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A case study in hospitals: Comorbidity modeling on Covid-19 mortality risk using logistic regression

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Abstract

Background: Comorbidities may have a role in Covid-19 patients' deaths. The goal of this research was to determine the impact of comorbidities on the risk of death from COVID-19.

Methods: The research took place at one of the Covid-19 patients' referral hospitals, from March 2020 to February 2021, data on inpatients was collected, and a logistic regression analysis was used to find co-morbid COVID-19 in patients at high risk of death.

Result: Model 1 predicts the risk of death from covid-19 based on age, sex, and the top ten co-morbid covid-19 with an accuracy of 85.3% and an R2 of 62.4%. With a p-value>0.05, sex (SEX), hypertension (HP), diabetes mellitus (DM), cardiac arrest (CA), anemia (AN), hyperuricemia (HR), and urinary tract infection (UTR) do not affect the probability of death in Covid-19 patients in model 1. Model 2 is based on the variables that affect the risk of death (p-value 0.05) are age (AGE), moderate malnutrition (MM), unspecified malnutrition (MU), obesity (OB), and chronic renal disease (CKD). Model 2 is Ln $\left(\frac{p}{(1-p)}\right)$= -3,295 +0,046*AGE +0,667*OB +0,611*MM +1,53*MU +1,248*CKD showed an accuracy of 69.4% with an R2 of 17.1%.

Conclusion: Model 2 is more effective since it only considers diseases with high mortality risk. The results of the model 2 simulation show that the higher the age and comorbid complications, the greater the risk of death for Covid-19 patients.

Keywords: Comorbidity modeling; Mortality risk; Comorbid; Logistic regression; Covid-19; Logistic Regression

1 Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory disease caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and spreads mostly through the respiratory system. [1]. The rapid spread of the virus that resulted in the COVID-19 pandemic occurring in almost all countries in the world triggered a public health emergency where the number of deaths per million population varied widely internationally [2]. Age and comorbidities are risk factors for the severity and mortality of SARS-CoV-2 [3][4][5]. Older age, comorbid heart failure, coronary artery disease, hypertension, type 2 diabetes mellitus, and chronic obstructive pulmonary disease are factors that significantly affect the mortality of COVID-19 patients [6][7]. While the most common comorbidities suffered by COVID-19 patients are diabetes, cardiovascular disease, and hypertension [8][9][10]. Identification of risk factors for the death of COVID-19 patients is useful for determining the level of risk, optimizing the reallocation of hospital resources, and public health

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interventions [11]. COVID-19 patients' characteristics, such as age, sex, and co-morbidities, can be used to identify risk factors for COVID-19 co-morbidities [12][13]. A risk model can be developed using logistic regression analysis to determine the effect of risk factors on COVID-19 mortality [14]. Knowing the comorbid COVID-19 risk factors and models can help manage at-risk groups, assess their mortality risk, and prioritize COVID-19 patient treatment, potentially lowering the number of COVID-19 deaths [15][16]. Logistic regression analysis on the risk of comorbid COVID-19 has been carried out in several previous studies [17][18] to determine the effect of comorbidities on the risk of death through the Odd ratio and P-value, but the use of the logistic regression model to calculate the risk of death from COVID-19 is still rarely found, especially in Indonesia. As a result, a study employing logistic regression analysis and a case study at one of the COVID-19 referral hospitals in Semarang was done on the COVID-19 comorbid risk model. As a result, a study employing logistic regression analysis and a case study at one of the COVID-19 referral hospitals in Semarang was done on the COVID-19 comorbid risk model.

2 Material and methods

The study was conducted in March-May 2021, with the research location at one of the referral hospitals in Semarang. The population for this study was medical record data from Covid-19 inpatients from March 2020 to February 2021, which included 954 patients with a total sample sampling technique. The data used is secondary data from the patient's medical record, in the form of a recapitulation of co-morbid conditions in positive COVID-19 individuals. Age, sex, length of stay (LOS), the source of the patient's referral, the major diagnosis (Covid-19), the patient's secondary diagnosis, and the patient's life and death status were among the information gathered. From the secondary diagnosis, the patient was diagnosed with comorbid and then analyzed descriptively and inferentially. The top 10 comorbidities that most suffered by patients were taken, age and sex as independent variables, while the dependent variable was the patient's life or death status. The following are research variables and data types presented in table 1.

Table 1 Variable and data type

Variable		Data Type
Constant		Number (n)
"AGE"	Age	Number (n)
"SEX"	Sex	Men(1) or Women(0)
"HP"	Hypertension (I10)	Yes(1) or No(0)
"DM"	Diabetes mellitus (E11.9)	Yes(1) or No(0)
"CA"	Cardiac arrest (I46.9)	Yes(1) or No(0)
"OB"	Obesity (E66.9)	Yes(1) or No(0)
"MM"	Malnutrition moderate (E44.0)	Yes(1) or No(0)
"MU"	Malnutrition unspecified (E43)	Yes(1) or No(0)
"AN"	Anemia (D63.8)	Yes(1) or No(0)
"HR"	Hyperuricemia (E79.0)	Yes(1) or No(0)
"UTR"	Urinary tract infection (N39.0)	Yes(1) or No(0)
"CKD"	Chronic kidney disease (N18.5)	Yes(1) or No(0)
Mortality risk		Recover (0) or Died (1)

A descriptive analysis was carried out on the characteristics of the respondents and the top 10 co-morbidities of covid-19, while on the risk model a logistic regression analysis was carried out to determine the effect of age, sex and the top 10 co-morbidities of covid-19 on the death of Covid-19 patients. A mortality risk prediction model was built using the logistic regression formula, namely $\mathrm{Ln}\left(\frac{p}{(1-p)}\right)$= α +β1*AGE + β2*SEX + β3*HP +β4*DM +β5*CA +β6*OB +β7*MM +β8*MU +β9*AN + β10*HR +β11*UTR + β12*CKD where p is the risk of death, α is a constant and β is the regression coefficient

of the variable. Logistic regression analysis processed using SPSS 16 will produce output Odd ratio (OR), p-value and regression coefficient with 95% confidence level. The next step is to simulate the results of the prediction of the risk of death from the model. The graphical simulation of the relationship between mortality risk, age, sex and comorbidity was carried out using Maple 18 software.

3 Result and Discussion

A descriptive analysis of the respondent's characteristics and the patient's death status was conducted using 954 medical record data of hospitalized COVID-19 patients. Table 2 shows the findings of the study of the respondents' characteristics based on a recapitulation of the patient's medical data.

Table 2 Characteristics of Respondents

Risk Factor		**Recover (%)**	**Died (%)**	**Total (%)**
Sex	Men	364 (38%)	191 (20%)	555 (58%)
	Women	259 (27%)	140 (15%)	399 (42%)
Age	<=15 y	19 (2%)	(0%)	19 (2%)
	16-30 y	53 (6%)	11 (1%)	64 (7%)
	31-45 y	170 (18%)	46 (5%)	216 (23%)
	46-60 y	268 (28%)	151 (16%)	419 (44%)
	>60 y	113 (12%)	123 (13%)	236 (25%)
Frecuency Diagnose Secondary	<=5	528 (55%)	187 (20%)	715 (75%)
	6-10	93 (10%)	121 (13%)	214 (22%)
	> 10	2 (0%)	23 (2%)	25 (3%)
Length Of Stay (LOS)	<=7 d	93 (10%)	206 (22%)	299 (31%)
	8-14 d	345 (36%)	92 (10%)	437 (46%)
	15-21 d	139 (15%)	25 (3%)	164 (17%)
	>21 d	46 (5%)	8 (1%)	54 (6%)
Referral from	Gov Hospital	31 (3%)	24 (3%)	55 (6%)
	Private Hospital	56 (6%)	41 (4%)	97 (10%)
	Polyclinic	1 (0%)	0 (0%)	1 (0%)
	Family doctor	0 (0%)	1 (0%)	1 (0%)
	Self arrive	535 (56%)	265 (28%)	800 (84%)
Total		623 (65%)	331 (35%)	954 (100%)

From table 2, it is known that 58% of COVID-19 patients are male, of which 20% have died. While female patients were 42% with 15% mortality. It can be seen that the number of male and female patients did not differ much. In terms of age, the most COVID-19 patients are 46-60 years old (44%), with the number of deaths at that age 151 patients or 16%, followed by patients aged > 60 years as many as 25% with 13% mortality. From this it is known that many Covid-19 patients are old and the number of patients who died is also many who are old. Length of stay ranged from 8-14 days (46%) with mortality 10%, but as many as 22% of patients who died with length of stay <= 7 days. Almost all patients came alone to the hospital (84%). As many as 75% or 715 COVID-19 patients have a secondary diagnosis of COVID-19 ranging from <= 5 secondary diagnoses, with a death rate of 20%. In total, it is known that the number of deaths due to COVID-19 who are hospitalized is 35% and those who have recovered are 65%. Comorbid covid-19 is included in the

secondary diagnosis, here are the top 10 comorbid covid-19 based on the medical records of covid-19 patients which are presented in table 3.

Table 3 Top 10 Comorbid on Life and Death Status

ICD Code	Top 10 Co-Morbid Covid-19	Have Comorbid	Recover (%)	Died (%)	Total (%)
I10	Hypertension (HP)	yes	212 (22%)	108 (11%)	320 (34%)
		no	411 (43%)	223 (23%)	634 (66%)
E11.9	Diabetes mellitus (DM)	yes	143 (15%)	87 (9%)	230 (24%)
		no	480 (50%)	244 (26%)	724 (76%)
I46.9	Cardiac arrest, cause (CA)	yes	0 (0%)	187 (20%)	187 (20%)
		no	623 (65%)	144 (15%)	767 (80%)
E66.9	Obesity (OB)	yes	48 (5%)	39 (4%)	87 (9%)
		no	575 (60%)	292 (31%)	867 (91%)
E44.0 & E43	Moderate & Unspecified malnutrition (MM & MU)	yes	51 (5%)	69 (7%)	120 (13%)
		no	572 (60%)	262 (27%)	834 (87%)
D63.8	Anemia (AN)	yes	25 (3%)	22 (2%)	47 (5%)
		no	598 (63%)	309 (32%)	907 (95%)
E79.0	Hyperuricemia (HR)	yes	33 (3%)	10 (1%)	43 (5%)
		no	590 (62%)	321 (34%)	911 (95%)
N39.0	Urinary tract infection (UTR)	yes	22 (2%)	21 (2%)	43 (5%)
		no	601 (63%)	310 (32%)	911 (95%)
N18.5	Chronic kidney disease (CKD)	yes	16 (2%)	26 (3%)	42 (4%)
		no	607 (64%)	305 (32%)	912 (96%)

Based on table 3, it is known that 34% of COVID-19 patients have comorbid hypertension, 24% of patients have comorbid diabetes mellitus. Although comorbid hypertension and diabetes mellitus are quite common in Covid-19 patients, the mortality percentage is around 9-11%. 20% of patients Covid-19 have cardiac arrest where all patients with cardiac arrest die. From the table above, it is known that the highest number of deaths is due to comorbid cardiac arrest, as many as 20% of patients suffering from cardiac arrest all died. Malnutrition (moderate & unspecified) affects 13% of patients, while obesity affects 9% of Covid-19 patients. Anemia, hyperuricemia, urinary tract infections each suffered 5% of patients and chronic kidney disease was experienced by 4% of Covid-19 patients with a low number of deaths. To determine the risk factors for death by age, sex and the top 10 comorbidities, a logistic regression analysis was carried out whose results are presented in table 4 below.

Table 4 Model 1 risk mortality for age, sex, and 10 comorbidities in of covid-19 patients

Variable	B	Sig	OR
Constant	-3,894	0,000	0,020
“AGE”	0,046	0,000	1,047
“SEX”	-0,161	0,424	0,851
“HP”	-0,431	0,051	0,650
“DM”	-0,205	0,385	0,815
“CA”	22,585	0,994	6,44E+09
“OB”	0,768	0,017	2,156

"MM"	0,838	0,011	2,313
"MU"	1,507	0,000	4,513
"AN"	-0,354	0,526	0,702
"HR"	0,765	0,058	2,149
"UTR"	-0,643	0,272	0,526
"CKD"	1,564	0,009	4,779
Hosmer & Lomeshow test	0,221		
R square	62,4%		
Accuracy	85,3%		
Model 1	$\text{Ln}\left(\frac{p}{(1-p)}\right)$= -3,894 +0,046*AGE -0,161*SEX -0,431*HP -0,205*DM +22,585*CA +0,768*OB +0,838*MM +1,507*MU -0,354*AN +0,765*HR -0,643*UTR +1,564*CKD		

Based on the table of risk model 1, it is known that partially affecting the risk of death from covid-19 are age, obesity, moderate and unspecified malnutrition, and chronic kidney disease with sig < 0.05. Meanwhile, sex, hypertension, diabetes mellitus, heart failure, anemia, hyperuricemia and urinary tract infections did not affect the risk of death of Covid-19 patients because sig > 0.05. Based on the Odd ratio (OR) it is known that the biggest risk factors for death are heart failure (OR=6.44E+09), acute kidney disease (OR=4.779), unspecified malnutrition (OR=4.513), moderate malnutrition (OR=2.313), Obesity (OR=2.156), Hyperuricemia (OR=2.149) and age (OR=1.047). The value of Hosmer & Lomeshow test > 0.05 indicates a fit model to use. There is an effect of age, sex and 10 comorbidities on the risk of death of 62.4%. Prediction results show the level of prediction accuracy is quite high, namely 85.3%. This means that the mortality risk prediction model is quite good at predicting with a prediction accuracy of 85.3%. Model 1 risk of death that is formed is $\text{Ln}\left(\frac{p}{(1-p)}\right)$= -3.894 +0.046*AGE -0.161*SEX -0.431*HP -0.205*DM +22.585*CA +0.768*OB +0.838*MM +1.507*MU -0.354*AN +0.765*HR -0.643*UTR +1.564*CKD. However, because the risk model 1 above still contains variables that do not affect the risk of death, a new risk model will be formed that contains variables that affect the risk of death, namely age, obesity, moderate and unspecified malnutrition, and chronic kidney disease.

Table 5 Model 2 risk mortality for age and 4 comorbidities in of covid-19 patients

Variable	**B**	**Sig**	**OR**
Constant	-3,295	0,000	0,037
"AGE"	0,046	0,000	1,047
"OB"	0,667	0,005	1,949
"MM"	0,611	0,021	1,841
"MU"	1,530	0,000	4,620
"CKD"	1,248	0,000	3,484
Hosmer & Lomeshow test	0,437		
R square	17,1%		
Accuracy	69,4%		
Model 2	$\text{Ln}\left(\frac{p}{(1-p)}\right)$ = -3,295+ 0,046*AGE +0,667*OB +0,611*MM +1,53*MU +1,248*CKD		

Based on table 5, model 2 shows that all variables affecting the risk of death from COVID-19 are age, obesity, moderate and unspecified malnutrition, and chronic kidney disease with sig < 0.05. Based on the Odd ratio (OR), the biggest risk factors for death were malnutrition (OR=4.620), acute kidney disease (OR=3.484), obesity (OR=1.949) and age (OR=1.047). The value of Hosmer & Lomeshow test > 0.05 indicates a fit model to use. There is an effect of age, sex and 4 comorbidities on the risk of death by 17.1% with a fairly high level of prediction accuracy, namely 69.4%. The model 2 risk of death formed is $\text{Ln}\left(\frac{p}{(1-p)}\right)$= -3.295 +0.046*AGE +0.667*OB +0.611*MM +1.53*MU +1,248*CKD. The risk model can be used to calculate the risk of death of a Covid patient by entering the data types as shown in Table 1. The following is a graphical simulation of the risk 1 disease model using the first model presented in Figure 1.

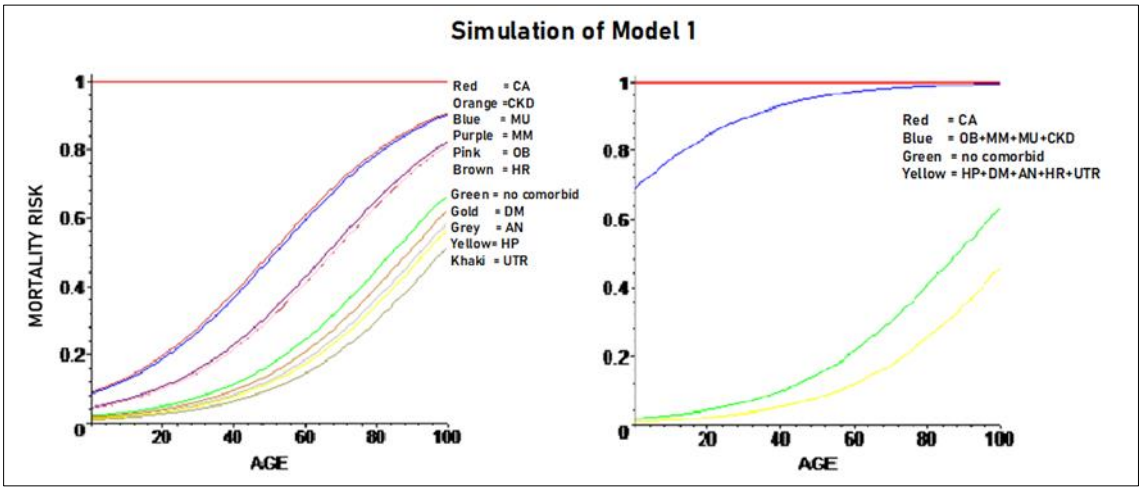

FIGURE 1 Simulation of model 1 risk of covid-19 death by age and comorbidity for female sex

Based on Figure 1, it is known that in model 1 the patient has no comorbidities (green color) the predicted risk of dying at the age of 40 is around 10%, but when the patient has a comorbid heart failure in the second simulation, the risk of dying is 100%. Patients with comorbidities that do not affect the risk of death, namely hypertension, diabetes mellitus, anemia, hyperuricemia and urinary tract infections, actually have a lower risk of death than those without comorbidities. Meanwhile, patients with comorbidities that affect the risk of death, namely obesity, moderate & unspecified malnutrition, chronic kidney disease have a higher risk of death compared to patients without comorbidities.

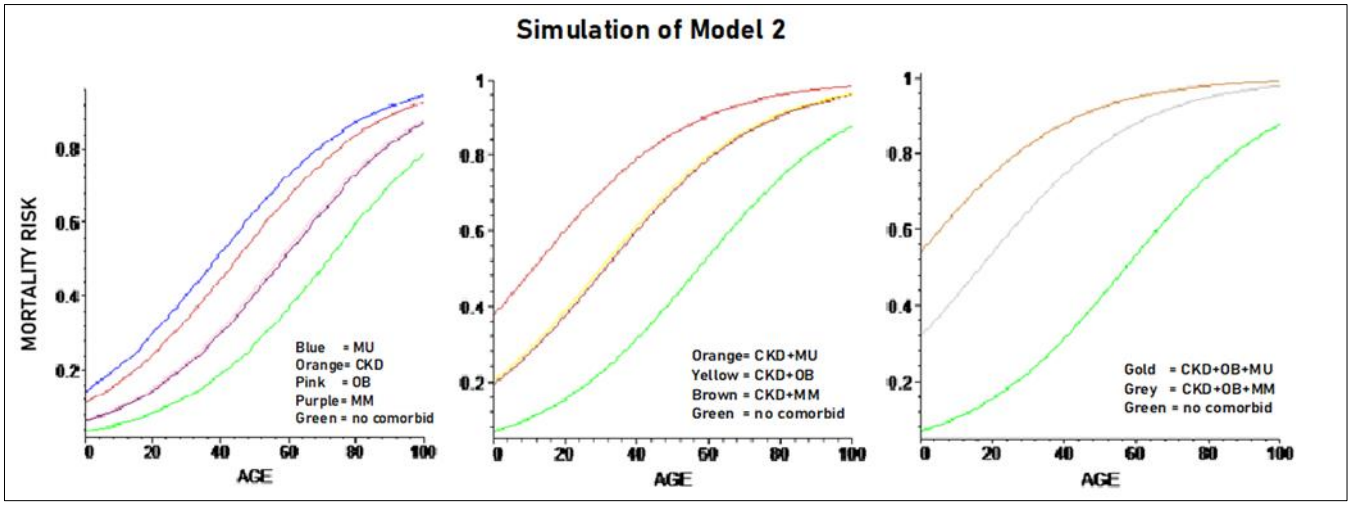

Figure 2 Simulation model 2 risk of covid-19 death by age and comorbidities

On the other hand, patients with comorbid complications that do not affect death have a lower risk of death than patients without comorbidities and patients with comorbid complications that affect death. From the simulation, it can be

concluded that model 1 is not good at predicting risk because patients with comorbid complications of hypertension, diabetes mellitus, heart failure, anemia, hyperuricemia and urinary tract infections will reduce the body's resistance so that it is at risk of death, but in model 1 the risk opportunities are actually reduce. Furthermore, a simulation of the risk of Covid-19 death is carried out in model 2 which is presented in Figure 2.

Based on Figure 2, it is known that the older you get, the higher the risk of death from COVID-19, whether patients have no comorbidities or have comorbidities. For patients with one comorbid, the risk of death is highest if the patient has a comorbid unspecified malnutrition, followed by chronic kidney disease, moderate malnutrition and obesity. For patients with one comorbid, the risk of death is highest if the patient has a comorbid unspecified malnutrition, followed by chronic kidney disease, moderate malnutrition and obesity. For patients who have two comorbidities, the risk of death is highest if these patients have comorbidities of unspecified malnutrition and chronic kidney disease. For patients who have three comorbidities, the risk of death is highest if these patients have comorbidities of unspecified malnutrition, obesity and chronic kidney disease. From the graph, it can be seen that patients with one comorbid age of 1 year have the largest mortality risk of around 20%, but in patients with two comorbidities the greatest mortality risk is known to be 40%, while patients with three comorbidities have the greatest mortality risk of around 60%. This shows that the more comorbid complications, the higher the mortality risk. From the model 2 simulation graph, it can be concluded that the higher the age and comorbid complications, the higher the risk of death for COVID-19 patients.

From the simulation of model 1 and model 2, it can be concluded that model 1 is not good at predicting risk, while model 2 can be used because it focuses more on high-risk diseases. But keep in mind that model 2 has a small effect (17.1%) and lower accuracy (69.4%) compared to model 1 (85.4%). Although the R2 value and accuracy of model 1 are higher than model 2, model 1 is not good at predicting risk, while model 2 is better because it only takes into account diseases that have a high risk of death.

Based on the results of the study, it is known that age and comorbidities affect the risk of Covid-19 death while sex has no effect on the risk of Covid-19 death. From the predictors of age, sex, comorbidities and occupation, it is known that only age and comorbidities significantly affect mortality, while sex and occupation are not significant predictors of death [19]. From the analysis of the risk factors for the death of Covid-19, it is known that the number of men who died was more than the number of women who died. This is in accordance with the results of research which states that male COVID-19 patients are more at risk than women [20][21][22]. Based on the results of the study, patients aged 40-60 years and aged > 60 years were more at risk of death than young people. Elderly COVID-19 patients are more at risk of death, especially if they are accompanied by comorbidities [23][24][25]. It is also known that 75% of patients have a secondary diagnosis of <=5 and almost all patients come alone to the hospital and the length of stay ranges from 1-14 days.

From the results of logistic regression analysis model 1, the factors that influence the risk of death from COVID-19 are age, obesity, moderate and unspecified malnutrition, and chronic kidney disease. Meanwhile, sex, hypertension, diabetes mellitus, heart failure, anemia, hyperuricemia and urinary tract infections did not affect the risk of death of Covid-19 patients. This is different from the results of studies which state that hypertension and diabetes mellitus are associated with the risk of death from COVID-19 [26][27]. Meanwhile, the results of logistic regression analysis model 2 that affect the risk of death from COVID-19 are malnutrition, acute kidney disease, obesity, and age. Renal failure, diabetes and obesity increase the risk of death and so do heart failure and ischemic heart disease [28]. Comorbid acute kidney disease is a major factor in death from COVID-19 [29][30]. Malnutrition and obesity are also co-morbidities of COVID-19 that are at risk for COVID-19 patients [31][32]. The older the patient, the higher the risk of dying from COVID-19. In the simulation of risk models 1 and 2, it can be seen that model 1 is not good at predicting risk on variables that have no effect, so model 2 is better used in predicting the risk of death from covid. From the model 2 simulation graph, it can be concluded that the higher the age and comorbid complications, the higher the risk of death for COVID-19 patients.

4 Conclusion

Risk factors for Covid-19 death, namely male sex is more at risk than female, patients aged 40-60 years and age > 60 years are more at risk of death than young people, almost all patients have a secondary diagnosis <=5 and come alone to the hospital. hospital, and length of stay ranging from 1-14 days. Comorbid covid affects the risk of death in model 1, namely acute kidney disease, moderate and unspecified malnutrition, obesity, and age. From model 1, it is known that the risk of death of patients with heart failure is very high with OR=6.44E+09. Although the R2 value and accuracy of model 1 are higher than model 2, model 1 is not good at predicting risk, while model 2 can be used because it only takes

into account diseases that have a high risk of death. The 2 risk model formed is Ln(p/((1-p)))= -3.295 +0.046*AGE +0.667*OB +0.611*MM +1.53*MU +1,248*CKD. The higher the age and comorbid complications, the higher the risk of death for COVID-19 patients. This risk model can be used as a starting point for forecasting the impact of concomitant COVID-19 on mortality, although it is limited to data from a case study at a hospital in Semarang.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Statement of informed consent

This study was conducted in compliance with international research standards, and all of the study's authors supplied their informed consent..

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