13	N-Altshuler	0.0501	-1.1149	0.0137	0.5590
	14	N-Harris-Albert	-0.0337	-1.1209	0.0155	0.5597
	15	N-Moreau	0.0503	-1.1149	0.0137	0.5590
	16	N-Prentice	-0.0172	-1.1196	0.0153	0.5596
	17	N-Prentice-Marek	0.0503	-1.1149	0.0137	0.5590
	18	Modified Altshuler	0.0474	-1.1151	0.5903	0.559
	19	Modified Harris-Albert	-0.0362	-1.121	0.6687	0.5597
	20	Modified Moreau	0.0476	-1.115	0.5902	0.559

According to the standard errors of parameter estimates, Cox regression model with weighting functions entitled as Gehan, Tarone-Ware, N-Altshuler, N-Harris-Albert, N-KM, N-Moreau, N-Prentice, N-Prentice-Marek have smaller standard errors for the covariate that does not satisfy the PH assumption than the Cox regression model. Thus, using Cox regression model with weighted estimation is more adequate than Cox regression model under nonproportional hazards for this data set.

4. THE SIMULATION STUDY

In the simulation study, we compare the use of different weighting functions for weighted estimation in Cox regression model and study the effect of the censoring rates and sample sizes on the estimates obtained from weighted Cox regression. All computations were carried out on a computer program prepared in MATLAB.

In this study, two dichotomous variables (x_1, x_2) are taken into consideration and x_1 is generated to have nonproportional hazards and x_2 is generated to have proportional hazards. Survival times are generated from Weibull distribution. Population regression model is taken as follows:

$$y = [(0.8 + \beta_1 x_1)(0.8 + \beta_2 x_2)] / 0.8 \quad (4.1)$$

where $\beta_1 = 0.7$, $\beta_2 = 1.4$. Over model (4.1), scale (α) and shape (γ) parameters of Weibull(α, γ) distribution are determined for x_1 and x_2 as follows; $\alpha = 0.8$, $\gamma = 1$ for $x_1 = 0$, $x_2 = 0$; $\alpha = 1.5$, $\gamma = 3$ for $x_1 = 1$, $x_2 = 0$; $\alpha = 2.2$, $\gamma = 1$ for $x_1 = 0$, $x_2 = 1$; $\alpha = 4.125$, $\gamma = 3$ for x_1=1, $x_2 = 1$. This setting of α and γ is chosen to get nonproportional hazards. The probability of having proportional hazards in the simulated data is as low as to be considered as Monte Carlo error. To generate censoring times and determine the censored observations, we utilize the studies of Persson and Khamis [17]. Censoring time C_i's, $i = 1, 2, ..., n$ are drawn from the uniform distribution $U(0, a)$ where a is chosen to ensure a desired censoring rate (CR). Censoring rates are chosen to be 10%, 30%, and 60%, respectively. It is checked while the simulation code is running that observed censoring rates are in the range of ± 0.05 of the predetermined censoring rates. Sample sizes are taken as 25, 50 and 100. 1000 samples are generated for each combination of censoring rate and sample size.

The sample mean square error (MSE) values are obtained to compare the performance of the models examined in the simulation study and the results are given in Table 4.

Table 4. Obtained MSE values for traditional and weighted Cox regression model with different weighting functions.

Models		Sample size	Censoring rate		
			10%	30%	60%
Traditional Cox regression model		25	15.2438	16.9941	19.8103
		50	12.8969	14.2500	17.7627
		100	11.5927	13.1218	15.4229
Weighted Cox regression model					
Weighting function	Altshuler	25	17.3874	18.4305	20.5561
		50	14.4647	15.1886	18.2294
		100	12.8118	13.9015	15.7815
	Andersen	25	17.5349	18.5643	20.6943
		50	14.5103	15.2270	18.2650
		100	12.8290	13.9161	15.7925
	Gehan	25	16.8123	18.1558	20.0587
		50	14.3226	15.3052	18.2744
		100	12.8164	14.1425	16.0131
	Harris-Albert	25	17.6045	19.0905	21.4381
		50	14.6248	15.6521	18.8077
		100	12.9513	14.2930	16.2273
	Moreau	25	17.2960	18.3813	20.5356

		50	14.4323	15.1726	18.2231
		100	12.7988	13.8947	15.7790
	Peto-Peto (KM)	25	17.4929	18.4858	20.5789
		50	14.4995	15.2055	18.2362
		100	12.8253	13.9086	15.7842
	Prentice	25	16.5521	18.3480	21.0423
		50	13.8537	15.1656	18.5744
		100	12.3403	13.8882	16.0514
	Prentice-Marek	25	17.2993	18.3826	20.5362
		50	14.4343	15.1736	18.2235
		100	12.8003	13.8955	15.7793
	Tarone-Ware	25	15.8336	17.3474	19.5566
		50	13.5453	14.6871	17.8582
		100	12.1157	13.5878	15.6488
	N-Altshuler	25	16.1821	17.1991	18.6952
		50	13.9878	14.6771	17.4450
		100	12.6049	13.6795	15.4520
	N-Harris-Albert	25	16.3115	17.5637	19.1646
		50	14.1127	15.0430	17.8613
		100	12.7279	14.0282	15.8314
	N-KM	25	16.2619	17.2371	18.7082
		50	14.0178	14.6917	17.4499
		100	12.6173	13.6856	15.4541
	N-Moreau	25	16.1129	17.1650	18.6832
		50	13.9596	14.6643	17.4403
		100	12.5928	13.6722	15.4502

Table 4. Obtained MSE values for traditional and weighted Cox regression model with different weighting functions (Continued).

Weighted estimation in Cox regression model		Sample size	Censoring rate		
			10%	30%	60%
Weighting function	N-Prentice	25	15.4963	17.0134	18.9095
		50	13.4334	14.6257	17.6767
		100	12.1579	13.6533	15.6749
	N-Prentice-Marek	25	16.1154	17.1659	18.6836
		50	13.9614	14.6650	17.4405
		100	12.5938	13.6730	15.4503
	Weighted Peto-Peto	25	17.2460	18.3408	20.4926
		50	14.4222	15.1643	18.2231
		100	12.7971	13.8926	15.7800
	Modified Altshuler	25	17.1822	18.1837	19.9720

		50	14.3440	15.0050	17.9025
		100	12.7564	13.8171	15.6303
	Modified Harris-Albert	25	17.4059	18.7648	20.8469
		50	14.4971	15.4479	18.4521
		100	12.8917	14.1974	16.0595
	Modified Moreau	25	17.0921	18.1379	19.9516
		50	14.3131	14.9896	17.8964
		100	12.7438	13.8104	15.6279
	Modified Peto-Peto	25	17.7345	18.6701	20.7387
		50	14.5747	15.2591	18.2778
		100	12.8539	13.9292	15.7974

As seen in Table 4, traditional Cox regression model has better results than weighted Cox regression model according to MSE for censoring rates 10%, and 30% and also for all sample sizes. However, for censoring rates 10%, and 30%, N-Prentice has the minimum MSE for n=25 and n=50 whereas Tarone-Ware has the minimum MSE for n=100 within the weighting functions.

For censoring rate 60%,

- When n=25, weighted estimation in Cox regression model with weighting functions N-Altshuler, N-KM, N-Prentice, N-Prentice-Marek, N-Harris-Albert, N-Moreau, Tarone-Ware has better results than traditional Cox regression model. Besides, N-Moreau has the minimum MSE within the weighting functions.
- When n=50, weighted Cox regression model with weighting functions N-Altshuler, N-KM, N-Prentice, N-Prentice-Marek, N-Moreau has better results than that of Cox regression model. Besides, N-Prentice-Marek has the minimum MSE within the weighting functions.
- When n=100, traditional Cox regression model gives better results than weighted Cox regression model. However, N-Moreau has the minimum MSE within the weighting functions.

The simulation study implies that for sample sizes 25 and 50 and 60% censoring rates, we get weighting functions that give better results than Gehan and N-KM weighting functions. Weighted estimation in Cox regression model with Tarone-Ware, N-Altshuler, N-Harris-Albert, N-KM, N-Moreau, N-Prentice, N-Prentice-Marek weighting functions should be used for sample size 25, whereas N-Altshuler, N-KM, N-Moreau, N-Prentice, N-Prentice-Marek weighting functions should be used for sample size 50 under nonproportional hazards.

5. DISCUSSION

The most popular survival model, Cox regression model, can lead the researcher to unreliable results, if its main assumption called as PH assumption does not hold. In this study, Cox regression model with weighted estimation under nonproportional hazards is examined and different weighting functions for this model are illustrated on a data set. Cox regression model with weighted estimation has some advantages over models such as stratified Cox regression model and Cox regression model with time-dependent covariates, because there is no requirement of distributional assumption, additional parameters and determination of a strata variable. A breast cancer data that contains nonproportional hazards is used for illustration of the models in the study. Parameter estimates of covariates are obtained to decide the appropriate weighting function for the breast cancer data set. Cox regression model with weighting functions entitled as Gehan, Tarone-Ware, N-Altshuler, N-Harris-Albert, N-KM, N-Moreau, N-Prentice, N-Prentice-Marek give reasonable results than Cox regression model.

Furthermore, a simulation study is carried out to show the utility of new weighting functions. According to the MSE of the models, sample sizes 25 and 50 under 60% censoring rates, Cox regression model with weighted estimation gives better results than traditional Cox regression model. Finally, weighted Cox regression model gives more reasonable results than the traditional Cox regression model for small sample sizes and large censoring rates. Therefore use of weighted estimation in Cox regression model is highly recommended in areas working with small sample size such as medicine, reliability, event history analysis, duration analysis.

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