COST-EFFECTIVENESS ANALYSIS OF ANTICOAGULANT USAGE IN COVID-19 PATIENTS AT 45 KUNINGAN HOSPITAL

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ABSTRACT

Cost-effectiveness analysis (CEA) is a pharmacoeconomic method that compares prices from all sources consumed (cost) with the outcome value of a program or intervention to obtain objective answers to the selection of drugs that are effective in terms of benefits and costs. COVID-19, or Coronavirus Disease 2019, is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2) and causes acute respiratory distress, including fever, coughing, and shortness of breath. Fondaparinux, aside from heparin and enoxaparin, can be given as an anticoagulant therapeutic option in hospitalized COVID-19 patients, according to the third edition of the COVID-19 care recommendations. This study aimed to find the most cost-effective therapy among heparin, enoxaparin, and fondaparinux in COVID-19 patients at the RSUD'45 Kuningan. It also applied descriptive non-experimental research methods with retrospectively collected data. The intervention that had been studied was the administration of anticoagulant medication, where the effectiveness of the drug was observed in the reduction of D-dimer levels to normal levels. Meanwhile, the costs were observed from the perspective of a healthcare provider, specifically the RSUD'45 Kuningan. The study sample included 107 patients, with 13 receiving heparin, 41 receiving enoxaparin, and 53 receiving fondaparinux. Bivariate analysis using the chi-square test revealed no significant difference between the drug groups in the proportion of patients who improved and did not improve (sig. value = 0.610). Bivariate analysis using the Mann-Whitney test revealed a significant difference in the total direct care costs per patient between the heparin and enoxaparin, heparin and fondaparinux, and enoxaparin and fondaparinux groups (sig. = 0.000, 0.029, and 0.011, respectively). Heparin has an effectiveness of 7%, enoxaparin of 19.5%, and fondaparinux of 17% for anticoagulants. Enoxaparin is the anticoagulant that works the best. Heparin costs Rp40,177,305, enoxaparin costs Rp61,892,199, and fondaparinux costs Rp51,251,622 per patient for each group. Heparin Rp40,177,305 is an anticoagulant that has the highest cost-effectiveness. The results of calculating The average cost-effectiveness ratios (ACER) for heparin, enoxaparin, and fondaparinux in patients with improved D-dimers were Rp521,783,181, Rp317,395,892, and Rp301,480,129, respectively. Fondaparinux is an anticoagulant with the lowest cost-effectiveness.

Keywords: **Cost-Effectiveness Analysis, Anticoagulants, D-dimer, COVID-19**

INTRODUCTION

The World Health Organization (WHO) reports that from August 23 to August 29, 2021, more than 4.4 million new cases of COVID-19 were documented, with a mortality toll of more than 67,000 million. Thus, there have been more than 4.5 million mortality and 216 million cases worldwide. Southeast Asia had 596,000 new cases, with Indonesia experiencing the newest deaths at 5551 (World Health Organization, 2021). Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2) is an infectious agent that causes the Coronavirus Disease 2019 (COVID-19), a contagious illness. Acute respiratory diseases, such as fever, coughing, and shortness of breath, are among the most frequent symptoms of COVID-19. In more serious cases, it can result in pneumonia, acute respiratory syndrome,

kidney failure, and even death (Kementrian Kesehatan Republik Indonesia, 2020). Although the respiratory system is the primary site of clinical manifestations, COVID-19 patients can develop coagulopathy, which is linked to higher mortality. The infection with COVID-19 can cause a cytokine storm and systemic inflammation, which can increase coagulation activation and result in hypercoagulation (Willim et al., 2020).

Unless contraindicated, preventive anticoagulation has been suggested by recent guidelines for all hospitalized COVID-19 patients (Willim et al., 2020). According to research by Tassiopoulos AK, Mofakham S, Rubano JA, Labropoulos N, and Bannazadeh M from the year 2021, anticoagulants substantially reduced the death rate of COVID-19. Anticoagulants may also be offered prophylactically, temporarily, or as long-term definitive therapy (Akbar T, 2020). However, these can enhance coagulation activation, resulting in hypercoagulation (Willim et al., 2020). Low-molecular-weight heparin (LMWH) or fondaparinux has been selected over unfractionated heparin (UFH) as anticoagulant thromboprophylaxis in hospitalized acute COVID-19 patients, according to CHEST international recommendations (Moores LK, Tritschler T, Brosnahan S, Carrier M, Collen JF, 2020). Both fondaparinux and enoxaparin anticoagulants proved equally effective in treating acute coronary syndrome in patients without ST-segment elevation; however, fondaparinux remains safer than enoxaparin (Hapsari DC, Suwaldi, 2014).

Based on these findings, heparin and fondaparinux treatments were expected to cost Rp5,793,088.75, and Rp5,799,219.84, respectively. The study's findings also indicated that there was no discernible difference in the cost of therapy for patients receiving heparin versus fondaparinux, even though the duration of stay for fondaparinux patients was 9 days less than that for heparin patients, at 12.05 days (Ariyani RM., 2016). Considering that patients who received fondaparinux therapy for up to 30 days had an average cost-effectiveness ratio (ACER) of Rp8,833,736, whereas patients who received heparin therapy paid an average cost of Rp10,878,243, it can be said that fondaparinux was more cost-effective than heparin (MPL & L, 2013). When the therapeutic effects of fondaparinux and enoxaparin were compared in 100 hospitalized COVID-19 patients, there was no statistically significant difference in prophylaxis for venous thromboembolism, indicating that fondaparinux was superior to enoxaparin (Viggiano et al., 2021). Among hospitalized COVID-19 patients, fondaparinux has been demonstrated to be both safer and more effective than enoxaparin in VTE prevention (Russo et al., 2020). The findings of this study additionally indicated that there were no appreciable differences in clinical trials of patients receiving fondaparinux or enoxaparin as thromboprophylaxis for SARS-CoV2 (Cardillo et al., 2021).

One of the clinically significant results of fibrin breakdown, including an increase in pulmonary embolism, was evaluated using D-dimer levels (Departemen Kesehatan Republik Indonesia, 2006). In COVID-19 people in general, elevated D-dimer levels are a sign of coagulopathy that is frequently discovered and linked to the severity of the illness. Hospitalized Covid-19 patients need to have their coagulation markers, namely D-dimer, periodically assessed (Willim et al., 2020). A three to fourfold increase in D-dimer levels can be regarded as substantial, but a precise threshold cannot be established (PDPI et al., 2020). When defining patterns of thromboprophylaxis and tracking the effectiveness of therapy, D-dimer levels can be a useful solitary predictor (Sakka et al., 2020).

RSUD'45 Kuningan offers heparin, enoxaparin, and fondaparinux as the 3 forms of anticoagulants for COVID-19 patients. Fondaparinux may be administered as an alternative to anticoagulant medication in COVID-19 patients who have received treatment since the third edition of the COVID-19 care recommendations was released (PDPI et al., 2020), and the researchers concluded that a cost-effectiveness analysis of the use of anticoagulants in COVID-19 patients at RSUD'45 Kuningan a regional public hospital, was necessary to compare the cost-effectiveness and efficiency of anticoagulant drugs in lowering D-dimer levels in COVID-19 patients at the RSUD'45 Kuningan. This study compared the use of heparin, enoxaparin, and fondaparinux in COVID-19 patients to discover what would be the most cost-effective treatment.

RESEARCH METHODS

This study used ethical clearance number KET-147/UN2.FI/ETIK/PPM.00.02/2023 examined the cost-effectiveness of treating COVID-19 patients at the RSUD'45 Kuningan with anticoagulants such as heparin, enoxaparin, and fondaparinux from January 2021 to December 2021. A non-experimental descriptive research design was adopted in this investigation, and secondary medical record data were retrospectively collected. Total sampling was the method used to choose the study sample, and it complied with the inclusion and exclusion criteria. All COVID-19 patients at RSUD'45 Kuningan in 2021 served as the research sample. These patients met the following inclusion criteria: being above the age of 18 years, having a verified COVID-19 status, having an initial D-dimer level greater than 1500 ng/mL, and being prescribed one of the anticoagulants heparins, enoxaparin, or fondaparinux. Patients who passed away or had D-dimer data with only one point dropped from the assessment process. Complete inclusion of patient data was used instead. Following sample analysis, 107 patients were identified, of whom 13 were receiving heparin, 41 were receiving enoxaparin, and 53 were receiving fondaparinux.

The information used consisted of the patient's name, sociodemographic information (age and gender), comorbidities, severity of illness symptoms, information about anticoagulant medications, and laboratory information (D-dimer and most recent PCR). The criteria for the assessment of pharmacological effectiveness included a reduction in D-dimer levels and the overall direct cost incurred during therapy. Based on the initial D-dimer value and the end D-dimer value (the percentage of D-dimer levels decreased until it improved) following anticoagulant treatment, the efficacy of each medication group was assessed. The nonparametric statistical tests Kruskal Wallis, Mann Whitney, and Chi-square were used during data analysis.

Research Procedure

The following parts of this research were carried out in RSUD'45 Kuningan throughout the 3 months of data collection:

1. Stage 1: Established the population and sample
   Researchers computed the total population from January to December 2021, and based on the inclusion and exclusion criteria, they established the sample size. A total of 107 patients with C0VID-19 were included in this study. Data were collected using a total sampling technique when the sample met the inclusion and exclusion criteria.
   The inclusion criteria were as follows.
   a) Patients over the age of 18 who have a verified COVID-19 status
   b) Initial D-dimer concentration > 1500 ng/mL
   c) Making use of an anticoagulant, such as heparin, enoxaparin, or fondaparinux
   d) Complete patient information for evaluation
   The exclusion criteria were as follows:
   a) Patient passes away
   b) D-dimer data only shows one point
   Samples of heparin were given to 13 patients, enoxaparin to 41 patients, and **fondaparinux to 53 patient**
2. Stage II: Data Collection
   The data were collected retrospectively by reviewing the medical records of COVID-19 patients using anticoagulants, D-dimer results, and total direct expenditures incurred during the patient's treatment.
3. Stage III: Descriptive and Pharmacoeconomic Analysis of Data

Data Analysis

	Univariate Analysis			
No	Parameter	Analysis	Variables	Measurement types
1	Patient Demographic Data	The researcher counted the total of patients with the percentage in each category. Percentage = Number of each category / total number of patients whose data were used in the study X 100%	1. Age 2. Gender 3. Comorbid 4. Degree of symptoms of COVID-19 disease 5. duration of being hospitalized 6. Percentage of drug use	Descriptive analysis
3	CER	Total direct costs and clinical outcomes were calculated Percentage = the average total direct costs of each category divided by the patient's average D-dimer reduction	1. Total Direct Costs during COVID-19 treatment 2. Clinical Outcome	Pharmacoeconomic analysis
4	CEA	The comparison of CER results for each category was calculated. The lower the CER value, the more effective cost can be obtained because low costs can provide higher therapeutic results	CER in each group of this research	Pharmacoeconomic analysis

	Bivariate analysis		
No	Parameter	Analysis	Statistical measurement type
1	The difference in the total cost of each alternative treatment	The analysis was used to find out whether there was a significant difference in the total direct cost of patients receiving anticoagulant therapy in each group tested	Kruskal Wallis-Test
2	Differences in the percentage of patients who experience decreased levels of D-Dimer	The analysis was used to see if there was a significant difference in the number of patients who experienced a decrease in D-dimer levels in each group tested	Chi Square-Test

RESULTS AND DISCUSSION
Drug Use as a Percentage

From the findings of this study, it could be inferred that Fondaparinux, with a 49.6% usage rate, was the anticoagulant most frequently used in RSUD'45 Kuningan. In contrast to the findings of earlier studies by Pratiwi et al., which indicated that enoxaparin was the most commonly used anticoagulant (44.7%), followed by fondaparinux (42.1%) and heparin (7.90%)%) (Pratiwi & Adhityasmara, 2021). The current finding is similar to that of Donna et al. Fondaparinux is the most widely used anticoagulant (Donna Perdana Putra et al. 2022). The data for the majority of anticoagulant use vary between studies; this is possible because the hospitals handled COVID-19 patients' coagulation issues following their own set of policies.

Table I. Data of Characteristic COVID-19 patients at the Regional Public Hospital 45 Kuningan

Variables	Categories	The Subject of research n=107					
		Heparin n=13		Enoxaparin n=41		Fondaparinux n=53	
		n	%	n	%	n	%
Percentage of Drug Use	Anticoagulants	13	12,2	41	38,3	53	45,5
Gender	Male	4	11,1	12	33,3	20	55,6
	Female	9	12,7	29	40,8	33	46,5
Age	18 – 25 years old	0	0	2	50	2	50
	26 - 35 Years old	4	22,2	4	22,2	10	55,6
	36 - 45 years old	2	15,4	8	61,5	3	23,1
	46 - 55 years old	3	12	12	48	10	40
	>56 years old	4	8,5	15	31,9	28	59,6
Degree of Symptoms of Disease	Low	4	10,2	14	35,9	21	53,9
	Medium	6	13,4	16	35,5	23	51,1
	Hard	3	13	11	47,8	9	39,2
Comorbid	Comorbid	7	10,6	28	42,4	31	47
	No Comorbid	6	14,6	13	31,7	22	53,7

Characteristics of the Patient

Under the study's findings, more female than male patients were registered. The findings of this study are consistent with those reported by Khaerunnisa et al., Patrisia et al., and Kurnianto et al.. (Cibro et al., 2022; Khaerunnisa et al., 2022; Kurnianto et al., 2021) and found that a higher proportion of patients were female than male. This could be explained by the fact that women experience stress more easily when dealing with it. It could be concluded that there were more women than men with COVID-19 at RSUD'45 Kuningan, with 66.4% female and 33.6% male.

The patient age information in **Table I** shows that the age group of COVID-19 patients at RSUD 45 was >56 years, with a total of 47 patients (43.92%). Aeda et al., Hadian et al., Cibro et al., and Khaerunisa et al. showed that the age group of COVID-19 patients was also significant (Cibro et al., 2022; Ernawati, 2021; Hildan Hadian & Sadeli Masria, 2022; Khaerunnisa et al., 2022). The majority belonged to the over-56 age group. This was the case because older patients tend to go through a degenerative period, which exposes

them to illnesses that lower immunity and are more likely to sign COVID-19. In addition, old age could result in recklessness in upholding protocols, increasing the risk of contracting COVID-19 (Hidayani, 2020). It is clear that, with a proportion of 43.92%, the majority of COVID-19 patients at the regional public hospital 45 Kuningan belong to the age category of >56 years.

Degree of Comorbidity of Disease Symptoms

Based on the study's findings, it was determined that patients with a moderate level of disease symptoms (42.1 %) had the highest degree of COVID-19 disease symptoms at RSUD'45 Kuningan. According to the overall sample, the fondaparinux group had a majority of mild patients (53.9%), a majority of moderate patients (51.1%), and a majority of severe patients (47.8%), except for the enoxaparin group. The number of patients with light degrees was 30.8%, moderate degrees was 46.2%, and severe degrees was 23% in the heparin group when examined from the proportions in each group. The percentage of enoxaparin-treated patients in the mild group was 34.2%, 39%, and 26.8%, respectively. Fondaparinux was classified as mild, moderate, or severe by 39.6%, 43.4%, and 17%, respectively. The enoxaparin group, with a patient prevalence of 26.8%, had the highest percentage of patients exhibiting severe disease symptoms, it could be inferred.

This study had several limitations, one of which was the challenge of reducing the variability between groups due to the unequal distribution of samples among the groups. Each group had a variety of disease symptoms, which ultimately affected how well the groups were measured. The percentage of disease symptoms was not significantly different between each medication group, based on the results of bivariate analysis using the chi-square test (p-value> 0.05).

Comorbidity

The majority of COVID-19 patients at the two COVID-19 referral hospitals in Ambon City in 2020 had comorbidities, according to Theresia's research findings, which were also consistent with Ichsan et al. 's study (Ichsan et al., 2022), which found that out of 107 total samples, 66 patients had comorbidities (61.6%), and 41 patients did not. Based on the study's findings, it should be noted that 61.6% of COVID-19 patients at the 45 Kuningan Regional Public Hospital had comorbidities.

According to the study findings, the Fondaparinux group had the highest number of comorbid patients, with 31 patients (47%), followed by the enoxaparin and heparin groups with 28 and 28.3 patients, respectively. In contrast, the enoxaparin group had the largest proportion of patients with comorbidities (68.3%), followed by fondaparinux (58.5%), and heparin (53.8%) when each group was regarded as a whole. The fact that the number of samples used in this study was disproportionally distributed among the groups, meaning that each group had a different number of comorbidities, and that it would be difficult to minimize the variability between groups in the future, which would have an impact on their ability to be effective and cost-effective, was one of its weaknesses. The percentage of comorbidities between each pharmacological group was not significantly different according to the findings of bivariate analysis using the chi-square test (p-value > 0.05).

Analysis of Effectivities of Anticoagulants

Table II. Data on the Efficacy of Treatment

Efficacy of Treatment	Category	Research Subject n= 107						p-value chi-square
		Heparin n=13		Enoxaparin n=41		Fondaparinux n=53		
		n	%	n	%	n	%	
The Average of D-Dimer	Increase	1	5.9	9	52.9	7	41.2	0,684
	Decrease	11	13.3	29	34.9	43	51.8	
	Constant	1	14.2	3	42.9	3	42.9	

Percentage Number of Patients with D-dimer Levels	Better	1	7.7	8	19,5	9	17	
	Worse	12	92.3	33	80,5	44	83	0,61
Percentage of number of PCR patients	Positive	9	11	37	44,5	37	44,5	0,046

The greatest percentage of decreased D-dimer levels (43 patients, 51.8 %) was in the fondaparinux group, according to **Table II**; however, when viewed from each patient's perspective, the total number of patients who experienced decreased D-dimer levels was lower. Heparin had the highest percentage reduction in terms of proportion in each group at 84.6% (11 of 13 patients), followed by fondaparinux (81.2%; 43 patients out of 53 patients), and enoxaparin at 70.7% (29 patients). The low percentage of the enoxaparin group in lowering D-dimer levels was caused by the proportion of patients who had higher comorbidities than patients in the other groups, which resulted in a lower reduction percentage than the other groups. The average percentage of rising D-dimer levels, falling D-dimer levels, and unchanged D-dimer levels in each drug group were not significantly different according to the findings of bivariate analysis using the chi-square test (p-value > 0.05).

The enoxaparin group, with a D-dimer improvement rate of 19.5%, was followed by the fondaparinux group, with a D-dimer improvement rate of 17%, and the heparin group, with a D-dimer improvement rate of 7.7%. Enoxaparin has the largest patient percentage among the three groups whose D-dimer levels are improving, indicating that it is the most effective anticoagulant. According to Viggiano et al., fondaparinux is the most effective anticoagulant among COVID-19 patients who have received treatment (Cardillo et al., 2021). However, the findings of this study disagree with these findings. According to the 2020 CHEST Guidelines, DOAC or rivaroxaban can be considered in COVID-19 patients who experienced venous thromboembolic complications (deep vein thrombosis or pulmonary embolism) with a stable clinical condition and did not receive therapy or medications that could potentially worsen the condition (500 ng/ml). This is also a cause because it refers to the anticoagulant study's outcome of lowering the patient's D-dimer level. Thus, when laboratory results (D-dimer) and clinical signs indicate improvement, doctors can replace the injectable anticoagulant with rivaroxaban tablets. The doctor then stopped monitoring D-dimer levels, which can harm the number of patients who experience a decrease in D-dimer levels until they improve (500 ng/ml) in very small amounts.

The number of patients who improved and did not improve across the drug groups was not significantly different, according to the results of bivariate analysis using the chi-square test (p-value > 0.05). The findings of this study were consistent with those of Russo et al. in that there were no appreciable variations among COVID-19 patients. A study by Hapsari et al. indicated that the efficiency of fondaparinux was the same as that of enoxaparin (Hapsari DC, Suwaldi, 2014) when 19 patients who used fondaparinux were compared with those who used enoxaparin therapy (Cardillo et al., 2021). The percentage of patients who were discharged from the hospital with positive PCR results was higher than that of patients with negative results, and more patients were discharged from the hospital in situations where the PCR results were still positive, including 83 patients out of the 107 total samples (77.6%), and negative PCR results in 24 patients (22.4%). This information was obtained from the results of the patient's last PCR test before leaving the hospital. When comparing the proportions of each drug group, the enoxaparin group had the highest number of patients with positive discharges (90%; 37 positives out of a total of 43 patients), followed by the fondaparinux and heparin groups (70 %).

The findings of this study support those of Khaerunisa et al., in that there are still patients leaving hospitals with positive PCR results, necessitating the need for independent isolation. This is because the patient's PCR results still returned positive 14 days after the treatment period ended, even though the patient's symptoms had begun to fade, and he or she was improving. The presence of virus remnants in the body may be the cause of the positive PCR results, even if these viruses are not communicable. Doctors advise their patients to practice self-isolation to stop the spread of the virus if they have positive PCR results and return home (Khaerunnisa et al. 2022). The study findings indicated that 77.6% of patients with positive PCR test results who were released from the regional public hospital 45 Kuningan still had such results. There was a significant difference between the pharmacological groups in terms of the number of patients discharged from the hospital with positive and negative PCR results (p-value 0.05), according to the findings of bivariate analysis using the chi-square test.

Cost Analysis of Anticoagulant Drug Therapy

Table III. Cost Data for Patient Care

Average Cost for Patient Care	Category	Heparin n=13	Enoxaparin n=41	Fondaparinux n=53	p-value Kruskal-Wallis
Average Cost for Patient Care	Drug Cost	Rp3.936.439	Rp5.436.957	Rp4.951.304	0,001
	Supporting Fees	Rp4.606.904	Rp6.237.057	Rp4.753.730	
	Maintenance costs	Rp31.633.962	Rp51.042.614	Rp41.546.588	
	Total cost of care	Rp40.177.305	Rp61.892.199	Rp51.251.622	
Average Cost for Drug	Anticoagulant Drugs	Rp538.462	Rp1.632.282	Rp2.094.255	0,113
	Other Drugs	Rp3.397.978	Rp3.804.675	Rp2.919.496	
	Total Cost of Drug	Rp3.936.439	Rp5.436.957	Rp5.013.751	

The average total direct cost per patient in the enoxaparin group was the highest, possibly because of the proportion of patients with comorbidities being higher among other drug groups, which causes the length of stay to be longer than in other drug groups, and the largest was in the enoxaparin group, which was Rp61,892,199. The lowest cost was in the heparin group, which was Rp40,177,305. the three medication groups had the highest average dosage per patient. Heparin is the drug class with the lowest average total direct cost per patient, with a cost of Rp40177305, according to the conclusions drawn from **Table III**. The sampling approach used for data collection was one of the weaknesses of the research because it implied an imbalanced ratio between the number of samples and the sample's characteristics, which threw doubt on the results.

Cost Effectiveness Analysis

Table IV. Data Comparison of Anticoagulant Cost-Effectiveness Ratio

No	Type of Cost	Heparin (n=13)	Enoxaparin (n=41)	Fondaparinux (n=53)	P- Value
1	Average Total Cost per patient	Rp40.177.305	Rp61.892.199	Rp51.251.622	0,001

	(Cost)			
2	Percentage Number of patients whose D-dimer levels improved (Effectiveness)	7.7%	19,5%	17%	0,610
	Average Cost Effectiveness Ratio (ACER)	Rp521.783.181 Each patient has an improvement of D-dimer	Rp317.395.892 Each patient has an improvement of D-dimer	Rp301.480.129 Each patient has an improvement of D-dimer

The cost-effectiveness ratio was calculated using the following equation.

$$\text{Cost Effectiveness ratio (CER)} = \frac{Cost}{Effectiveness} \quad \text{……………………... (1)}$$

Comparing the enoxaparin group to the fondaparinux and heparin groups, the enoxaparin group had the highest percentage of patients whose D-dimer levels improved, although the expenses associated with using enoxaparin were higher. While heparin was less expensive than enoxaparin and fondaparinux, it had the lowest rate of patients whose D-dimer levels improved at least 7.7%, as opposed to enoxaparin (19.5 %) and fondaparinux (17 %). The anticoagulant with the highest effectiveness ratio at the lowest cost was expected to be chosen based on the computation of the cost-effectiveness ratio (CER) of each anticoagulant used. Compared to enoxaparin and fondaparinux, heparin had the lowest average total direct cost and the lowest proportion of patients whose D-dimer levels improved. Compared to heparin and fondaparinux, the enoxaparin group had the largest percentage decrease in D-dimer levels when the percentage of patients who experienced a decrease in D-dimer levels was calculated. However, when the average cost-effectiveness ratio (ACER) was calculated, the fondaparinux group had the lowest ACER value, with a cost of Rp51,251,622 and an effectiveness of 17%. Fondaparinux is the most economical option for anticoagulant treatment in COVID-19 patients at the regional public hospital 45 Kuningan because its ACER value is lower than those of enoxaparin and heparin.

CONCLUSION
1. According to this study, anticoagulant use among COVID-19 patients at RSUD 45 Kuningan was as follows: in 53 patients (49.6%), 41 patients (38.3%), and 13 patients (12.1%), fondaparinux, enoxaparin, and heparin were the most frequently used anticoagulants.
2. From the standpoint of health service providers, specifically RSUD 45 Kuningan, the components of total direct costs per patient included treatment costs, drug costs, and supporting costs for three groups of drugs, namely heparin Rp40,177,305, enoxaparin Rp61,892,199, and fondaparinux Rp51,251,622. Heparin, at a cost of Rp40,177,305, was the anticoagulant with the best value.
3. The analysis of the effectiveness of anticoagulant medications in the three drug groups heparin 7%, enoxaparin 19.5%, and fondaparinux 17% showed no statistically significant differences in the effectiveness of anticoagulant medications in any of the three drug groups. This could be a result of several factors, including an unbalanced sample size, unequal severity of disease symptoms, and an unequal percentage of comorbidities between groups, all of which may alter the outcomes of research and statistical analyses. Therefore, enoxaparin, with a 19.5% reduction in D-dimer level, was the most effective anticoagulant.
4. According to the ACER values for the three drug groups, the cost-effectiveness of treatment with heparin, enoxaparin, and fondaparinux were Rp521,783,181, Rp317,395,892, and Rp301,480,129 per patient with enhanced D-dimer, respectively.

Fondaparinux is an anticoagulant medication with the lowest cost-effectiveness ratio. Heparin or fondaparinux could be utilized as anticoagulant therapy in COVID-19 patients as a matter of policy.

SUGGESTIONS

1. The quality and thoroughness of medical records must be improved in cases where they are not cleanly organized, some of the data are missing, and other records are dispersed throughout the room, making it challenging for researchers to gather information.

2. To ensure that the findings drawn from the research results accurately reflect the study population, additional research on the analysis of the cost-effectiveness of anticoagulant medication must be conducted with a proportionate number of samples.

3. As the Ministry of Health is responsible for covering the costs of all COVID-19 patients, additional research is required to determine whether comparing the total direct costs derived from the calculation of the unit cost of health service providers when compared to the rates paid by the guarantor is reasonable.

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