The Influence of Vitamins, Comorbid Status and Advanced Age in Modelling Survival Time for Covid-19 Patients Using the Cox Proportional Hazard Model in Southeast Sulawesi

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Abstract

There has been an increase of the COVID-19 case in December, 2023.. For this reason, learning from previous data is needed to anticipate so that the spike in COVID-19 cases does not happen again. This study aims to identify risk factors that influence the survival of COVID-19 patients using the Cox proportional hazard model from medical record of COVID-19 patients at RSU Bahteramas for the period March to December 2020. The results of the study show that the Cox proportional hazards model in COVID-19 patients is $h(t) = h_0(t)exp(1{,}5274X_2 - 1{,}4639X_4)$. The risk factors that influence the survival of COVID-19 patients are age (X_2) and administration of drugs and vitamins (X_4) from the fourth independent variables involved. The hazard ratio value for the age variable is 4.6063 > 1, which indicates that the risk of COVID-19 patients aged > 60 years experiencing death is 4.6063 times faster than COVID-19 patients aged ≤ 60 years, while the hazard ratio value for drug administration and vitamins is 0.2313 < 1, which indicates that COVID-19 patients who take drugs and vitamins during the treatment period will be reduced by 0.2313 times compared to patients who only take drugs without vitamins.

Keywords: COVID-19, Cox Proportional Hazard, Hazard Ratio, Survival Analysis, Southeast Sulawesi

1. INTRODUCTION

The disease covid-19 is a disease that shocked the world at the end of 2019. Indonesia first reported COVID-19 cases on March 2, 2020. Since then, the number of COVID-19 cases has continued to increase spreading to almost all parts of Indonesia, including Southeast Sulawesi Province. Based on data released by the Central Statistics Agency of Southeast Sulawesi Province in 2021, there were 20,173 confirmed positive cases of COVID-19, of which 19,639 cases were declared cured and 528 cases were declared dead [1]. To handle the increasing number of cases, the government has established referral hospitals for COVID-19 services in Southeast Sulawesi, one of which is the Bahteramas General Hospital (RSU). Since 2020 to 2021, RSU Bahteramas has treated 1,699 patients who were confirmed positive for COVID-19, of whom 255 patients were declared dead. The mentioned data indicates that COVID-19 leads to individuals who survive (recover) and those who do not survive (die).

Several previous studies aimed to determine the factors that influence the survival of COVID-19 patients. Alam and Sultana, 2021 concluded that climate factors, especially temperature and humidity, contribute significantly to the transmission of COVID-19. The relationship between temperature and humidity has received greater attention than wind speed and precipitation from the scientific community [2] . Sajadi et. al (2020) concluded that a temperature of 8-100C and humidity of 60-90% are ideal conditions for the spread of the Coronavirus that causes COVID-19. The higher the temperature and the more humid, the lower the spread of Covid-19 [3]. Dhruba et al, 2022 concluded that factors of Gender, Age, Location, Vaccination Status, Pre-Disease Conditions, Place of Treatment, and Food Habits involved in this research showed that significant risk factors were pre-disease, location, and eating habits which could prolong recovery time from COVID-19. Meanwhile, gender and age do not affect extending the recovery time for Covid-19 patients in India [4]. Speakman et al (2021) conducted a research review related to vitamins and supplements and COVID-19 without carrying out mathematical modelling and concluded that vitamins and supplements do not provide

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sufficient evidence to justify their use compared to pharmacological therapy and other prevention techniques that have been proven to be used in the management and prevention of COVID-19. [5]

Even though starting on June 21st, 2023 the government of the Republic of Indonesia has revoked the status of the COVID-19 pandemic, but according to the report of the ministry of health of the Republic of Indonesia there has been an increase of the COVID-19 case as reported in the published kompas newspaper on December 5th, 2023 [6]. This is a warning to the public that COVID-19 has not disappeared around us. For this reason, learning from previous data is needed to anticipate so that the spike in COVID-19 cases does not happen again.

With indications of an increase in COVID-19 cases, research needs to be carried out to determine the factors that influence the resilience of COVID-19 patients, especially in Southeast Sulawesi, based on historical COVID-19 data. The factors involved in this research are vitamins, gender, comorbid status and advanced age with the aim of modeling the survival time of COVID-19 patients based on the factors that influence them in Southeast Sulawesi. Mathematical modeling uses the Cox proportional hazard model.

2. MODEL FORMULATION

The survival function is denoted by S(t). The definition of S(t) is the probability that an individual will be able to survive beyond time t which is formulated as follows: $S(t) = P(T \geq t) = \int_t^{\infty} f(x)\,dx$. Furthermore, based on the definition of the cumulative distribution function F(t), the survival function can be written as

$$F(t) = 1 - S(t) \tag{1}$$

Equation (1) derived to t on both sides is obtained

$$f(t) \quad = -\frac{d(S(t))}{dt} = -S'(t) \tag{2}$$

In theory, the survival function can be described in a survival curve. The characteristics of the survival function are as follows: (1). The survival function is a non-increasing monotone function, (2). At time t=0, S(t) = S(0) = 1, meaning that at the start of the research, because no individual had experienced the event, the probability of survival at time t=0 was 1 and (3). At time t = ∞, S(t) = 0, meaning that if the research period increases without limit, then at the end of time no individual will survive, so the survival curve will move towards 0. [7]

The probability that an individual experiences an event in the time interval (t, t+Δt) with the condition that the individual still survives until time t is called the hazard function (h(t)). h(t) which mathematically can be written as follows:

$$h(t) = \lim_{x\to\infty}\left(\frac{P(t \leq T < t + \Delta t | T \geq t)}{\Delta t}\right) \tag{3}$$

Based on probability theory, the conditional probability P(A|B) is formulated as follows:

$$P(A|B) = \frac{P(A \cap B)}{P(B)} \tag{4}$$

Equation (4) is applied to equation (3), then the equation (3) is obtained as follows:

$$h(t) = \frac{F'(t)}{S(t)} = \frac{f(t)}{S(t)} \tag{5}$$

Substituting equation (2) into equation (5) we get:

$$h(t) \;= \frac{-\frac{d(S(t))}{dt}}{S(t)}$$

$$= \frac{1}{S(t)} \cdot -\frac{d(S(t))}{dt}$$

$$-h(t)dt = \frac{1}{S(t)} d(S(t)) \tag{6}$$

from equation (6) can be obtained from the relationship between the survival function and the hazard function where $t = u$ that is

$$-\int_0^t h(u)\, du = \ln S(t) - \ln S(0) \qquad (7)$$

when $t = 0$, $S(t) = S(0) = 1$ and it is known that the value of $\ln(1)$ is equal to 0, then Equation (7) becomes

$$H(t) = -\ln S(t) \qquad (8)$$

The cumulative hazard function H (t) is as follows

$$H(t) = \int_0^t h(x)\, dx$$

Equation (8) is changed to exponential form so it becomes

$$S(t) = \exp[-H(t)]$$

The characteristics of the hazard function are: (1). The hazard function is always positive ($h(t) \geq 0$). (2) The hazard function has no upper limit.

The Kaplan-Meier survival curve is a curve that describes the relationship between the estimated survival function at time t and the survival time which is formulated by

$$\hat{S}(t_{(j)}) = P_1 \times P_2 \times \ldots P_k = \prod_{j=1}^{k} P_j$$

$$\hat{S}(t_{(j)}) = \prod_{j=1}^{k} \left(1 - \frac{d_j}{n_j}\right)$$

The test used to estimate whether there are statistical differences in the Kaplan Meier survival curves for two or more groups is the log rank test with the following hypothesis

H_0: There is not a difference between the two Kaplan-Meier survival curves

H_1: There is a difference between the two Kaplan-Meier survival curves

The test statistic used in the log-rank test is

$$\text{log-rank} = \frac{(O_i - E_i)^2}{Var(O_i - E_i)}; i = 1,2$$

Hypothesis H_0 will be rejected, if log-rank$\approx \chi^2$ greater than $\chi^2_{(\propto,df)}$ with degrees of freedom equal to 1. The Cox proportional hazards model involving p predictor variables can be written using the following equation:

$$= h_0(t) \exp \sum_{j=1}^{p} \beta'_j X_j \qquad (9)$$

with

h(t,X): The function of the individual who experiences the event at time t is based on the predictor variable X

$h_0(t)$: The baseline hazard function is if all predictor variable values (X_j) are equal to zero

The hazard ratio in Cox proportional hazard regression is defined as the hazard value for category one individuals divided by the hazard value for different individuals which can be written with the following equation

$$\widehat{HR} = \frac{\hat{h}(t,X^*)}{\hat{h}(t,X)} = \frac{\hat{h}_0(t) e^{\sum_{i=1}^{p} \hat{\beta}_i X_i^*}}{\hat{h}_0(t) e^{\sum_{i=1}^{p} \hat{\beta}_i X_i}} = e^{\sum_{i=1}^{p} \hat{\beta}_i (X_i^* - X_i)} \qquad (10)$$

The hazard ratio value ranges from 0 to 1 with the following conditions:

1. If HR < 1 indicates that the predictor variable X is a protective factor against failure.
2. If HR = 0 indicates that there is no association between the predictor variable X and the occurrence of failure.
3. If HR > 1 indicates that the predictor variable X is a risk factor for failure. [7].

3. MODEL ANALYSIS

This research utilizes secondary data obtained through medical records of COVID-19 patients at RSU Bahteramas regarding survival times and factors thought to influence the survival of 98 COVID-19 patients. The variables include response variables (Y) and predictor variables (X). Response variables (Y) consist of survival time (T) and patient status (d) with the following conditions:

1. The initial time of the research was the time when COVID-19 patients began undergoing treatment at RSU Bahteramas.
2. The measurement scale in this study is recorded in days.
3. The event considered in this research is the death of a COVID-19 patient after undergoing treatment at RSU Bahteramas for the period March to December 2020.
4. The end time of the research is the condition when the COVID-19 patient was declared dead after undergoing treatment at the RSU Bahteramas for the period March–December 2020.
5. Censoring time is divided into patients who have recovered, have not recovered/need further treatment, are self-isolating, and patients whose progress is unknown during the study period are referred to as patients with right censored time.

Meanwhile, the predictor variable (X) consists of factors that are thought to influence the survival time of Covid-19 patients, including gender (X_1), age (X_2), comorbid status (X_3), medicine/vitamin administration (X_4) as presented in Table 1.

TABLE 1. Predictor Variables

Variable	Variable Name	Scale	Categorical
X_1	Gender	Nominal	1: Male 0: Female
X_2	Age	Nominal	1: Age >60 0: Age ≤ 60
X_3	Comorbid Status	Nominal	1: There are comorbidities 0: There are no comorbidities
X_4	Administration of medicine/vitamin	Nominal	1: Administration of medicines and vitamins 0: Administration of medicines

Based on equation (9) involving 4 predictor variables, the Cox proportional hazard equation model is

$$h(t, X) = h_0(t) \exp\left(\beta'_1 X_1 + \beta'_2 X_2 + \beta'_3 X_3 + \beta'_4 X_4\right) \quad (11)$$

To get the value of the parameter from equation (11), it is necessary to estimate it using the maximum likelihood method with the following stages:

1. The ordered survival time of r individuals who experience an event namely $t_{(j)}$ is denoted $t_{(1)} < t_{(2)} < \cdots < t_{(r)}$. The partial likelihood function of the Cox proportional hazard equation model is as follows

$$L(\beta) = \prod_{j=1}^{r} \frac{\exp(\boldsymbol{\beta}' \boldsymbol{x}_{(j)})}{\sum_{l \in R(t_{(j)})} \exp(\boldsymbol{\beta}' \boldsymbol{x}_{(l)})} \quad (12)$$

2. For example, the data consists of n observations of survival time, namely $t_1, t_2, \ldots, t_n$ and d_i is the status of the event for the i-th individual with a value

$$d_i = \begin{cases} 0; & ith\ individual\ censored \\ 1; & other \end{cases}$$

Equation (12) can also be written in the form of the following equation

$$L(\beta) = \prod_{i=1}^{n} \left(\frac{\exp(\beta' x_{(i)})}{\sum_{l \in R(t_{(j)})} \exp(\beta' x_{(l)})} \right)^{d_i}$$

3. So that the function above is linear, it needs to be linearized so that a new equation is obtained as follows:

$$\ln L(\beta) = \ln \left(\prod_{i=1}^{n} \left(\frac{\exp(\beta' x_{(i)})}{\sum_{l \in R(t_{(j)})} \exp(\beta' x_{(l)})} \right)^{d_i} \right)$$

4. differentiate lnL(β) with respect to β and obtain:
$\frac{d \ln L(\beta)}{d\beta} = 0$ (13)

5. To get an estimator maximum likelihood $\hat{\beta}$ in equation (13), then the Newton Raphson method will be used because the estimator is not unique.
6. Test the significance of model parameters simultaneously using the likelihood ratio test and partially using the Wald test.
The likelihood ratio test:

$$G^2 = -2ln\frac{L(\widehat{\omega})}{L(\widehat{\Omega})} \sim \chi^2{}_{a,p}$$

The wald test:

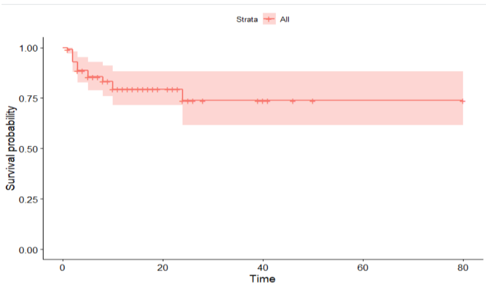
$$Z = \frac{\widehat{\beta_J}}{SE(\widehat{\beta_J})} \text{ for j =1,2,3,4}$$

7. Selecting the best model of Cox proportional hazards regression $AIC = -2lnL + 2K$
8. Calculate the hazard ratio of significant predictor variables in the model to determine the comparison of survival rates for COVID-19 patients for each category of predictor variables from equation (10).

4. SIMULATION

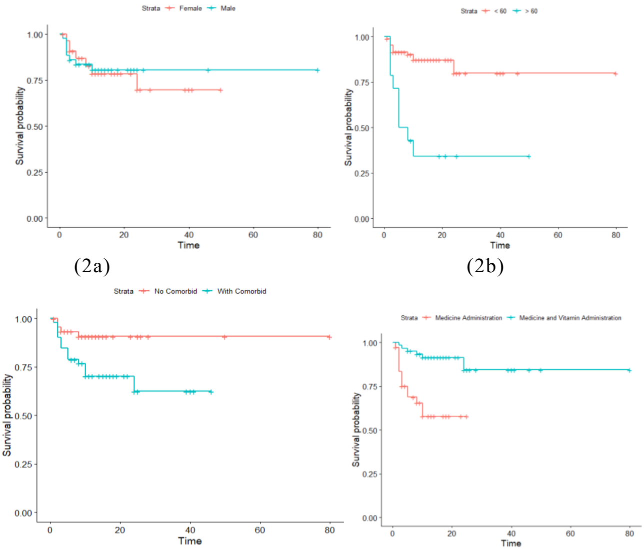
4.1.Kaplan Meier's Survival Curve

The survival characteristics of COVID-19 patients can be described using the Kaplan-Meier survival curve, which indicates whether there are differences in survival probability in the categories contained in a variable.



. **Figure 1.** Kaplan-Meier's Survival Curve of Covid-19 Patients at RSU Bahteramas

Based on the figure, the Kaplan-Meier survival curve decreases slowly because, in the research data, more patients are censored or survive than patients who experience death. The survival probability of COVID-19 patients remains relatively high, ranging from 1 to 0.75. Furthermore, the Kaplan-Meier survival curve based on factors thought to influence the survival of Covid-19 patients, such as gender(X_1), age(X_2), comorbid status(X_3), and administration of medicines/vitamins(X_4), is shown in Figure 2.



(2a) (2b)

(2c) (2d)

Figure 2. Kaplan-Meier's Survival Curve Based on Predictor Variables

Figure 2a graphically shows that the Kaplan-Meier survival curves for gender(X_1) coincide, indicating there is no difference in the Kaplan-Meier survival curves between male and female patients. In contrast, Figure 2b for the variables of age(X_2) fifugre 2c for comorbidity status(X_3), and figure 2d administration of medicines and vitamins(X_4), the lines on the Kaplan-meier'scurve do not coincide. This indicates that there are differences in survival curves between the categories of these three variables. In other words, during the March-December 2020 period, it is thought that there were differences in the probability of survival in patients aged ≤60 years and >60 years, patients who had comorbid status and those who did not, patients who were given medicines and vitamins and patients who were given only medicines.

4.2. Log-rank Testing

The results of the log-rank test analysis for each predictor variable are presented in Table 2.

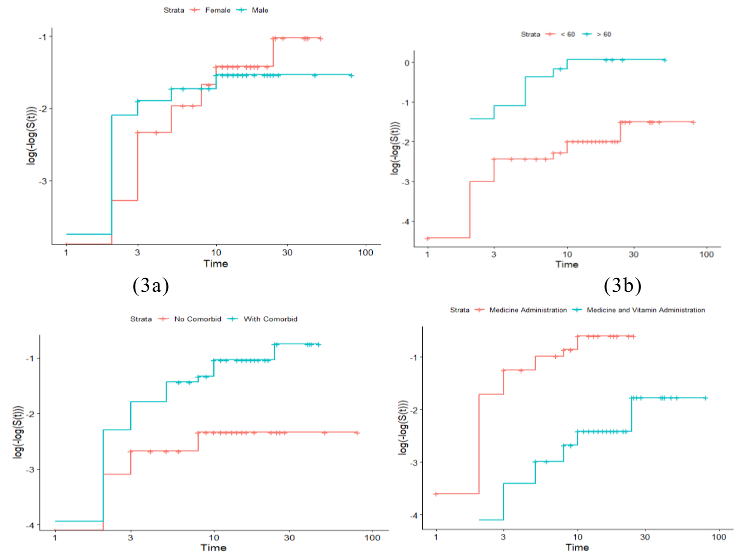
TABLE 2. Log-rank Test Result

Variable	df	Log-Rank	*P-value*
Gender (X_1)		0.0584	0.8
Age (X_2)		21.1	0.000004
Comorbid Status (X_3)	1	5.89	0.02
Administration of medicines/vitamins (X_4)		15.2	0.0001

Based on Table 2, it can be concluded that differences in the Kaplan-Meier survival curve exist in the variables age (X_2), comorbid status (X_3), and medicines/vitamins administration (X_4).

4.3 Test of Proportional Hazard Assumption

The proportional hazards assumption test was utilized to examine whether the factors thought to influence the survival of COVID-19 patients were independent of time. The test proportional hazard assumption is graphically shown in Figure 3. Figure 3 shows that gender (X_1) in Figure (3a) does not satisfy the proportional hazard assumption because the plots between the female and male categories are not parallel. On the other hand, the variables age (X_2) in Figure (3b), comorbid status (X_3) in Figure (3c), and medicines/vitamins administration (X_4) in Figure (3d) satisfy the proportional hazard assumption because the plots between categories in these variables are parallel.



(3c) (3d)

Figure 3. Plot $ln\left(-ln\hat{S}(t)\right)$ Predictor Variables

To confirm this analysis, the proportional hazard assumption should be tested using the goodness-of-fit test as shown in Table 3. Based on Table 4, the p-value for each variable > 0.05, indicating that the proportional hazard assumption is satisfied for all variables used in the research. Thus, as all variables satisfy the proportional hazard assumption, the research model can be continued using the Cox proportional hazard regression model.

TABLE 3. Goodness of Fit Test Result

Variable	Schoenfeld Residual	*P-value*
Gender	-0.3340	0.1500
Age	0.1065	0.6548
Comorbid Status	0.1613	0.4969
Administration of Medicines/Vitamins	0.2191	0.3532

4.4 Cox Proportional Hazard Model

The parameter estimation used to obtain the Cox proportional hazards equation model is the Breslow Partial Likelihood method. The Breslow Partial Likelihood method is one method that can be used to overcome ties in survival data. The results of estimating Cox proportional hazard model parameters using the Breslow partial likelihood method are showed in Table 4.

TABLE 4. Estimation Parameter of Cox Proportional Hazard Model

Variable	$\hat{\beta}$	$exp(\hat{\beta})$
Gender	0.2011	1.2228
Age	1.3727	3.9458
Comorbid Status	0.8045	2.2355
Administration of Medicines/Vitamins	-1.3891	0.2493

If it is assumed that all variables have a significant effect, then the initial Cox proportional hazards regressiion model is as follows:

$$h(t) = h_0(t)exp(0.2011X_1 + 1.3727X_2 + 0.8045X_3 - 1.3891X_4)$$

4.5. Parameter Testing

Parameter significance testing divided into simultaneous tests and partial tests. The simultaneous test shows the likelihood ratio value $(G^2) = 25.08 > \chi^2_{0,05,4} = 9.4877$ and *p-value*< 0.05. Then, reject H_0 indicating that there is at least one predictor variable significant to the model.Furthermore, the partial test results are shown in Table 6. Based on Table 5, it can be seen that the variables age and medicines/vitamins administration have a significant effect on the model because $Z_{test} > Z\alpha/_2$ and *p-value*< 0.05. In contrast, the variables gender and comorbid status do not has a significant effect because $Z_{test} < Z\alpha/_2$ and *p-value*> 0.05.

TABLE 5. Partial Test Result

Variables	Z	$Z\alpha/_2$	*P-value*
Gender(X_1)	0.4203	1.96	0.6741
Age(X_2)	2.8410		0.004
Comorbid Status(X_3)	1.3720		0.170
Administration of Medicines/Vitamins(X_4)	-2.7430		0.006

4.6. Selection of The Best Model

The best model was selected using backward elimination by gradually eliminating variables that were not significant. The models formed will be compared by examining at the smallest Akaike's Information Criterion (AIC) value. The results of selecting the best model through backward elimination and AIC values are presented in Table 6. Table 6 shows the smallest AIC value which explains the goodness of the best model is in step 2 (155.17). Therefore, it can be concluded that the best Cox proportional hazards regression model to describe the survival time of COVID-19 patients at RSU Bahteramas for the period March to December 2020 is a model with variables of age $(X_2)$and medicines/vitamins administration(X_4).

TABLE 6. Selection of The Best Model Results

Step	Model Formed	AIC
0	All variables	157.02
1	Without gender (X_1)	155.19
2	Without gender (X_1) and comorbid status (X_3)	155.17

Subsequently, parameter estimates involving only the best model are shown in Table 7.

TABLE 7. Parameter Estimation of The Best Cox Proportional Hazard Regression Model

Variable	$\hat{\beta}$	$exp(\hat{\beta})$
Age (X_2)	1.5274	4.6063
Medicines/Vitamins Administration (X_4)	-1.4639	0.2313

Based on the Table 7, the best Cox proportional hazards regression model that can be used to model the survival time of Covid-19 patients at RSU Bahteramas, for the period March – December 2020 is as follows:

$$h(t) = h_0(t)exp(1.5274X_2 - 1.4639X_4)$$

This model can be explained by calculating the hazard ratio value using equation (10):

If $X_2^*$is the category of patients aged >60 years which is symbolized by 1 and $X_2$is the category of patients aged ≤60 years which is symbolized by 0, then the hazard ratio value for age (X_2) is:

$$\widehat{\mathrm{HR}} = \exp[1,5274] = 4,6063$$

The hazard ratio value of 4.6063 > 1 indicates that age is a risk factor for death for patients aged > 60 years or the risk of COVID-19 patients aged >60 years dying is 4.6063 times faster than COVID-19 patients aged ≤60 years.

If $X_4^*$is a category of patients who are given medicines and vitamins symbolized by 1 and $X_4$is a category of patients who are only given medicines symbolized by 0, thenthen the hazard ratio value

$$\widehat{\text{HR}} = \exp[-1{,}4639] = 0{,}2313$$

The hazard ratio value of 0.2313 < 1 indicates that giving medicines and vitamins to Covid-19 patients is a protective factor for death compared to Covid-19 patients who only take medicines.In the other words, the risk of death for Covid-19 patients who take medicines and vitamins during the treatment period is greater. Reduced by 0.2313 times compared to patients who only took medicines.

4.7. Probability Estimation

To obtain the estimated value of the opportunity, it is necessary to have information about the life table of COVID-19 patients at the RSU Bahteramas for the period March- December 2020. Life Table is a table that provides information about the estimated survival function and hazard function of the individual at a certain time interval. The life table of COVID-19 patients at RSU Bahteramas for the period March-December 2020 is shown in Table 8.

TABLE 8. Life Table of COVID-19 Patients at RSU Bahteramas

j	Δt	n_j	w_j	d_j	n'_j	$\hat{q}_j$	$\hat{p}_j$	$\hat{h}_j$	$\hat{S}_j$	$\hat{H}_j$
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
1	[0,1)	98	0	0	98	0	1	0	1	0
2	[1,2)	98	1	1	97,50	0,0102	0,9897	0.0103	0,9897	0,0103
3	[2,3)	96	0	6	96	0,0625	0,9375	0.0645	0,9279	0,0748
4	[3,4)	90	2	4	89	0,0449	0,9550	0.0459	0,8860	0,1210
5	[4,5)	84	1	0	83,50	0	1	0	0,8860	0,1210
6	[5,6)	83	1	3	82,50	0,0363	0,9636	0.0370	0,8540	0,1578
7	[6,7)	79	2	0	78	0	1	0	0,8540	0,1578
8	[7,8)	77	1	0	76,50	0	1	0	0,8540	0,1578
9	[8,9)	76	2	2	75	0,0266	0,9733	0.0270	0,8310	0,1851
10	[9,10)	72	7	0	68,50	0	1	0	0,8310	0,1851
11	[10,11)	65	5	3	62,50	0,0480	0,9520	0.0491	0,7911	0,2343
12	[11,12)	57	7	0	53,50	0	1	0	0,7911	0,2343
13	[12,13)	50	8	0	46	0	1	0	0,7911	0,2343
14	[13,14)	42	4	0	40	0	1	0	0,7911	0,2343
15	[14,15)	38	4	0	36	0	1	0	0,7911	0,2343
16	[15,16)	34	2	0	33	0	1	0	0,7911	0,2343
17	[16,17)	32	2	0	31	0	1	0	0,7911	0,2343
18	[17,18)	30	4	0	28	0	1	0	0,7911	0,2343
19	[18,19)	26	5	0	23,50	0	1	0	0,7911	0,2343
20	[19,20)	21	2	0	20	0	1	0	0,7911	0,2343
21	[21,22)	19	2	0	18	0	1	0	0,7911	0,2343
22	[22,23)	17	2	0	16	0	1	0	0,7911	0,2343
23	[23,24)	15	1	0	14,50	0	1	0	0,7911	0,2343
24	[24,25)	14	3	1	12,50	0,08	0,92	0.0833	0,7280	0,3174
25	[25,26)	10	2	0	9	0	1	0	0,7280	0,3174
26	[26,27)	8	1	0	7,50	0	1	0	0,7280	0,3174
27	[28,29)	7	1	0	6,50	0	1	0	0,7280	0,3174
28	[39,40)	6	1	0	5,50	0	1	0	0,7280	0,3174
29	[40,41)	5	1	0	4,50	0	1	0	0,7280	0,3174
30	[41,42)	4	1	0	3,50	0	1	0	0,7280	0,3174
31	[46,47)	3	1	0	2,50	0	1	0	0,7280	0,3174
32	[50,51)	2	1	0	1,50	0	1	0	0,7280	0,3174
33	[80,81)	1	1	0	0,50	0	1	0	0,7280	0,3174

By substituting $\hat{h}_0(t_{(j)})$contained in Table 8 into the best Cox proportional hazards regression model, the probability of failure of a COVID-19 patient at RSU Bahteramas at certain points in time can be calculated. For example, in the time interval [1,2), the probability of failure for COVID-19 patients aged >60 years can be calculated as follows:

$$\hat{h}(t) = 0.0474$$
$$\hat{S}(t) = 0.9525$$

This means that the probability of failure for COVID-19 patients aged >60 years in the time interval [1,2) is 0.0474, while the probability of survival for COVID-19 patients aged >60 years in the time interval [1,2) is 0.9525.

Furthermore, at a time interval of [5.6) days, the probability of failure for COVID-19 patients aged >60 years and taking medicines and vitamins during the treatment period can be calculated as follows:

$$\hat{h}(t) = 0.0394$$
$$\hat{S}(t) = 0.9605$$

This means that the probability of failure for COVID-19 patients aged >60 years and taking medicines and vitamins at a survival time interval of [5.6) days is 0.0394, while the probability of survival for COVID-19 patients aged >60 years and taking medicines and vitamins at survival time [5.6) days is 0.9605.

Conclusion

The results of descriptive analysis using the Kaplan-Meier survival curve show that during the March to December 2020 period there were differences in survival probability between categories in the variables of age, comorbid status, and medicines/vitamins administration while for the gender variable with the male categoryand women there is no difference in survival probability. This is proven by testing the hypothesis using the log-rank test. Cox proportional hazards regression model for survival time data for COVID-19 patients at RSU Bahteramas for the period March to December 2020 based on selecting the best model, namely:

$$h(t) = h_0(t)exp(1.5274X_2 - 1.4639X_4)$$

From this model it is known that the factors that influence the survival time of COVID-19 patients at RSU Bahteramas during the March–December 2020 period are age and administration of medicines/vitamins. COVID-19 patients aged >60 years are at risk of dying 4.6063 times faster than COVID-19 patients aged ≤60 years, while COVID-19 patients who take medicinesand vitamins during the treatment period are at 0.2313 times more riskdied more slowly than COVID-19 patients who only took medicine.

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