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Original Article

A simulation study to compare median survival time estimators for interval-censoring

Prapasiri Ratchaprapapornkul*, and Kanit Sriklaub

Department of Educational Research and Psychology, Faculty of Education, Chulalongkorn University, Bangkok, 10330, Thailand

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Abstract

The objective of this study is to compare nonparametric methods for estimating the median survival time from interval-censored data, under varying levels of right-censoring (30%, 40%, and 50%) and sample sizes (80, 200, and 400), using Monte Carlo simulation across scenarios. Survival times are simulated from a Weibull distribution with parameters representing constant, increasing, and decreasing hazard rates. Three methods – Turnbull's EM algorithm uses linear interpolation for a non-smooth ($TB_{lin-diag}$) stepwise survival function, the Iterative Convex Minorant (*ICM*), and the Kaplan-Meier applies midpoint imputation with linear interpolation (KM_{mid}) – are evaluated using mean squared error (MSE).

Simulation results indicate that all three methods perform well, with KM_{mid} achieving the lowest MSE especially when the sample size is 200 or 400 with non-increasing hazard rates. $TB_{lin-diag}$and *ICM* produce similar results, with relative MSE values ranging from 1.37% to 36.72% higher than KM. With increasing hazard rate and 50% censoring rate, $TB_{lin-diag}$ and *ICM* overestimated the median survival time, whereas KM_{mid} underestimated it. Additionally, increasing the sample size generally lowers the MSE for all methods when the hazard rate is decreasing or constant.

Keywords: nonparametric estimator, interval-censored, Kaplan-Meier estimator, Turnbull estimator, Iterative Convex Minorant

1. Introduction

In survival analysis, interval-censored data can occur in many areas, especially in the study of time to event where the data are only known to be as interval values (between bounds); and interval-censored data frequently arise in clinical trials and longitudinal studies, as well as in social or educational contexts, such as when studying school dropout rates, where the exact time of an event, such as disease progression, is unknown but is constrained within an interval between periodic observations. In social sciences and educational research, interval-censored data can arise in longitudinal studies that track student performance or societal outcomes over time. For instance, researchers may be interested in understanding the time it takes for students to reach educational milestones (e.g., completing a degree) or for individuals to exhibit certain social behaviors (e.g., employment after training). Similar to clinical trials, where exact event times are unknown due to periodic observation, educational and social science studies often collect data at intervals, leading to uncertainty in the exact timing of events. Even though most time-related data or events of interest are constrained by the duration of data collection, leading to right-censored data, interval-censored data can also involve right-censoring in many cases. Therefore, interval-censored data always mixes with right-censored data. The right-censored observations come from participants who missed follow-up or withdrew, or events beyond the end of the study.

Several well-known methods have been developed for estimating survival functions S(t) and median survival times from such data. The Kaplan-Meier (KM) estimator, originally designed for right-censored data, can be adapted to interval-censored data by imputing the event time as the midpoint or the endpoint of the observed interval (Giesecke *et al*., 1988; Grover *et al*., 2013; Harezlak, & Tu, 2006; Law & Brookmeyer, 1992; Støvring and Kristiansen, 2011; Sun *et al*., 2013; Williams *et al*., 2004). However, midpoint imputation may introduce biases, especially when intervals are wide or irregular. The

*Corresponding author
Email address: prapasiri.r@chula.ac.th

Turnbull estimator (Turnbull, 1976) offers a nonparametric maximum likelihood estimate (NPMLE) for interval-censored data but leaves the survival function undefined over certain intervals, which can be addressed by interpolation techniques (Fay & Shaw, 2010; Hebeisen, 2014; Ratchaprapapornkul & Ingsrisawang, 2019). The Iterative Convex Minorant (*ICM*) algorithm further refines survival estimates under monotonicity and convexity constraints (Chen *et al*., 2012; Groeneboom & Wellner, 1992; Jongbloed, 1998). Although the interval-censored data always mixes with right-censoring in real-world applications (Samuelsen, & Kongerud, 1994; Sun, 1995), the estimator of median survival time or the survival function are recommended for use in this mixed case that is quite challenging. The median survival function is commonly used to compare the effectiveness of treatments and to understand survival trends following a given treatment. It determines the time at which half of the population under study has experienced the event of interest, such as death, failure, or relapse. Specifically, the median survival time is the point at which the survival function (S(t)) equals 0.5, meaning that 50% of the subjects are still surviving while the other 50% have experienced the event. It is particularly valuable because it provides a more robust measure of central tendency compared to the mean, especially when dealing with skewed data or censored observations (Kleinbaum, & Klein,2012).

The Kaplan-Meier (KM) estimator and Turnbull (TB) estimator are widely recognized for estimating the median survival functions under right-censored and interval-censored data, respectively. There have been several studies comparing the performances of median survival function estimators and survival function estimators at other time points. Lindsey and Ryan (1998) evaluated both parametric and nonparametric approaches and noted that Kaplan-Meier estimators with midpoint or left/right-point imputation could introduce biases depending on interval width. Nishikawa and Tango (2004) showed that the mid-point imputed KM estimator often yielded smaller mean squared error (MSE) than Turnbull under regular interval spacing. Gorelick (2009) investigated crossover behaviors between KM and Turnbull estimators, influenced by factors such as sample size and the frequency of follow-up. Ratchaprapapornkul and Ingsrisawang (2019) further compared KM with midpoint imputation and Turnbull with linear interpolation, showing that while Turnbull had smaller bias, KM achieved smaller MSE overall.

Moreover, the Iterative Convex Minorant (*ICM*) algorithm is also widely used for estimating the survival function in cases of interval-censored data. The *ICM* algorithm works by iteratively refining an initial guess of the survival function, ensuring it is non-decreasing and convex, a requirement for survival estimates. At each iteration, the algorithm computes the largest convex function, known as the convex minorant, that fits under the current estimate, and continues refining until convergence to the nonparametric maximum likelihood estimate (NPMLE) is achieved (Chen *et al*., 2012).This lack of consensus encourages us to examine how well the *ICM* and other estimates perform, especially when using a linear interpolation on the intervals. The goal of this study was to evaluate the performance of nonparametric estimators for median survival time under different conditions of right-censoring, sample size, and hazard rate, using a simulation-based approach. We designed 27 simulation scenarios by varying the right-censoring rates (30%, 40%, and 50%), the sample sizes (80, 200, and 400), and the shape parameters of the Weibull distribution (0.8, 1.0, and 1.5). For each scenario, survival times were generated and follow-up visits were scheduled at 2-week intervals. The estimators were assessed based on bias, variance, mean squared error (MSE), and relative MSE. The estimator with the smallest MSE was considered the most efficient.

2. Materials and Methods

2.1 Imputation method and Kaplan-Meier estimator

Suppose t is the time to event and it is known to be within the interval $(L_i, R_i]$ for i^{th} subject where $i = 1, 2, \ldots, n$. The midpoint imputation $m_i = \frac{(L_i + R_i)}{2}$ can be obtained for each interval $(L_i, R_i]$ where $i = 1, 2, \ldots, n$. Then the imputed value m_i is treated as an exact observation, the KM method could be applied to the interval-censored data in order to estimate the $S(t)$. Moreover, KM estimator is a nonparametric maximum likelihood estimator of the survival function, which is also known as the product-limit estimator. It is a step function which depends on each time point associated with an uncensored observation. Suppose that there are n individuals with the time to event t and there are m unique times among the individuals, where $m \leq n$. Let $t_{(j)}$, $j = 1,2, \ldots, m$ be the ordered unique times of n individuals, n_j be the number of subjects at risk to an event at time $t_{(j)}$, and d_j be the number of subjects that have had the event at time $t_{(j)}$. Then the KM estimator of $S(t)$ was defined as follows (Kaplan & Meier, 1958) :

$$S(t) = \begin{cases} 1 & if\ t < t_{(1)} \\ \prod_{j=1}^{k} \left(\frac{n_j - d_j}{n_j} \right) & if\ t_{(q)} \leq t < t_{(q+1)} \end{cases} \quad (1)$$

2.2 Turnbull with linear interpolation estimator

Assume that the survival times $T_1, T_2 \ldots, T_n$ are iid with probability density function $f(t)$ and the cumulative distribution function $F(t)$. Let $(L_i, R_i]$ be the interval censored data for subject i, where $i = 1, 2, \ldots, n$. Let $A = \bigcup_{i=1}^{n} (L_i, R_i]$ and assume the likelihood function for these intervals is given by: $L(F) = \prod_{i=1}^{n} [F(R_i +) - F(L_i -)]$. The procedure for estimating the survival function using the TB follows the self-consistency algorithm, as described in Ratchaprapapornkul & Ingsrisawang (2019).

The TB intervals are defined as m disjoint intervals $(q_1, p_1], \ldots, (q_m, p_m]$, where the endpoints $q_j$and p_j are drawn from the sets $\{L_i\}$ and $\{R_i\}$, respectively and satisfy the ordering: $0 \leq q_1 \leq p_1 \leq q_2 \leq p_2 \ldots \leq q_m \leq p_m$. Let $B = \bigcup_{j=1}^{m} (q_j, p_j]$ be these intervals. The NPMLE of $S(t)$ over the set A is piecewise constant over the gaps in B , specifically on the intervals $[p_j, q_{j+1}]$ for $j = 1,2, \ldots, m-1$, as well as on $[0, q_1]$ and $[p_m, \infty)$. Let $\bar{s} = (s_1, s_2, \ldots, s_m)$ be the vector of probabilities where $s_j = Pr(q_j < T \leq p_j) = F(p_j +) - F(q_j -)$. The NPMLE is obtained by maximizing the likelihood with respect to $s_1, s_2, \ldots, s_m$:

$$L(\bar{s}) = \prod_{i=1}^{n}\sum_{j=1}^{m} \alpha_{ij} s_j \ , \ \text{where } \alpha_{ij} = \begin{cases} 1, & (q_j, p_j] \subseteq (L_i, R_i] \\ 0, & \text{Otherwise} \end{cases} \quad (2)$$

subject to $s_j > 0$ and $\sum_{j=1}^{m} s_j = 1$. (For more details, see Turnbull (1976), Gentleman & Geyer (1994).) The self-consistent algorithm updates each s_j using (Dempster, Laird, & Rubin, 1977)

$$s_j^{new} = \frac{1}{n}\sum_{i=1}^{n} \frac{\alpha_{ij} s_j^{old}}{\sum_{k=1}^{m} \alpha_{ik} s_k^{old}} \ , \quad for\ j = 1,..m\ , i = 1,..n \quad (3)$$

when the initial $s_j^{0} = \frac{1}{m}\ and\ \sum_{j=1}^{m} s_j^{0} = 1$. For $1 \le l \le m$.

Let $w_l = 1 - (\hat{s}_1 + \hat{s}_2 + \cdots + \hat{s}_l)$, where $\hat{s}_j$ is an estimated pseudo-probability obtained by iterating equation (3) until convergence for all $j = 1,2,\ldots,l$. Then the survival function $S(t)$ can be expressed as:

$$S(t) = \begin{cases} 1 & if\ t \le q_1 \\ w_l & if\ p_l \le t \le q_{l+1} \\ 0 & if\ t \ge p_m \end{cases} \quad \text{for } 1 \le l \le m-1 \quad (4)$$

Note that $S(t)$ is undefined within each TB interval $(q_j, p_j]$ and the corresponding estimators are represented by the gray regions in Figure 1.

In this study, to estimate $S(t)$ within each $(q_j, p_j]$, we apply linear interpolation along the diagonal of the region. This interpolation is denoted by $S(t)_{lin-diag}$. Define $w_0 = 1$ and $w_m = 0$. Then, within each TB interval, $S(t)_{lin-diag}$ can be estimated from equation (4) as:

$$S(t)_{lin-diag} = w_l + (t - p_l)\frac{(w_{l-1} - w_l)}{(q_l - p_l)} \quad (5)$$

for $q_l < t < p_l$, where $1 \le l \le m$. An example of the survival funtion estimated by $S(t)_{lin-diag}$ is shown in Figure 1.

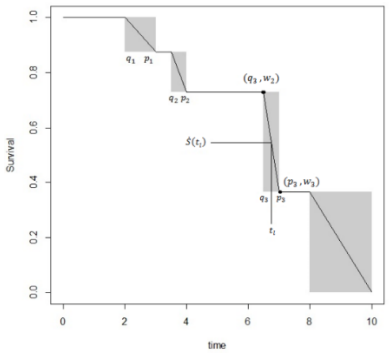

Figure 1. Example of the survival curve estimated by Turnbull's linear interpolation method

2.3 Iterative convex minorant estimator

Another approach is the iterative convex minorant (*ICM*) algorithm which is a special case of the generalized gradient projection optimization method that can maximize the log-likelihood function $L(F)$ with respect to $\hat{F} = (\hat{F}_1, \hat{F}_2, \ldots, \hat{F}_m)$ where $\hat{s}_j = \hat{F}_j - \hat{F}_{j-1}$ for j=1,2,...m by obtaining

$$\hat{F} = argmax_{F \in \theta_F} L(F) \quad (6)$$

To maximize the quadratic function respecting monotonicity constraints on F, at each iteration, the $\hat{F}$ estimate is based on its gradient projection and approximate Hessian taking the diagonal of the full Hessian:

$$\tilde{F} = \underline{F} - H^{-1} g \quad (7)$$

where $g = \nabla L(F)$ is the gradient vector of the log-likelihood with respect to F and H is the Hessian of $L(F)$. Then the update becomes the standard Newton–Raphson step. To obtain a feasible point, the update $\underline{\hat{F}} = Proj_{\theta_F}[\tilde{F}, H]$ is computed. At start of each new iteration $\underline{F}$ is replaced by $\underline{\hat{F}}$ and iteration is repeated until convergence (Groeneboom and Wellner (1992) and Jongbloed (1998)).

2.4 Simulation Design

2.4.1 Data notation and assumption

This study analyzes a sample of n subjects, with survival time t_i $(i = 1, 2, \ldots, n)$ for each subject i assumed to follow the Weibull distribution, which is frequently used in survival analysis due to its flexibility in modeling various hazard functions. Specifically, the Weibull distribution with shape parameter (α) and scale parameter ($\boldsymbol{\gamma}$) has the survival function $S(t) = exp\left(-\left(\frac{t}{\gamma}\right)^{\alpha}\right)$. In this study, the three shape parameters α = 0.8, 1, 1.5 represent decreasing hazard, constant hazard, and increasing hazard, respectively, with corresponding scale parameters γ=19.38,12.31, and 6.72 aligned with the desired study duration and ensuring 95% survival probability over the observation period. This study also assumed there are follow-ups twice a month and the total follow-ups are calculated based on each scenario's duration.

The interval-censored observations are defined as $(L_i, R_i]$. Each subject is scheduled for regular follow-up visits every 0.5 months,with a total k follow-ups of visit times $v_{i1}, v_{i2}, \ldots, v_{ik}$,. The study begins at $T = 0$, with $v_{i0} = 0$. The first visit time v_{i1} is generated from a uniform distribution $v_{i1} \sim Uniform\,(0,1)$ and each subsequent visit time is calculated as $v_{il} = v_{i1} + (l-1) * 0.5$. Participants may miss appointments with a probability of $p = 0.3$, except for the first and last visits, which are always attended. Left-censored data are not considered, and right-censoring is applied as type I censoring, occurring after the final scheduled visit. A data point is interval-censored if t_i falls between two visits $(L_i, R_i] = (v_{il}, v_{i(l+1)}]$ and right-censored if t_i exceeds v_{ik}, represented as (v_{ik}, ∞).

The primary outcome is the median survival time, which is defined as the time point at which the survival function $S(t)$ has dropped to 0.5, which is estimated using the three nonparametric methods.

2.4.2 Simulation procedure

A total of 27 different simulation scenarios were designed, based on three sample sizes (80, 200, and 400), three levels of right censoring (30%, 40%, and 50%) and three values of the shape paremeter for the survival time distribution (0.8, 1, and 1.5).The simulation for each scenario follows these steps:

1. Survival Time Generation; simulate event times t_i $(for\ i = 1, 2, \ldots, n)$ from Weibull distributions with parameter pairs (α, γ) = (0.8,19.38), (1,12.31), and (1.5,6.72).
2. Follow-Up Visits; generate follow-up times $v_{i1}, v_{i2}, \ldots v_{ik}$ per subject, allowing for probability of missed visits = 0.3
3. Censoring Definition; define interval-censored data $(L_i, R_i] = (v_{ij}, v_{il}]$ based on the nearest visits containing t_i. Right-censored observations $(R_i, \infty) = (v_{ik}, \infty)$ occur when t_i exceeds the last k-th visit.
4. Midpoint Estimation; impute event time using the midpoint of $(L_i, R_i]$. Estimate the survival time via KM_{mid}.
5. Turnbull Estimator; arrange Turnbull intervals and apply the self-consistency estimator iteratively for the median survival function, obtaining $TB_{lin-diag}$
6. ICM Estimation; use generalized gradient projection optimization to calculate the *ICM* estimator for the median survival function. Repeat steps 1–6 for 500 rounds and calculate MSE, variance, bias, and relative MSE.

All simulation steps can be seen in the diagram of Figure 2.

2.4.3 Performance evaluation criteria

These measures are calculated based on 500 Monte Carlo simulation replications for each scenario where $\bar{S}(t) = \frac{1}{500}\sum_{r=1}^{M} \hat{s}_r(t)$ is the average estimated median survival time. The measures of accuracy and consistency for the estimator are

(i) the bias of parameter (Bias) = $\bar{S}(t) - S(t)$

(ii) the variance of parameter (Var) = $\frac{1}{500}\sum_{r=1}^{500}[\hat{S}_r(t) - \bar{S}(t)]^2$

(iii) the mean squared error (MSE) = $\frac{1}{500}\sum_{r=1}^{500}[S(t) - \hat{S}_r(t)]^2$.

(iv) The relative MSE of method = $\frac{MSE_{Method} - MSE_{KM}}{MSE_{KM}} \times 100$

3. Results and Discussion

The objectives are to compare the performances of nonparametric estimators for the median survival function among the KM_{mid} , $TB_{lin-diag}$, and *ICM* estimators, and to evaluate effects of right censering and sample size. We used criteria such as mean square error (MSE), variance (VAR), bias (Bias), and relative MSE, which are calculated for each scenario as presented in Tables 1-4 and Figures 3-5.

Overall, all three methods, KM_{mid}, $TB_{lin-diag}$ and *ICM*, perform well for estimating median survival time across most cases. As shown in Figure 3 and Table 1, KM_{mid} consistently yielded the lowest MSE values, particularly when the sample size is large (n= 400) and shape parameter is 0.8 or 1.0. $TB_{lin-diag}$ and *ICM* have very similar MSE values up to the second decimal place in many cases. Additionally, when evaluated using relative MSE compared to KM_{mid} (Table 1), $TB_{lin-diag}$ and *ICM* are quite close, with relative MSE values ranging from 1.37% to 36.72% higher than those obtained by the KM_{mid} method, depending on the shape parameter, censoring rate, and sample size. In the case where the shape parameter is 1.5 and the sample size is 400, both $TB_{lin-diag}$ and *ICM* clearly have higher MSE values compared to the KM_{mid} . Moreover, increasing the sample size generally reduces the relative MSE, particularly when shape is 0.8 or 1.0 (Figure 3). For example, under shape = 0.8 and 50% censoring rate, relative MSE of $TB_{lin-diag}$ drops from 8.01% (n = 80) to 3.70% (n = 400). However, under shape = 1.5, the relative MSE unexpectedly increases with sample size.

When comparing the performances of the three methods across different factors, we found that KM_{mid} yielded the smallest variance (VAR), particularly with the shape parameter 1.5 (Figure 4 and Tables 2-4).

However, KM_{mid} also showed the most significant negative bias, which was greater than those of the other two methods (Figure 5). Moreover, the biases for KM_{mid} are noticeably further from the x-axis compared to the other methods, and this bias becomes more negative as the rate of

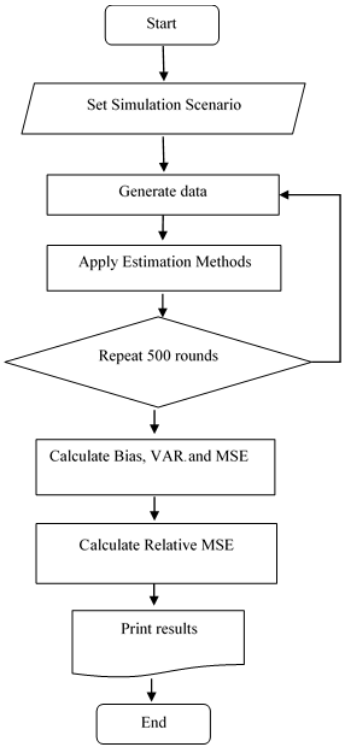

Figure 2. Monte Carlo simulation flowchart

Table 1. Relative MSE (%) of median survival estimators

The relative MSE (%)					
Shape parameter	Right censoring (%)	Method	Sample size		
			80	200	400
0.8	30	TB	2.97	5.11	4.37
		ICM	2.97	5.11	4.36
	40	TB	1.37	4.79	1.63
		ICM	1.37	4.78	1.62
	50	TB	8.01	7.22	3.70
		ICM	8.07	7.23	3.76
1	30	TB	6.47	3.30	12.60
		ICM	6.47	3.30	12.62
	40	TB	5.09	6.37	9.32
		ICM	5.09	6.36	9.33
	50	TM	8.19	3.23	5.97
		ICM	8.24	3.26	6.07
1.5	30	TB	17.82	30.27	33.34
		ICM	17.83	30.31	33.65
	40	TB	20.98	21.42	29.64
		ICM	20.99	21.49	29.86
	50	TB	9.73	27.39	36.15
		ICM	9.77	27.51	36.72

*TB = $TB_{lin-diag}$ and the KM = KM_{mid}

Table 2. Median survival estimates: mean, SD, bias, and MSE for shape parameter α = 0.8

r	Method	n=80				n=200				n=400			
		M (SD)	95%CI	BIAS (%)	MSE (%)	M (SD)	95% CI	BIAS (%)	MSE (%)	M (SD)	95% CI	BIAS (%)	MSE (%)
0.3	KM	.4986 (.0580)	.4859 - .5113	-0.1363	0.3360	.5017 (.0355)	.4968 - .5066	0.1670	0.1261	.4997 (.0250)	.4972 - .5022	-0.0323	0.0622
	TB	.4988 (.0588)	.4859 - .5117	-0.1154	0.3460	.5018 (.0364)	.4968 - .5068	0.1754	0.1326	.4995 (.0255)	.4970 - .5020	-0.0497	0.0649
	ICM	.4988 (.0588)	.4859 - .5117	-0.1154	0.3460	.5018 (.0364)	.4968 - .5068	0.1753	0.1326	.4995 (.0255)	.4970 - .5020	-0.0498	0.0649
0.4	KM	.4984 (.0562)	.4861 - .5107	-0.1650	0.3155	.5000 (.0348)	.4952 - .5048	0.0015	0.1209	.4994 (.0246)	.4970 - .5018	-0.0570	0.0605
	TB	.4982 (.0566)	.4858 - .5106	-0.1790	0.3199	.4999 (.0356)	.4950 - .5048	-0.0066	0.1267	.4992 (.0248)	.4968 - .5016	-0.0806	0.0615
	ICM	.4982 (.0566)	.4858 - .5106	-0.1790	0.3199	.4999 (.0356)	.4950 - .5048	-0.0067	0.1267	.4992 (.0248)	.4968 - .5016	-0.0806	0.0615
0.5	KM	.4960 (.0582)	.4846 - .5074	-0.3985	0.3400	.5015 (.0381)	.4962 - .5068	0.1459	0.1454	.5010 (.0268)	.4984 - .5036	0.0989	0.0719
	TB	.4944 (.0604)	.4812 - .5076	-0.5575	0.3672	.5017 (.0395)	.4962 - .5072	0.1679	0.1559	.5026 (.0272)	.4999 - .5053	0.2614	0.0745
	ICM	.4944 (.0604)	.4812 - .5076	-0.5578	0.3674	.5017 (.0395)	.4962 - .5072	0.1679	0.1559	.5026 (.0272)	.4999 - .5053	0.2612	0.0746

Table 3. Median survival estimates: mean, SD, bias, and MSE for shape parameter α = 1

r	Method	n=80				n=200				n=400			
		M (SD)	95%CI	BIAS (%)	MSE (%)	M (SD)	95%CI	BIAS (%)	MSE (%)	M (SD)	95%CI	BIAS (%)	MSE (%)
0.3	KM	.4989 (.0548)	.4869 - .5109	-0.1150	0.2997	.4990 (.0359)	.4940 - .5040	-0.1020	0.1291	.4999 (.0241)	.4975 - .5023	-0.0123	0.0582
	TB	.4982 (.0565)	.4858 - .5106	-0.1764	0.3190	.4989 (.0365)	.4938 - .5040	-0.1112	0.1333	.4998 (.0256)	.4973 - .5023	-0.0245	0.0655
	ICM	.4982 (.0565)	.4858 - .5106	-0.1761	0.3190	.4989 (.0365)	.4938 - .5040	-0.1112	0.1333	.4998 (.0256)	.4973 - .5023	-0.0247	0.0656

Table 3. Continued.

r	Method	n=80				n=200				n=400			
		M (SD)	95%CI	BIAS (%)	MSE (%)	M (SD)	95%CI	BIAS (%)	MSE (%)	M (SD)	95%CI	BIAS (%)	MSE (%)
0.4	KM	.5009 (.0545)	.4890 - .5128	0.0877	0.2969	.4986 (.0366)	.4935 - .5037	-0.1369	0.1337	.5001 (.0248)	.4977 - .5025	0.0096	0.0614
	TB	.5015 (.0559)	.4893 - .5137	0.1515	0.3121	.4990 (.0377)	.4938 - .5042	-0.1003	0.1422	.5002 (.0259)	.4977 - .5027	0.0170	0.0671
	ICM	.5015 (.0559)	.4893 - .5137	0.1515	0.3121	.4990 (.0377)	.4938 - .5042	-0.1004	0.1422	.5002 (.0259)	.4977 - .5027	0.0172	0.0671
0.5	KM	.4959 (.0596)	.4828 - .5090	-0.4123	0.3564	.4976 (.0369)	.4925 - .5027	-0.2362	0.1367	.4995 (.0262)	.4969 - .5021	-0.0503	0.0685
	TB	.4972 (.0621)	.4936 - .5108	-0.2808	0.3856	.5000 (.0376)	.4948 - .5052	0.0030	0.1411	.5009 (.0269)	.4983 - .5035	0.0942	0.0726
	ICM	.4972 (.0621)	.4936 - .5108	-0.2809	0.3857	.5000 (.0376)	.4948 - .5052	0.0028	0.1411	.5009 (.0269)	.4983 - .5035	0.0945	0.0726

Table 4. Median survival estimates: mean, SD, bias, and MSE for shape parameter α = 1.5

r	Method	n=80				n=200				n=400			
		M (SD)	95% CI	BIAS (%)	MSE (%)	M (SD)	95% CI	BIAS (%)	MSE (%)	M (SD)	95% CI	BIAS (%)	MSE (%)
0.3	KM	.5023 (.0544)	.4904 - .5142	0.2255	0.2965	.5009 (.0355)	.4960 - .5058	0.0943	0.1256	.5004 (.0257)	.4979 - .5029	0.0446	0.0661
	TB	.5017 (.0591)	.4887 - .5147	0.1650	0.3494	.5006 (.0405)	.4950 - .5062	0.0553	0.1637	.5001 (.0297)	.4972 - .5030	0.0068	0.0882
	ICM	.5016 (.0591)	.4886 - .5146	0.1648	0.3494	.5006 (.0405)	.4950 - .5062	0.0551	0.1637	.5001 (.0297)	.4972 - .5030	0.0066	0.0884
0.4	KM	.4990 (.0562)	.4867 - .5113	-0.1000	0.3157	.4994 (.0360)	.4944 - .5044	-0.0578	0.1298	.4990 (.0262)	.4964 - .5016	-0.0983	0.0685
	TB	.4991 (.0618)	.4856 - .5126	-0.0931	0.3819	.5006 (.0397)	.4954 - .5058	0.0615	0.1576	.4994 (.0298)	.4965 - .5023	-0.0555	0.0888
	ICM	.4991 (.0618)	.4856 - .5126	-0.0931	0.3820	.5006 (.0397)	.4954 - .5058	0.0609	0.1577	.4995 (.0298)	.4966 - .5024	-0.0538	0.0890
0.5	KM	.4950 (.0595)	.4820 - .5080	-0.5037	0.3564	.4962 (.0372)	.4917 - .5007	-0.3796	0.1393	.4965 (.0249)	.4941 - .4989	-0.3487	0.0629
	TB	.5036 (.0625)	.4899 - .5173	0.3607	0.3910	.5032 (.0420)	.4974 - .5090	0.3243	0.1775	.5037 (.0291)	.5008 - .5066	0.3733	0.0857
	ICM	.5036 (.0625)	.4899 - .5173	0.3597	0.3912	.5032 (.0420)	.4974 - .5090	0.3229	0.1777	.5037 (.0291)	.5008 - .5066	0.3731	0.0861

right censoring increases, especially for the shape parameter 1.5**.** In contrast, the biases for $TB_{lin-diag}$ and *ICM* perform similarly and tend to be more positive as the rate of right censoring increases. Alternatively, when the shape parameter is 1.5 with 50% right censoring, it is obvious that $TB_{lin-diag}$ and *ICM* overestimated the median survival function, whereas KM_{mid} clearly underestimated it. Moreover, sample sizes of 200 and 400 yield similar results for VAR and BIAS, with VAR decreasing as the sample size increases. However, the amplitude of bias is not affected by sample size; instead, it varies with the rate of right censoring or the shape parameter.

4. Conclusions

According to the objectives of this study, we compared the performances of the three nonparametric estimators Kaplan-Meier with midpoint imputation (KM_{mid}), Turnbull with linear interpolation ($TB_{lin-diag}$), and Iterative Convex Minorant (*ICM*), for estimating the median survival time from interval-censored data under various conditions of right-censoring rates, sample sizes, and hazard rate shapes.

The results showed that KM_{mid} consistently achieved the lowest mean squared error (MSE) across most scenarios. KM_{mid} exhibited a tendency to underestimate the median survival time, particularly when the right-censoring rate increased. However, even under extreme conditions, KM_{mid} remained relatively stable and efficient. In contrast, $TB_{lin-diag}$ and *ICM* generally performed similarly to each other, but their accuracy decreased when the hazard rate was high (shape = 1.5) and when right-censoring levels reached 40%–50%. Under such conditions, both $TB_{lin-diag}$ and *ICM* began to overestimate the median survival time, whereas KM_{mid} continued to underestimate it but with a smaller bias magnitude.

In comparison to previous studies (De Gruttola & Lagakos, 1989; Lindsey & Ryan, 1998; Nishikawa & Tango,

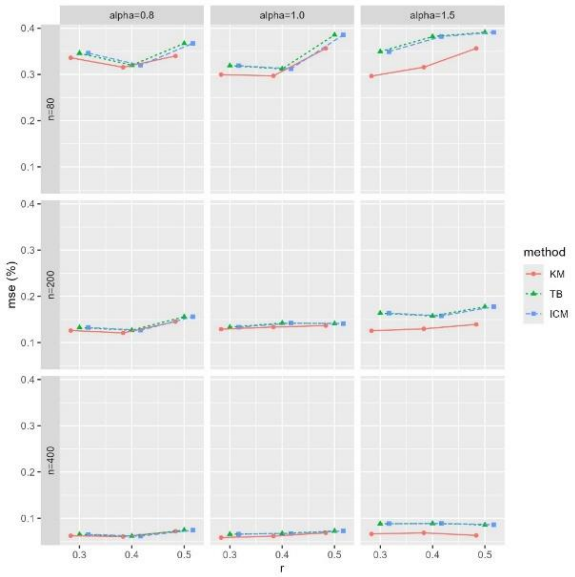

Figure 3. MSE (%) of median survival estimators

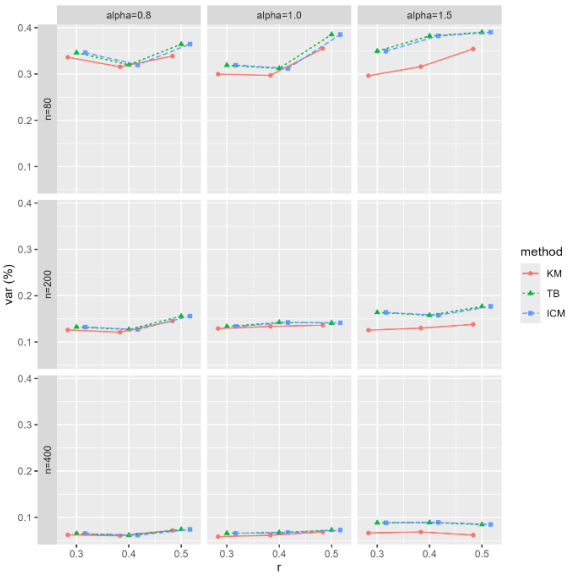

Figure 4. Variance (%) of median survival estimators

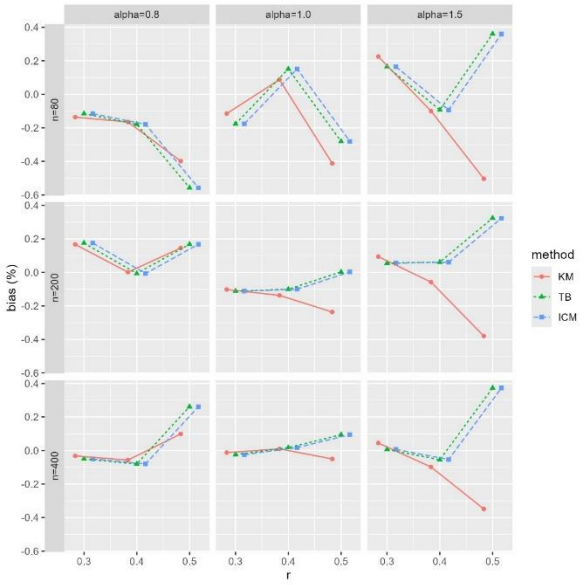

Figure 5. Bias (%) of median survival estimators

2004; Gorelick, 2009; Ratchaprapapornkul & Ingsrisawang, 2019), some consistencies and differences were observed. Both the current and earlier studies agreed that KM_{mid} tends to underestimate the median survival time, especially as the right-censoring rate increases. Consistent with previous findings, our study also confirmed that the Turnbull estimator exhibited both underestimation and overestimation depending on the shape parameter and interval length. However, a notable difference emerged: because the current study systematically varied right-censoring rates across multiple levels (30%, 40%, and 50%), it was possible to observe more clearly that $TB_{lin-diag}$ and *ICM* tended to shift toward overestimation when facing high hazard rates and heavy censoring. This insight extends previous understanding, which had mainly observed underestimation without considering multiple censoring levels systematically.

From a practical perspective, the results offer important observations for selecting appropriate survival estimators depending on data characteristics. KM_{mid} demonstrated relatively stable performance across a wide range of conditions, particularly when follow-up intervals were frequent and right-censoring was moderate. Meanwhile, $TB_{lin-diag}$ and *ICM* showed comparable performances in many scenarios, but their tendency to overestimate under high hazard rates and heavy censoring suggests that researchers may need to consider data characteristics carefully when applying these methods. Further research could investigate different time intervals between visits, various time-to-event distributions, and settings with higher right-censoring rates, to better understand the robustness and limitations of these nonparametric estimators.

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