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Comparison of unfractionated heparin and fondaparinux in relation to the incidence of recurrent myocardial infarction

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ABSTRACT: Acute Myocardial Infarction (AMI) is a cardiovascular condition that involves necrosis of the heart muscle because of a decrease in blood supply to the heart caused by an obstruction of the coronary arteries. The prevalence of cardiac disease is 1.5% including AMI, and ranked 4th above all provinces in Indonesia. Anticoagulants are administered for the management of AMI treatment. Anticoagulants are treatments utilized to prevent thrombosis and reduce ischemic injury, preventing hemorrhage from developing in the heart's arteries and veins. Unfractionated heparin (UFH) and fondaparinux are both anticoagulants, that are utilized frequently in the treatment of AMI-EST patients. In decreasing the production of thrombin and preventing coagulation, unfractionated heparin, and fondaparinux can avoid death and recurrent myocardial infarction. The research was conducted as an observational study with retrospective data collection from medical records of inpatients diagnosed with acute transmural myocardial infarction of the anterior wall at Prof. Dr. Margono Soekarjo Purwokerto from January 2019 to December 2021. The chi-square test was used to examine the association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the incidence of recurrent myocardial infarction. The statistical analysis showed a significant association between the type of anticoagulant therapy and the incidence of recurrent myocardial infarction ($p < 0.05$). A higher proportion of patients treated with fondaparinux did not experience recurrent myocardial infarction compared to those treated with unfractionated heparin, suggesting that fondaparinux may be more effective in preventing recurrence.

KEYWORDS: Acute myocardial infraction; fondaparinux; unfractionated heparin.

INTRODUCTION

Acute myocardial infraction (AMI) is a cardiovascular disease associated with necrosis of the heart muscle caused by decreased blood supply to the heart due to occlusion of the coronary arteries [1]. The American Heart Association (AHA) reported 8.5 million Myocardial Infraction cases in 2010. The disease was responsible for 7.2 million (12.2%) deaths worldwide [2]. The prevalence of coronary artery disease in Indonesia was approximately 1.5%, including AMI, based on a doctor's diagnosis. Central Java had the fourth highest prevalence of heart disease in Indonesia, at 1.6% or approximately 132,565 cases. AMI is classified into two types : transmural infarction and nontransmural infarction. Transmural infarction involves the entire thickness of the myocardium from the epicardium to the endocardium. Meanwhile, nontransmural infarctions are not widespread, and only the inner third of myocardium. The main clinical symptom that occurs in AMI patients is pain. The pain feels like pressure or heaviness in the middle of the chest, radiates to the left arm, neck, jaw, shoulder, or epigastrium, and persists for >20 minutes. Shortness of breath, nausea/vomiting, cold sweat, and pallor because of vasoconstriction can occur with pain symptom [4].

Old-generation anticoagulants such as unfractionated heparin (UFH) and new-generation anticoagulants such as fondaparinux are used in the treatment of acute myocardial infarction (AMI). Unfractionated heparin is a parenteral anticoagulant that utilizes a narrow therapeutic window [5]. The recommended dose, according to the Guidelines for the Management of Acute Coronary Syndromes in Indonesia [4], is an intravenous bolus of 60 IU/kgBW (maximum 4000 IU), followed by an intravenous infusion of 12 IU/kgBW (maximum 1000 IU/hour). The dose of unfractionated heparin infusion is adjusted to sustain the Activated Partial Thromboplastin Time (aPTT) during therapy at 1.5 - 2 times the normal range [4]. Fondaparinux is given

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subcutaneously at intervals of once a day for 5-8 days or until the patient leaves the hospital in AMI-EST patients undergoing fibrinolytic or without reperfusion therapy [4]. Various randomized controlled trials have shown the efficacy of unfractionated heparin in acute coronary syndromes. The frequency of recurrent myocardial infarction incidents wares consistently decreased in trials. Meta-analysis testing with or without unfractionated heparin showed that unfractionated heparin was effective in preventing death [6]. The use of fondaparinux sodium shows many advantages compared to unfractionated heparin therapy, such as not requiring close monitoring therapy because the drug is fully bioavailable when administered subcutaneously and has less risk of bleeding side effects [7], [8]. The effectiveness of therapy using unfractionated heparin or fondaparinux in IMA-EST patients is to prevent recurrent myocardial infarction [9]. This medical condition can be recognized from the clinical signs and symptoms of recurrent myocardial infarction, which include chest pain that spreads to the left arm, neck, jaw, shoulder, or epigastrium and lasts for more than 20 minutes, shortness of breath, and cold sweats [4]. According to De Luca (2021), fondaparinux was more effective than unfractionated heparin in managing out-of-hospital cardiac arrest due to acute myocardial infarction by reducing early bleeding complications in one month [10]. The incidence of adverse drug events in patients with fondaparinux was lower compared to patients with heparin, at 11.11% and 25.86%, respectively, thus providing a better safety profile [11].

Monitoring the efficacy of fondaparinux as a new generation anticoagulant should be done to assess its effectiveness in preventing recurrent myocardial infarction when compared to unfractionated heparin, which has long been utilized and effective in the treatment of patients with AMI-EST. A prior study conducted in Italy indicated that fondaparinux was safer than unfractionated heparin (UFH) in the management of out-of-hospital cardiac arrest (OHCA) secondary to acute myocardial infarction (AMI), as it reduced early bleeding complications at one month; however, the incidence of recurrent myocardial infarction (re-MI) was not significantly different between the two therapies (p-value = 1) [10]. There is limited data in Indonesia, and no research has been conducted on how the type of anticoagulant therapy (unfractionated heparin or fondaparinux) affects clinical outcomes in patients with acute myocardial infarction at Prof. Dr. Margono Soekarjo Hospital in Purwokerto.

▪ MATERIALS AND METHODS

Materials

The study was approved by the Research Ethics Committee at Prof. Dr. Margono Soekarjo Hospital, Purwokerto with post number 420/04627. Patient data were kept confidential and used solely for research purposes. This study employed an observational design, with data collected retrospectively from patient medical records between January 2019 and December 2021. The inclusion criteria comprised inpatients aged ≥18 years who were diagnosed with acute myocardial infarction, specifically acute transmural myocardial infarction of the anterior wall (I21.0) [32], and received intravenous UFH therapy or subcutaneous fondaparinux during the study period. Eligible patients had complete medical record data, including demographic details (age, gender, body weight), anticoagulant use (drug name, dose, frequency, and duration), and clinical outcomes following anticoagulant therapy. The exclusion criterion was patients who died during anticoagulant treatment. Sampling was conducted using a total sampling method based on the inclusion and exclusion criteria, followed by simple random sampling of fondaparinux users to equalize the number of samples between the UFH and fondaparinux groups. Data were obtained from electronic medical records meeting the criteria and transcribed into a case report form (CRF). After data collection, 63 patients received UFH and 188 received fondaparinux. The fondaparinux sample was then adjusted to match the UFH group, resulting in 63 patients in each group.

The independent variable in this study was the type of anticoagulant used (intravenous UFH or subcutaneous fondaparinux). The dependent variable was the clinical outcome of anticoagulant therapy, assessed based on clinical signs of recurrent myocardial infarction, such as chest pain radiating to the left arm, neck, jaw, shoulder, or epigastrium lasting >20 minutes, shortness of breath, and cold sweats. Data were analyzed using univariate and bivariate analyses. Univariate analysis was conducted to describe the characteristics of each variable, including patient demographics (gender, age, and secondary diagnoses). The analysis of UFH and fondaparinux usage patterns included drug name, dosage, frequency, interval, and duration of administration, presented in tabular form. Bivariate analysis was performed to examine the

association between the type of anticoagulant (UFH or fondaparinux) and the incidence of recurrent myocardial infarction, as indicated by clinical signs, using the Chi-square test in IBM SPSS Statistics version 26. The hypothesis test results were interpreted based on the p-value, with $p < 0.05$ indicating a statistically significant association.

Instrument

The intsrument used in this study was the case report form (CRF). The CRF contains medical record numbers, patient identity (initial name, gender, patient age, and patient weight), date of treatment (date of admission and exit from the hospital), diagnosis (primary and secondary diagnosis), hospital admission complaints, anticoagulant therapy given to the patient (name of the drug, type of preparation, dose, route of administration, and frequency of administration), and post-administration conditions. The association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the occurrence of recurrent myocardial infarction was assessed based on clinical signs observed after discontinuation of the anticoagulant therapy. According to Indonesian Heart Association [4], clinical signs of recurrent myocardial infarction include chest pain that spreads to the left arm, neck, jaw, shoulder, or epigastrum and lasts more than 20 minutes; shortness of breath; and cold sweating after unfractionated heparin or fondaparinux administration is discontinued.

Methods

The research used an observational study design with retrospective data collection by accessing patient CRF data. Data were analyzed univariately by calculating the percentage and quantity of patient demographic parameter data, such as patient characteristics including gender, age range, and secondary diagnosis, as well as patterns of use of unfractionated heparin and fondaparinux, including the name of the drug, dosage, frequency, method of administration, and duration of administration. The effectiveness of treatments with unfractionated heparin compared to fondaparinux against the incidence of recurrent myocardial infarction in patients was analyzed bivariately to determine whether or not there is a difference in outcome clinic between the uses of the two drugs if seen through clinical signs of the occurrence of a recurring myocardial infarct after the drug administration is discontinued. Clinical signs of recurrent myocardial infarction include chest pain that spreads to the left arm, neck, jaw, shoulder, or epigastrum and lasts more than 20 minutes; shortness of breath; and cold sweating after unfractionated heparin or fondaparinux administration is discontinued. Data processing was performed using comparative statistical analysis, using the chi-square test. Interpretation of the hypothesis test results is based on the p-value. If the interpretation results are $p<0.05$, a significant comparison was considered.

▪ RESULTS

Characteristic of patients

According to the results of this study, the majority of patients in the group using unfractionated heparin were male, namely 49 patients (77.78%), while in the fondaparinux group, there were 50 male patients (79.36%), with ages ranging from 46 to 65 years (29 patients, or 46.04%) for unfractionated heparin and (36 patients, or 57.14%) for fondaparinux. Patients in the unfractionated heparin group mostly had secondary cardiovascular diagnoses of atrial fibrillation and flutter (10 patients (6.76%)) and ventricular premature depolarization (10 patients (6.76%)), while patients in the fondaparinux group mostly had secondary cardiovascular diagnoses of essential (primary) hypertension, namely 13 patients (12.63%). Patients in the unfractionated heparin and fondaparinux user groups mostly had secondary non-cardiovascular diagnoses in the form of non-insulin-dependent diabetes mellitus without complications, namely 13 patients (8.78%) and 10 patients (9.71%). More complete patient characteristics in this study can be seen in Table 1.

Table 1. Characteristics of patients.

No	Characteristic	*Unfractionated Heparin* (n=63)	*Fondaparinux* (n=63)	Total (n=126)
		n (%)	n (%)	n (%)
1	Gender			
	Male	49 (77.78)	50 (79.36)	99 (78.57)
	Female	14 (22.22)	13 (20.64)	27 (21.43)
	Total	63 (100)	63 (100)	126 (100)
2	Age (y.o)			
	18-25	0 (0)	0 (0)	0 (0)
	26-45	6 (9.52)	9 (14.29)	15 (11.90)
	46-65	29 (46.04)	36 (57.14)	65 (51.59)
	>65	28 (44.44)	18 (28.57)	46 (36.51)
	Total	63 (100)	63 (100)	126 (100)
3	Secunder Cardiovasculer Diagnose			
	Essential (primary) hypertension (I10)	6 (4.05)	13 (12.63)	19 (7.57)
	Atrial fibrillation and flutter (I48)	10 (6.76)	6 (5.83)	16 (6.37)
	Ventricular premature depolarization (I49.3)	10 (6.76)	7 (6.79)	17 (6.77)
	Hyperlipidaemia, unspecified (E78.5)	5 (3.38)	10 (9.71)	15 (5.98)
	Congestive heart failure (I50.0)	8 (5.41)	6 (5.82)	14 (5.58)
	Others Diagnose*	29 (19.6)	27 (26.21)	56 (22.32)
	Non-cardiovascular			
	Non-insulin-dependent diabetes melitus: Without complications (E11.9)	13 (8.78)	10 (9.71)	23 (9.16)
	Unspecified kidney failure (N19)	13 (8.78)	0 (0)	13 (5.18)
	Dyspepsia (K30)	4 (2.70)	8 (7.77)	12 (4.78)
	Hyperkalaemia (E87.5)	9 (6,08)	2 (1.94)	11 (4.38)
	Urinary tract infection, site not specified (N39.0)	4 (2.70)	2 (1.94)	6 (2.39)
	Others Diagnose	37 (25)	12 (11.65)	49 (19.52)
	Cases Total	148 (58.96)	103 (41.04)	251 (100)

Profile of unfractionated heparin and fondaparinux use in patient

According to the results in Table 2, fondaparinux was administered subcutaneously at a dose of 2.5 mg every 24 hours to 63 patients (100%) for a duration of 5 days. In this study, patients receiving an intravenous bolus of 60 IU/kgBB (maximum 4000 IU) were followed by a maintenance dose of 12 IU/kgBB/hour intraveneous droplets (maximum 1000 IU per hour) for 5 days in 28 patients (44.44%) and 26 patients (41.27%) for 3 days.

Table 2. Using unfractionated heparin dan fondaparinux in AMI patients at Prof. Dr. Margono Hospital Period January 2019-December 2021.

No	Anticoagulan dose	Duration (days)	Frequency (n)	Percentage (%)
1	Fondaparinux subcutan 2.5 mg/ 24 hr	5	63	100
	Total		63	100
2	Unfractionated heparin			
	iv bolus 60 IU/kgBB (max 4000 IU) continued iv drip 12 IU/kgBB/hr (max 1000 IU/hr)	5	28	44.44
	iv drip 12 IU/kgBB/hr (max 1000 IU/hr)	5	26	41.27
	iv bolus 60 IU/kgBB (max 4000 IU) continued iv drip 12 IU/kgBB/hr (max 1000 IU/hr)	3	5	7.94
	iv drip 12 IU/kgBB/hr (max 1000 IU/hr)	3	4	6.35
	Total		63	100

Association of unfractionated heparin and fondaparinux use with recurrent myocardial infarction

Based on the data obtained in Table 3, the outcome clinic of therapy in patients receiving unfractionated heparin therapy included 36 patients (57.14%) having clinical signs of recurrent myocardial infarction, and 27 patients (42.86%) had no clinical evidence of recurrent myocardial infarction. Patients receiving fondaparinux therapy: 20 patients (31.75%) had clinical signs of recurrent myocardial infarction, and 43 patients (68.25%) did not have a clinical sign of recurrent myocardial infarction. Therefore, the results of the study showed that, based on the clinical signs of recurrent myocardial infarction, patients receiving fondaparinux had better clinical outcomes compared to those treated with unfractionated heparin, as clinical symptoms of recurrent myocardial infarction occurred less frequently in patients receiving fondaparinux, namely in 20 patients (31.75%) and 36 patients (57.14%). The p-value obtained from the results of statistical analysis with the Chi-square test in this study was 0,004 ($p<0.05$). Based on the Chi-square test results, there was a significant association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the incidence of recurrent myocardial infarction in patients with acute myocardial infarction.

Table 3. The association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the occurrence of recurrent myocardial infarction.

Anticoagulan	Effectiveness of the treatment		Total (n=63)	*p-value*
	Clinical indicators of recurrent MI episodes are present n (%)	Clinical indicators of recurrent MI episodes are absent n (%)	n (%)	
Unfractionated heparin	36 (57.14)	27 (42.86)	63 (100)	0.004
Fondaparinux	20 (31.75)	43 (68.25)	63 (100)	

▪ DISCUSSION

Characteristic of patients

The population of patients with ST-segment elevation myocardial infarction (STEMI) who used unfractionated heparin (UFH) or fondaparinux in this study was 332 patients. 81 patients were excluded because 59 patients died and 22 patients did not have complete medical record data, resulting in a sample size of 251 patients for this study. Out of the 251 patients, 188 used fondaparinux and 63 used UFH. Fondaparinux sampling was adjusted to the number of UFH patients using simple random sampling to avoid bias, resulting in a sample size of 63 patients for both UFH and fondaparinux. UFH as an anticoagulant can be given to patients with STEMI undergoing primary intervention coronary percutaneous reperfusion therapy or fibrinolytic therapy, while fondaparinux can be given to STEMI patients undergoing fibrinolytic therapy but was not recommended for patients with primary intervention coronary percutaneous [4]. Men are more likely than women to have an acute myocardial infarction. Because the hormone estrogen protects against the development of atherosclerosis, women encounter their first myocardial infarction nine years later than men. Women's risk of acute myocardial infarction can increase after menopause [12]. Increased risk factors such as smoking, associated diseases (hypertension and diabetes mellitus), and elder age can result in women having incidences of acute myocardial infarction similar to men [13]. Women who have a recent history of smoking and diabetes mellitus are more likely to have an acute myocardial infarction [14]; [15]. It was in accordance with previous research Khaznadar, A.A. J., et.al, (2020) which found that most heart disease patients were aged ≥ 45 years, and that patients receiving AMI-EST were predominantly between the ages of 41 and 65 [16]; [17]. The characteristics of a secondary diagnosis are divided into cardiovascular and non-cardiovascular disorders. A secondary diagnosis is an illness that occurs concurrently with hospitalization, develops later, influences treatment, or has been present for a long period. The study's results found 251 secondary diagnostic cases in 126 patients with acute myocardial infarction, which were classified as secondary cardiovascular and non-cardiovascular disorders. There were 148 cases (58.96%) of unfractionated heparin use, with the most common secondary diagnoses of cardiovascular disease being atrial fibrillation and flutter (I48) and ventricular premature depolarization (I49.3), which are estimated to be 10 cases each (6.76%).

According to Indonesian Heart Association [4], atrial fibrillation is a problem that affects 6-28% of IMA-EST patients and is frequently associated with significant left ventricular damage and cardiac failure.

According to several studies, the presence of atrial fibrillation during an acute myocardial infarction is a predictor of the cause of all deaths and is unrelated to treatment. Clinical signs of recurrent myocardial infarction include chest pain that spreads to the left arm, neck, jaw, shoulder, or epigastrum and lasts more than 20 minutes; shortness of breath; and cold sweating after unfractionated heparin or fondaparinux administration is discontinued.

Patients with atrial fibrillation had a significant risk of suffering from acute myocardial infarction, with an increased risk of acute myocardial infarction three times {18], [19]. In patients with atrial fibrillation, a rapid atrial rate is associated with increased thrombocyte activation and thrombus formation, which is a causative factor for acute myocardial infarction. The formed thrombus can block the coronary arteries so that the coronary blood flow decreases and the available oxygen supply cannot meet the oxygen needs of the myocardium [20]. Non-insulin-dependent diabetic mellitus without complications was the most common secondary diagnosis with the use of unfractionated heparin or fondaparinux, with thirteen incidents (8.78%) and ten incidents (9.71%), respectively.

Accordance Cui [21] and Einarson [22] reported that people with non-insulin-dependent diabetes mellitus (DMT2) had an increased risk of suffering acute myocardial infarction with a >40% recurrence. According to Rathore [23] patients with DMT2 showed higher cardiovascular morbidity and mortality, with acute myocardial infarction responsible for 75% of the deaths caused by coronary heart diseases. Diabetes increases the risk of an acute myocardial infarction through accelerated atherosclerosis improvement, affecting the levels of lipids, and speeding up the creation of atherosclerotic plaques. Furthermore, patients with diabetes have a higher risk of plaque rupture.

Profile of unfractionated heparin and fondaparinux use in patient

Use of IMA-EST treatment with anticoagulant drugs to avoid thrombosis and decrease reperfusion injury, which decreases hemorrhage in arterial blood vessels and cardiac veins [5], [27]. The analysis of typical usage of unfractionated heparin and fondaparinux aims to determine the dosage, route, intervals of administration, and duration that are commonly used in patients with acute myocardial infarction type acute transmural myocardial infarction of the anterior wall treated in hospital at RSUD Prof. Dr. Margono Soekarjo Purwokerto from January 2019 to December 2021.

According to the 2018 Guidelines for the Management of Acute Coronary Syndrome [4], the dose of fondaparinux for IMA-EST patients receiving fibrinolytic therapy is 2.5 mg subcutaneously administered once daily or every 24 hours for 5-8 days or until hospitalization. This is in accordance with research De Luca [10] where the dose of fondaparinux used for patients with acute myocardial infarction is 2.5 mg once a day by subcutaneous injection. The subcutaneous administration route of fondaparinux demonstrates rapid absorption with 100% bioavailability, so no monitoring is required for dose adjustment [25].

The rules for the use of unfractionated heparin (UFH) are based on the patient's body weight to determine the appropriate dose. The maintenance dose of unfractionated heparin is always adjusted by looking at the results of an aPTT examination to always reach the therapeutic range, which can be assisted with the use of nomograms. The aPTT value that meets the therapeutic range of unfractionated heparin is 1.5–2.5 times the control value already determined by each laboratory, or 50–70 seconds [4]. The normal value of APTT in Prof. Dr. Margono Soekarjo Hospital, Purwokerto margin, is 26.4–37.5 seconds, so the therapeutic range is 39.6–93.75 seconds.

The route of administration of unfractionated heparin is fully intravenously with a bolus interval of administration once a day on the first day of administration, while intravenous drops are given continuously and the infusion rate is adjusted every 6 hours. The duration of administration of unfractionated heparin in patients with acute myocardial infarction in RSUD Prof. Dr. Margono Soekarjo Purwokerto is 3-5 days. According to Indonesian Heart Association, unfractionated heparin is administered with an interval of once a day for at least 48 hours [4]. The European Society of Cardiology Guidelines recommend iv bolus doses for IMA patients of 60–70 IU/kg up to a maximum of 5000 IU, followed by infusions of 12–15 IU/kg/hour up to a maximum of 1000 IU [26]. According to the Guidelines for the Management of Acute Coronary Syndromes in Indonesia, the recommended dose is an iv bolus of 60 IU/kg (maximum 4000 IU), followed by an iv infusion of 12 IU/kg/hour. Unfractionated heparin infusion doses are regularly adjusted to maintain activated partial thromboplastin time (aPTT) while therapy reaches 1.5 to 2 times the normal range [4].

Intravenous bolus administration is not always given to all patients. In this study, only 33 of the 63 patients received intravenous boluses, while 30 patients only received intravenous drops without boluses. This was because in the administration of unfractionated heparin doses, it is necessary to look at the value of aPTT so that the dose is always within the therapeutic range. If the patient's aPTT results are in the sub-therapeutic range, then intravenous bolus administration of unfractionated heparin should be carried out to reach the therapeutic range as quickly as possible. that unfractified heparin can be administered without a bolus when patients' aPTP values are already in the therapy range. The administration of an unfractionated heparin bolus can speed up aPTT to reach the therapeutic range [27].

The association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the occurrence of recurrent myocardial infarction

Clinical signs of recurrent myocardial infarction include chest pain that spreads to the left arm, neck, jaw, shoulder, or epigastrum and lasts more than 20 minutes; shortness of breath; and cold sweating after unfractionated heparin or fondaparinux administration was discontinued. The Chi-square test was used to examine the association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the incidence of recurrent myocardial infarction. The analysis yielded a p-value of 0.004 ($p<0.05$), indicating a statistically significant association between the type of anticoagulant used and the occurrence of recurrent myocardial infarction in patients with acute myocardial infarction. These results indicate that the use of fondaparinux provides better effectiveness than unfractioned heparin when considering the incidence of recurrent myocardial infarction.

This research was accordance with De Luca [10] stated that the adverse cardiovascular incidence, including the incidence of recurrence myocardial infarction, associated with the use of unfractionated heparin was higher than that of fondaparinux, which was 65.9% and 35.8%, respectively. Recurrent myocardial infarction involves chest pain such as feeling depressed, spreading to the left arm, neck, jaw, shoulder, or epigastrum that persists for more than 20 minutes, shortness of breath, and cold sweat more than 24 hours and 5 days after treatment [28]. Fondaparinux provide higher effectiveness compared to heparin in reducing D-dimer levels, especially in patients with more severe coagulation ($p<0.005$) [29]. It was consistent with the mechanism of action of fondaparinux, which inhibits factor Xa in the blood coagulation cascade, making it more selective and effective in controlling coagulation [30]. In another study, it was shown that fondaparinux once daily has been proven to have better clinical benefits than LMWH (enoxaparin) twice daily in preventing VTE in COVID-19 patients [31].

▪ CONCLUSION

In this study, the effectiveness of using anticoagulant drugs in preventing recurrent myocardial infarctions, was based only on anticoagulant drugs alone. There was a significant association between the type of anticoagulant therapy (unfractionated heparin or fondaparinux) and the incidence of recurrent myocardial infarction in patients with acute myocardial infarction ($p<0.05$). These results indicate that the use of fondaparinux provides better clinical outcomes than unfractioned heparin when considering the incidence of recurrent myocardial infarction. Further research needs to be carried out regarding monitoring the effectiveness of therapy for the incidence of recurrent myocardial infarction in patients by looking at overall drug use and by looking at objective data related to symptoms and signs of recurrent myocardial infarction.

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