ASSOCIATION BETWEEN 72-H CUMULATIVE FLUID BALANCE AND MORTALITY IN COVID-19 PATIENTS AT RSUD DR. SOETOMOSURABAYA

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ABSTRACT

Cumulative fluid balance (CFB) with positive values mentioned in many studies is associated with mortality risk. In general, positive CFB was found in patients with sepsis, acute kidney injury (AKI), and heart failure. Meanwhile, COVID-19 is one of the causes of the conditions mentioned above. This study is a retrospective observational study using a cross-sectional method. Of the 97 samples obtained, 78 samples met the inclusion criteria. Obtained 69.2% male and 30.7% female. In this study, 45 (57.7%) patients had positive CFB, and 33 (42.3%) patients had negative CFB out of a total of 78 patients. The mortality rate was 32 (41.1%) patients who died from 78 patients in August 2020 s.d. October 2020. The optimal cut-off value for the amount of CFB in 72 hours is 516 ml (sensitivity 59.4%; specificity 71.7%). The result of the significant value of the number of CFB in 72 hours and mortality is (p) = 0.019 then p<0.05, which means there is a relationship between the number of CFBs in 72 hours and mortality in COVID-19 patients in the Ruang Isolasi Khusus (RIK) 1 RSUD Dr. Soetomo Surabaya Period August 2020-October 2020. Positive cumulative fluid balance (>516 ml) predicted to increase mortality of COVID-19 patients in Ruang Isolasi Khusus (RIK) 1 RSUD Dr. Soetomo Surabaya Period August 2020-October 2020.

Keywords: COVID-19, Cumulative Fluid Balance, Mortality

INTRODUCTION

An observational study in 198 ICUs in 24 European countries showed an association of cumulative fluid balance (CFB) in the first 72 hours with the onset of sepsis and increased mortality (1). Several studies stated that an increase in CFB was associated with the death of patients with acute kidney injury in the intensive care unit (ICU) (2). Reported in one study that 1,177 patients with sepsis had a positive cumulative fluid balance (CFB), associated with an increased risk of mortality (3). CFB is the sum of daily fluid balances within a certain period, which can be calculated by the formula [Sum of (total fluid intake—total fluid output) in the first 72 hours of care] and CFB is used as a reference for monitoring ICU patients and fluid resuscitation (1). Daily fluid balance is the daily difference of fluid in and out and does not

include fluid loss without cause. Patients with sepsis who receive adequate initial fluid resuscitation have a better life expectancy and shorter duration of ventilator use (4).

In December 2019, the outbreak of pneumonia caused by SARS-CoV-2 viruses began in Wuhan, the People's Republic of China; the virus has spread rapidly throughout China, with the risk of a continuing pandemic. The COVID-19 outbreak has been one of the world's health care problems in recent years. Strategies for adequate fluid resuscitation for the specific characteristics of the disease, for example, fluid overload (FO) and circulatory system failure, will help optimize the care of these patients (5). Understanding cardiovascular disorders caused by COVID-19 and knowledge of the mechanisms of disease occurrence are essential to treat patients effectively so that the mortality rate due to COVID-19 can be minimized (6). Until now, there have not been many studies discussing the direct association between COVID-19 and CFB and its effect on mortality; therefore, we want to know if there is an association between CFB and mortality rate in COVID-19 patients at RSUD Dr. Soetomo Surabaya within August 2020 to October 2020.

METHODS OF THE STUDY

This research uses a retrospective observational study using a cross-sectional method. The population in this study was diagnosed as COVID-19 patients with 72 h cumulative fluid balance monitoring in Ruang Isolasi Khusus (RIK) 1 RSUD Dr. Soetomo Surabaya within August 2020 until October 2020. Sampling was carried out by consecutive sampling, namely the technique of taking all samples that met the inclusion and exclusion criteria within a certain period. This research was conducted at the Ruang Isolasi Khusus (RIK) 1 RSUD Dr. Soetomo Surabaya as an intensive care unit for COVID-19 patients, particularly within May-August 2021. We use secondary data in the form of patient medical records. Our inclusion criteria were patients with complete cumulative fluid balance data in the first 72h of treatment who had been diagnosed with confirmed COVID-19 pneumonia. We used analysis of difference and receiver operating characteristic (ROC) to obtain the significance of the CFB 72h and mortality variables and determine the optimal cut-off of CFB 72h based on Youden's index.

RESULTS

This research's data collection and processing were carried out from May to August 2021 in the Special Isolation Room of RSUD Dr. Soetomo Surabaya. The samples obtained were 97 samples from patient medical record data; 78 samples had met the inclusion criteria in

the period range of August 2020 s.d. October 2020, the following statistical analysis tests will be carried out.

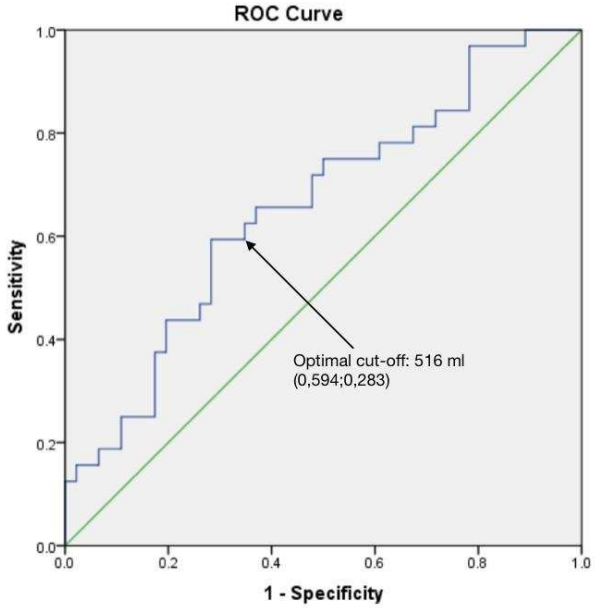
		All	Survivors	Non-survivors	p
Age, years [%}	**17-65**	63 [80,8%]	37 [80,4%]	26 [81,3%]	1,000
	≥ 65	15 [19,2%]	9 [19,6%]	6 [18,8%]	
Female, n [%]		24 [30,7%]	18 [39,2%]	6 [18,8%]	0,095

This study obtained the distribution of data based on age, 63 (80.8%) patients aged 17 to 59 years, 15 (19.2%) of the patients were aged 60 years and over, the mean value (mean) is 49 years, and the median value (median) is 51 years. There is no data for patients aged 17 years and under. Of the patients aged 17 to 59 years, 37 (80.4%) patients survived, and patients aged 60 years and over there were 9 (19.6%) patients alive. Patients who died aged 17 s.d. 59 years, 26 (81.3%), and 6 (18.8%) patients who died were aged 60 years and over. Through the Chi-square analysis test with power (α) = 5%, we got a significance value (p) = 1.00 then p>0.05, which means there is no difference in mortality by age. 54 male patients (69.2%) and 24 (30.7%) female patients. The male patients who survived until the treatment period were 28 (60.8%) patients and 18 (39.2%) female patients who survived. Male patients who died were 26 (81.2%) patients, and the number of female patients who died was 6 (18.8%) patients. Using the Chi-square analysis test with power (α) = 5%, we got a significance value (p) = 0.095 then p>0.05, which means there is no difference in mortality by sex. In general, this study obtained a distribution of data based on mortality, with 46 (58.9%) patients surviving and 32 (41.1%) patients dying out of 78 patients.

		All	Survivors	Non-survivors	p
CFB 72h (ml)	**Mean±SD**	382,6 ±209,59	-93,44 ±222,19	1066,94 ±370,57	0,019
	Median	240	-109	657,50	

In this study, we collected data on the number of patients' CFBs in the first 72 hours from entering RIK RSUD Dr. Soetomo. The results were obtained from the mean (mean) of all patients with a value of 382.6±209.59 ml and a median value of 240 ml. The surviving patients

received an average CFB count of -93.44±222.19 ml with a median value of -109 ml. However, in patients who died, the average number of CFBs was 1066.94 ± 370.57 ml and a median of 657.5 ml. Then from the data described above, we carried out the Mann-Whitney analysis test and obtained the results of a significance value (p) = 0.019 then p <0.05, which means a relationship between the number of CFBs and mortality.



From the analysis above, we get the value of Youden's index is 0.311, which shows the optimal cut-off value of 516 ml (sensitivity 59.4%; specificity 71.7%) on the CFB variable within 72 hours which can be seen in the table. So it can be concluded that 59.4% of patients with CFB at 72h>516 ml correctly predicted were more likely to die, and patients with CFB 72h<516 ml correctly predicted more likely to survive. The value of the AUC is 0.657 (95% CI 0.534 - 0.780), which means that this analytical model is acceptable for predicting patient mortality (7).

DISCUSSION

From the total number of 78 patient data we have analyzed, the mean value is 49 years, and the median is 51 years. Different weights are mentioned in the study. The age of patients with non-COVID-19 infection cases in the ICU ranges from an average value of 66 years, with research subjects monitoring CFB patients with/without AKI or CKD (1). In patients with septic shock without COVID-19 in the ICU with CFB monitoring, it was stated that the average age of living was 62 years, and the average age of patients who died was 65 years (8). In the case of COVID-19, the patient's older age may be a factor that is also considered related to increased mortality in the presence of associated comorbidities such as cardiovascular disease, diabetes, and hypertension (9). We got data on 46 patients (58.9%) alive, while 32 patients (41.1%). The

different percentages of research regarding CFB in ARDS patients without COVID-19 there were 444 living patients (74%) and 156 patients dying (26%) (8). As for the research of Chao, et al. stated that there were 241 patients (81.4%) who lived and 55 patients (18.5%) who died in the case of infected patients without COVID-19 who were treated in the ICU (10).

The results obtained from the CFB variable are 45 patients with positive CFB (57.7%) and 33 patients with internal negative CFB (42.3%). The significance value (p) of the number of CFBs in 72 hours and mortality was 0.019, so $p<0.05$, which means there is a relationship between the number of CFBs and mortality. We obtained a median value of -109 ml for the number of CFBs of living patients and 657.5 ml of patients who died. The average number of CFB in living patients was -93.44±222.19 ml, and in patients who died, the average was 1066.94±370.57 ml. In the 2015 study, a different value was stated. Namely the median amount of CFB for 72 hours experienced by patients admitted to the ICU with the infection without COVID-19 was 5,100 ml, ranging from 2,700 ml to 3,100 ml (11). As for the research of Chao et al., the number of CFBs during 72 hours of treatment for infectious patients was 1710ml±3011ml, meanwhile, for survivor patients, the number of CFBs was 1431ml±2807ml, and for non-survivors, it was 2930ml±3557ml (10). The research of Huang et al. stated that the number of CFB 72 hours of living patients was 1066.7ml±348.8ml while patients who died were 3067.7ml±446.1ml in the case of MODS in patients with septic shock (12).

From the analysis using the Receiver Operating Characteristic (ROC) method, we get the optimal cut-off result from the amount of CFB in 72 hours with a mortality of 516 ml (sensitivity 59.4%; specificity 71.7%). So it can be concluded that 59.4% of patients with CFB count at 72h>516 ml were correctly predicted to die, and patients with CFB at 72 h<516 ml were correctly predicted to live. Different things were reported in the study of Aragão et al. regarding positive CFB within 72 hours of ICU care patients; the optimal cut-off value was 3900 ml (sensitivity 72.7%, specificity 65.1%) (13). de Oliveira et al. reported that CFB greater than 3000 ml at 24 hours and 48 hours with a diagnosis of sepsis was an independent risk factor for mortality (14).

CONCLUSION

Positive cumulative fluid balance (>516 ml) predicted to increase mortality of COVID-19 patients in Ruang Isolasi Khusus (RIK) 1 RSUD Dr. Soetomo Surabaya Period August 2020-October 2020.

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