JMU
Jurnal Medika Udayana

ISSN: 2597-8012 JURNAL MEDIKA UDAYANA, VOL. 15 NO.1, JANUARI, 2026

Received: 2025-10-28 Revision: 2025-11-25 Accepted: 30-12-2025

USE OF ANTICOAGULANTS IN COVID-19 PATIENTS AS A PREVENTIVE EFFORT FOR HEART FAILURE MORTALITY

I Putu Dharma Yuda[1], I Made Putra Swi Antara[2], Luh Oliva Saraswati Suastika[2], Cyndiana Widia Dewi Sinardja[2]
[1]Medical Student, Faculty of Medicine, Udayana University
[2]Department of Cardiology, Faculty of Medicine, Udayana University
e-mail : dharmayuda2041@gmail.com

ABSTRACT

Background: Thrombosis and hypercoagulable states are complications that can arise in COVID-19 and heart failure patients. This occurs due to a cytokine reaction, leading to the activation and increase of coagulation factors. This condition can lead to complications such as DVT, VTE, and PE, which will increase the severity and mortality of the patient's disease. Anticoagulants are one of the effective therapies to prevent and treat various types of thromboembolic diseases. Heparin and enoxaparin are commonly used anticoagulants in hospitals.
Objective: This study aimed to determine whether the use of anticoagulants was associated with the mortality rate in COVID-19 patients diagnosed with heart failure.
Methods: This study was conducted using a cross-sectional analytic design. The sample consisted of 71 patients, including 51 who used enoxaparin, 15 who used heparin, and 5 who used a combination of both. After the data was obtained, it was then processed and presented in tabular form.
Results: While initial findings suggested that enoxaparin use was associated with lower mortality rates compared to heparin or a combination of both, subsequent analysis revealed no statistically significant difference in mortality rates among patients receiving enoxaparin, heparin, or a combination (p-value = 0,191).
Conclusion: There was no significant difference in mortality rates between patients given enoxaparin, heparin, or a combination.
Keywords : anticoagulant, heparin, enoxaparin, COVID-19, heart failure, mortality

INTRODUCTION

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. This virus originated in China and spread rapidly to various countries and on March 2, 2020 it spread throughout Indonesia [1]. Data from WHO on April 29, 2022 showed that there were 6,049,876 established cases and 156,438 deaths due to COVID-19 in Indonesia. Based on the Our World in Data report, the death rate in Indonesia until March 17, 2022 reached 2.58%, placing Indonesia in the second highest rank in Southeast Asia.[1,2]

COVID-19 depending on its severity has various clinical symptoms. Confirmed cases are categorized into several groups. The first group includes individuals who test positive for COVID-19 nucleic acid but show no symptoms, clinical signs, or abnormalities in chest imaging. The second group consists of patients with mild symptoms, such as signs of acute upper respiratory tract infection or gastrointestinal issues. The next category involves moderate pneumonia, characterized by frequent fever and coughing, but without noticeable hypoxemia, and chest CT scans showing lesions. More severe cases include those with pneumonia accompanied by hypoxemia (SpO2 <92%) and critical conditions such as acute respiratory distress syndrome (ARDS), which may lead to complications. Although SARS-CoV-2 attacks the lungs, damage to the vascular endothelium has been found in other organs. One of these complications is heart failure.[3]

Heart failure is a pathological condition characterized by the inability of the heart to pump blood to meet the metabolic needs of the tissue.[4] One study by Zhou et al. found that as many as 23% of COVID-19 patients had complications of heart failure.[5] This high prevalence is partly due to the release of cytokines that cause endothelial dysfunction and the formation of microthrombi that can damage the endocardium. In addition to being a complication, heart failure can also be a condition that already exists before the patient is infected with SARS-CoV-2. In a study by Bashir et al., as many as 4.9% to 13% of COVID-19 patients heart failure. Patients with heart failure comorbid tend to have a poor prognosis and a higher risk of death than patients without comorbid heart failure.[6]

Thromboembolic event such as VTE, DVT, and PE are complications that occur in COVID-19 patients and heart failure patients. Based on the results of a study by Cheng et al., among COVID-19 patients treated in intensive care units, the incidence of thromboembolic complications was reported to be as high as 69%.[7] Meanwhile, in the study by

Xu et al. the incidence of VTE and PE 1.57 and 2 times higher in patients with heart failure than in patients without heart failure. This increased risk can be attributed to several mechanisms, such as blood stasis due to enlargement of the heart chamber, decreased myocardial contractility, increased plasma viscosity and coagulability, and endothelial.[8]

Based on guidelines from the International Society on Thrombosis and Hemostasis (ISTH) and the National Institutes of Health (NIH), the use of anticoagulants is recommend for most hospitalized COVID-19 patients unless they have contraindications. Anticoagulants are a type of drug used to reduce the risk of blood clots. Blood clots are masses formed from platelets and fibrin to stop bleeding. This drug works by preventing or destroying blood clots in the blood vessels.[9] This therapy is useful for preventing thromboembolic complications, improving patient prognosis, reducing the risk of intensive care, and reducing mortality.[10] Some anticoagulants that are often used are Low Molecular Weight Heparin (LMWH) such as enoxaparin and Unfractionated Heparin (UFH) such as heparin.[11]

Enoxaparin and heparin are anticoagulants that work through antithrombin activity. The difference between the two anticoagulants is the ability to inhibit factor Xa and thrombin, size and structure, and the location of their elimination. The enoxaparin complex binds factor Xa and catalyzes its inactivation so that enoxaparin shows higher activity against factor Xa and Factor IIa. Not only that, enoxaparin also binds less to platelets and has a weaker affinity for endothelial cells and von Willebrand factor. Therefore, enoxaparin has fewer bleeding complications than heparin.[12] Enoxaparin also has smaller structure and lower molecular weight than heparin. This small structure cause enoxaparin to have higher bioavailability, longer half-life, and better access to cell receptors.[13] Although enoxaparin has a lower risk of bleeding and superior efficacy, heparin is the main choice for patients with chronic kidney disease (CKD). This because heparin has higher efficacy and safety because it will be metabolized and eliminated by the liver. Meanwhile, enoxaparin requires dose adjustment when given to patients with CKD because it is eliminated through the kidneys.[14]

MATERIALS AND METHODS

This research employs an observational study design with an analytical cross-sectional approach. The samples were obtained through total sampling of medical records from inpatient COVID-19 patients diagnosed with heart failure at Prof. Dr. IGNG Ngoerah Hospital during the 2021–2022 period. The study was carried out from April 2024 to December 2024 and received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Udayana University, under protocol number 2024.01.1.0113. Data collected were reviewed for completeness and assessed based on inclusion and exclusion criteria. Subsequently, the data were processed using the SPSS software for analysis. The statistical method applied was the chi-square test, with results presented in crosstab format.

RESULTS

Based on the inclusion and exclusion criteria there are 71 samples. The sample characteristics will be presented in Table 1.

Table 1. Characteristics of the Samples

Patient Characteristic	Total (%)
Gender	
Male	43 (60,56%)
Female	28 (39,44%)
Age Group	
<40 years	5 (7,04%)
40-49 years	6 (8,45%)
50-59 years	14 (19.72%)
60-69 years	22 (30.99%)
>70 years	24 (33.80%)
Length Of Stay	
≥ 10 days	33 (46,48)
< 10 days	38 (53,52)
COVID-19 Severity	
Severe symptom	62 (87,32%)
Moderate symptom	9 (12,68%)
Comorbid	
Hypertension	42 (59,15%)
Diabetes mellitus	25 (35,21%)

Anemia	7 (9,86%)
Obesity type I	17 (23,94%)
Obesity type II	4 (5,63%)
CAD	27 (38,03%)
Atrial fibrillation	16 (22,53%)
Atrial flutter	1 (1,4%)
STEMI	4 (5,63%)
NSTEMI	3 (4,22%)
Myocardial infarct	1 (1,4%)
COPD	5 (7.04%)
Asthma	2 (2,81%)
CKD	29 (40,84%)
Outcome	
Survivor	33 (46,5%)
Non survivor	38 (53,5%)
Cause Of Death	
ARDS	15 (21,12%)
Pneumonia	3 (4,22%)
Cardiogenic shock	6 (8,45%)
Sepsis shock	10 (14,09%)
Pulmonary embolism	2 (2,81%)
Cardiac arrest	2 (2,81%)

From Table 2, there was no significant relationship between the type of anticoagulant and the mortality rate of the sample with p-value = 0.191. It was also found that the mortality rate of patients given anticoagulants in the form of enoxaparin (n = 24, 47.1%) was lower than the mortality rate of patients given heparin (n = 10, 66.7%) or patients given enoxaparin and heparin (n = 4, 80%).

Table 2. Effects of the Type of Anticoagulant to the Mortality Rate

Type of Anticoagulant	Outcome		Total	p
	Survivor	Non-Survivor		
	People (%)	People (%)		
Heparin	5 (33,3%)	10 (66,7%)	15 (100%)	0,191
Enoxaparin	27 (52,9%)	24 (47,1%)	51 (100%)	
Enoxaparin + Heparin	1 (20%)	4 (80%)	5 (100%)	
Total	33 (46,5%)	38 (53,5%)	71 (100%)	

DISCUSSION

One of the main mechanisms that worsens the condition of COVID-19 patients is the formation of blood clots or thrombosis. This virus triggers an excessive inflammatory response in the body, which can damage blood vessels and disrupt the blood clotting system. This response can increase blood clotting factors, such as factor VIII and von Willebrand, as well as damage to the endothelial lining that worsen this condition. Blood clots have the potential to lead to a range of severe complications, including stroke, heart attacks, ischemia, DVT, or PE.[7] Research by Nahum et al., revealed that individuals with COVID-19 undergoing treatment in intensive care units faced an elevated risk of developing thrombotic events, reaching as high as 69%.[15]

In addition to COVID-19, patients with heart failure also have a high risk of thrombosis. A study conducted at the San Paolo Heart Institute during the period 2000 to 2006, found that around 39% of patients in the study experienced thromboembolism, and in most cases, thromboembolism was the main cause or one of the risk factors for death. The most common type of blood clot found was pulmonary embolism, which occurred in around 23% of all cases of death from heart failure in the study. The researchers suspect that one of the reasons why patients with heart failure are more susceptible to blood clots is because of the much higher production of tissue factor than healthy people when examined.[16]

Anticoagulants are one of the main therapies for treating various types of thromboembolic diseases. In a study by Hi et al., patients who did not receive anticoagulant therapy experienced a 4.2 times higher mortality rate compared to those who did. This indicates that administering anticoagulants to COVID-19 patients with cardiovascular conditions can help minimize thromboembolic complications and reduce patient mortality.[17]

In Table 2, there was no significant relationship between the type of anticoagulant and the mortality rate of hospitalized COVID-19 patients who had been diagnosed with heart failure and received anticoagulants at Prof. Dr. IGNG Ngoerah Hospital in the period 2021-2022 with a p-value = 0.191. This is different from the research conducted by Pawlowski et al. and Rosnarita et al. which states that the difference in the administration of anticoagulant types in the form of heparin or enoxaparin in COVID-19 patients has a significant relationship in reducing patient mortality. The difference due to the high mortality rate in the sample. This high mortality rate cause by many factors such as gender, age, and comorbidities.[18,19]

Research conducted by Ningrum & Syahrizal et al., elderly patients has higher risk of mortality compared to younger individuals. With advancing age, the immune system's response becomes less effective making individuals more vulnerable to COVID-19 infection and associated complications, including ARDS and an increased likelihood of fatal outcomes.[20]

Research conducted by Ningrum & Syahrizal et al., proportion of male COVID-19 patients (57.5%) was greater than the proportion of female patients (42.5%).[20] This result also simillar to Liu et al. where male patients have a higher disease severity, ICU admission, mortality, and morbidity than female patients. The mechanism underlying this difference in prevalence is thought to be related to higher expression of the ACE2 enzyme in male individuals, which is the main receptor for the SARS-CoV-2 virus.[21] Men are also more susceptible to cardiovascular disease due to unhealthy lifestyles, such as smoking and alcohol. Meanwhile, women have the hormone estrogen which can protect and prevent the risk of atherosclerosis by increasing the high-density lipoprotein ratio.[22]

In the study by Suryaputra et al., significant relationship found between the mortality rate and comorbidities in COVID-19 patients. The mortality of patients with comorbidities (76.9%) was higher than the mortality of patients without comorbidities (23.1%).[23] This study supported by other literature stating that comorbidities such as hypertension, DM, obesity, cardiovascular disease, and kidney disease are associated with poor prognosis and death in COVID-19 patients.[5]

In COVID-19 patients, comorbid hypertension can increase patient mortality. In China, 23% of hypertension cases with COVID-19 were reported to have a CFR of 6%.[24] In research carried out by Abdillah et al., COVID-19 patients with comorbid hypertension were 5.23 times more at risk of dying than COVID-19 patients without comorbid hypertension.[25]

In COVID-19 patients, comorbid diabetes can increase patient mortality. 11–58% of all COVID-19 patients suffer from diabetes with a mortality rate of 8%.[24] In a study conducted by Abdillah et al., diabetes mellitus increased the risk of mortality by 18.30 times compared to patients without diabetes mellitus in COVID-19 patients.[25]

Research carried out by Mahamat-Saleh et al. revealed a 12% higher mortality rate among COVID-19 patients with a BMI of 30 kg/m² or higher compared to those with a BMI below 30 kg/m². Additionally, patients with a BMI between 40 and 45 kg/m² were found to have a mortality rate 1.5 to 2 times higher than those with a BMI in the range of 22 to 24 kg/m².[26]

Study conducted by Dan et al., revealed a link between increased troponin levels and the severity as well as mortality in patients with cardiovascular conditions. Among 187 COVID-19 patients studied, 35% had a prior history of cardiovascular disease, and 28% of them showed elevated troponin levels. The mortality rates were 7.6% for patients without cardiovascular disease and normal troponin levels, 13.3% for those with cardiovascular disease but normal troponin levels, 37.5% for patients with elevated troponin but no cardiovascular disease, and 69.4% for those with both cardiovascular disease and elevated troponin levels.[27]

Research conducted by Wang et al., COVID-19 patients with acute kidney injury had a 5.3 times higher mortality risk than COVID-19 patients without acute kidney injury.[29] Meanwhile, another research condected by Hakami et al. showed that acute kidney injury increased the risk of mortality and a worse prognosis by 3.6-6.8 times compared to patients without acute kidney injury in COVID-19 patients.[29,30]

From table 2 we also found that the mortality rate of patients given anticoagulants in the form of enoxaparin (n = 24, 47.1%) was lower than the mortality rate of patients given heparin (n = 10, 66.7%) or patients given enoxaparin and heparin (n = 4, 80%). This in line with study conducted by Pawlowski et al. and Rosnarita et al. which stated that enoxaparin has a lower incidence of death than heparin in COVID-19 patients. From this study, 38 (29.9%) of 127

COVID-19 patients died while receiving COVID-19 treatment with 54.5% of patients dying in the heparin group and 8% in the enoxaparin group. The low mortality in patients given enoxaparin is related to several factors such as the higher effectiveness of enoxaparin, the lower risk of heparin-induced thrombocytopenia (HIT) in patients given enoxaparin, and the choice of anticoagulant.[18,19]

Research conducted by AlLehaibi et al., patients given enoxaparin had a 53% lower risk of pulmonary embolism compared to those given heparin. The researchers suspect that this effectiveness is related to the weight and structure of the molecule. Heparin has a large structure with an average molecular weight of 15 to 19 kDa while enoxaparin has a smaller structure with a molecular weight of 3.0 to 6.5 kDa. The smaller structure cause enoxaparin to have higher bioavailability, longer half-life, and better access to cell receptors, thus having better anti-inflammatory effects.[13]

One contributing factor to the elevated mortality rate among patients receiving heparin is the occurrence of HIT. Research has shown that HIT is less commonly observed in patients treated with enoxaparin compared to those treated with heparin. In a researcj conducted by Junqueira et al., the risk of HIT was 22 cases per 1000 patients for those administered unfractionated heparin (UFH), whereas it dropped to 5 cases per 1000 patients for those receiving enoxaparin.[31,32]

Another contributing factor that can cause higher mortality rates among patients receiving heparin is the presence of comorbid kidney disease. Heparin is often the preferred parenteral anticoagulant for individuals with CKD due to its superior safety and efficacy profile. In contrast, enoxaparin requires careful dose adjustments in CKD patients. This is because heparin is metabolized by the liver, eliminating the need for dose modifications in advanced CKD stages (stages four and five). Conversely, low molecular weight heparin (LMWH) like enoxaparin is primarily cleared by the kidneys, and failure to adjust the dose can result in prolonged drug half-life, increased systemic exposure, and heightened bleeding risk. As a result, unfractionated heparin (UFH) is typically used for patients with significantly reduced creatinine clearance or advanced CKD. This may explain the elevated mortality rates observed in patients receiving a combination of heparin and enoxaparin as anticoagulant therapy.[14]

In addition to the factors that can influence mortality, there are other factors that do not contribute to differences in mortality between the use of heparin and enoxaparin. These include the effectiveness in reducing D-dimer levels and the bleeding risk associated with each anticoagulant. According to research from Rosnarita et al., there was no significant difference between the decrease in D-dimer with the administration of enoxaparin and heparin anticoagulants with an average decrease in heparin of 552.8 ng/mL in the heparin group and 622.6 ng/mL in the enoxaparin group with a p-value = 0.444. from this study, it was found that the use of enoxaparin or heparin as a treatment was equally effective in reducing D-dimer values in COVID-19 patients. Another study from Rosnarita et al. found no significant difference in the risk of bleeding, the risk of major or minor bleeding. As many as 36.2% of the 127 samples in this study experienced bleeding events due to the use of prophylactic anticoagulants. The highest number of bleedings occurred in the heparin group, which was 40% of the total patients receiving heparin (22 cases of bleeding from 55 samples), while in the enoxaparin group the incidence of bleeding was 33.3% (24 cases from 72 samples) the data was then analyzed and obtained a p value = 0.372. from this study it was found that the use of enoxaparin or heparin had the same risk of bleeding.[19]

This study has limitations in terms of the number of sample data which is quite small, especially in samples given heparin anticoagulant which amounted to 15 samples and those given a combination of heparin and enoxaparin anticoagulant which amounted to 5 samples. The small amount of data can produce false results and cause bias. In addition, there are other factors that can cause bias such as factors that increase mortality such as age and comorbidities, and also other factors such as CrCl value and CKD stage which influence the choice of anticoagulant used.

CONCLUSION AND RECOMMEDATION

Based on the result there was no significant mortality difference between the use of enoxaparin, heparin and the combination of heparin and enoxaparin in hospitalized COVID-19 patients who had been diagnosed with heart failure and received anticoagulants at Prof. dr. IGNG Ngoerah Hospital in the period 2021-2022. These results are different from other studies, this difference can be caused by factors that increase mortality such as age, gender, and comorbidities.

In future studies, it is recommended to increase the sample size and select patients with fewer comorbidities or patients with chronic kidney disease at more consistent stages. This approach is expected to enhance the accuracy and reliability of the research findings.

REFERENCES

1. Menteri Kesehatan RI. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MenKes/413/2020 Tentang Pedoman Pencegahan dan Pengendalian Corona Virus Disease 2019 (Covid-19). *MenKes/413/2020*. 2020;2019:207.
2. WHO. WHO Coronavirus Disease (COVID-19) Dashboard. Published 2022. Accessed May 14, 2022. https://covid19.who.int/
3. Natalie VP, Lay DS, Sitanggang FP, Srie N, Laksminingsih, Martadiani ED. HUBUNGAN ANTARA HIPERTENSI DENGAN KEJADIAN

COVID-19 YANG BERGEJALA DI RSUP SANGLAH TAHUN 2020. *E-Jurnal Med*. 2023;12(2):51-56.
4. Nurkhalis, Adista RJ. Manifestasi Klinis dan Tatalaksana Gagal Jantung. *J Kedokt Nanggroe Med*. 2020;3(3):36-46.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3
6. Bashir H, Yildiz M, Cafardi J, Bhatia A. A Review of Heart Failure in Patients with COVID - 19. 2020;(January).
7. Cheng NM, Chan YC, Cheng SW. COVID-19 related thrombosis: A mini-review. *Phlebology*. 2022;37(5):326-337. doi:10.1177/02683555211052170
8. Xu T, Huang Y, Liu Z, et al. Heart failure is associated with increased risk of long-term venous thromboembolism. *Korean Circ J*. 2021;51(9):766-780. doi:10.4070/KCJ.2021.0213
9. Devi GAPGL, Aryabiantara W, Hartawan IU. Profil Penggunaan Antikoagulan Pada Pasien Kardiovaskular Yang Dirawat Di Ruang Iccu Rsup Sanglah Periode Januari 2016 - Juni 2016. *E-Jurnal Med*. 2018;7(10):1-11.
10. Putra BDP, Suprapti B, Sari ADP, Sundari M. Profil Penggunaan Antikoagulan Pada Pasien Covid-19 Di Irna Fatmawati Rsud Dr M Yunus Bengkulu. *J Media Kesehat*. 2022;15(1):54-63. doi:10.33088/jmk.v15i1.741
11. Pratiwi ADE, Adhityasmara D. Gambaran Penggunaan Antikoagulan Pada Pasien Covid-19 Di Salah Satu Rumah Sakit Rujukan Covid-19 Di Kota Semarang. *Sebatik*. 2021;25(2):442-448. doi:10.46984/sebatik.v25i2.1619
12. Megasafitri D, Wiargitha, Maliawan S. Low-Molecular Weight Heparin (Lmwh) Sebagai Profilaksis Deep Vein Thrombosis (Dvt) Pada Pasien Trauma. *E-Jurnal Med*. 2017;1(1):1-19.
13. AlLehaibi LH, Alomar M, Almulhim A, et al. Effectiveness and Safety of Enoxaparin Versus Unfractionated Heparin as Thromboprophylaxis in Hospitalized COVID-19 Patients: Real-World Evidence. *Ann Pharmacother*. 2023;57(4):361-374. doi:10.1177/10600280221115299
14. Erlanda W, Karani Y. Penggunaan Antikoagulan Pada Penyakit Ginjal Kronik. *J Kesehat Andalas*. 2018;7(Supplement 2):168. doi:10.25077/jka.v7i0.845
15. Nahum J, Morichau-Beauchant T, Daviaud F, et al. Venous Thrombosis Among Critically Ill Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Netw open*. 2020;3(5):e2010478. doi:10.1001/jamanetworkopen.2020.10478
16. Goldhaber SZ. Venous Thromboembolism in Heart Failure Patients: Pathophysiology, Predictability, Prevention. *J Am Coll Cardiol*. 2020;75(2):159-162. doi:10.1016/j.jacc.2019.11.028
17. Hi RA, Febri A, Andriani F. Profil Penggunaan Antikoagulan pada Pasien COVID-19 dengan Komorbid Hipertensi di Rawat Inap RSUD Panembahan Bantul Yogyakarta. *Lumbung Farm J Ilmu Kefarmasian*. 2023;4(1):141-148.
18. Pawlowski C, Venkatakrishnan AJ, Kirkup C, et al. EClinicalMedicine Enoxaparin is associated with lower rates of mortality than unfractionated Heparin in hospitalized COVID-19 patients. *EClinicalMedicine*. 2021;33:100774. doi:10.1016/j.eclinm.2021.100774
19. Rosnarita IA, Zaimatuddunia I, Yasin NM, Ikawati Z. Evaluasi Penggunaan Heparin dan Enoxaparin Sebagai Antikoagulan Profilaksis pada Pasien COVID-19. *Maj Farm*. 2023;19(4):2023.
20. Ningrum RI, Syahrizal. The Indonesian Journal of Health Promotion MPPKI Media Publikasi Promosi Kesehatan Indonesia Hubungan Usia dan Jenis Kelamin terhadap Kematian Covid-19 di Kota Depok. *Indones J Heal Promot*. 2023;6(2):267-271. https://doi.org/10.31934/mppki.v2i3
21. Qian Z, Lu S, Luo X, Chen Y, Liu L. Mortality and Clinical Interventions in Critically ill Patient With Coronavirus Disease 2019: A Systematic Review and Meta-Analysis. *Front Med*. 2021;8(July):1-15. doi:10.3389/fmed.2021.635560
22. Priandani, Hendra, Kusumajaya, Permatasari. I. Faktor-Faktor Yang Berhubungan Dengan Kejadian Congestive Heart Failure (Chf) Pasien. *J Penelit Perawat Prof*. 2022;4(November):1377-1386.
23. Suryaputra GP, Apriningsih H, Wardani MM. Hubungan Komorbid dengan Mortalitas dan Lama Rawat Inap pada Pasien COVID-19 di Rumah Sakit UNS Surakarta. *Plex Med J*. 2022;1(1):32-41. doi:10.20961/plexus.v1i1.20
24. Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . 2020;(January).
25. Abdillah MN, Rauf NI, Andi Muhammad Ardan, Nur Hamdani Nur, Darwin Safiu. Analisis Faktor Risiko Kematian Pasien Covid-19 di RSUD Sayang Rakyat Kota Makassar. *Media Publ Promosi Kesehat Indones*. 2023;6(1):130-136. doi:10.56338/mppki.v6i1.2966
26. Mahamat-Saleh Y, Fiolet T, Rebeaud ME, et al. Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: A systematic

review and meta-analysis of observational studies. *BMJ Open*. 2021;11(10). doi:10.1136/bmjopen-2021-052777

27. Dan S, Pant M, Upadhyay SK. The Case Fatality Rate in COVID-19 Patients With Cardiovascular Disease: Global Health Challenge and Paradigm in the Current Pandemic. *Curr Pharmacol Reports*. 2020;6(6):315-324. doi:10.1007/s40495-020-00239-0
28. Wang L, Li X, Chen H, et al. Coronavirus disease 19 infection does not result in acute kidney injury: An analysis of 116 hospitalized patients from Wuhan, China. *Am J Nephrol*. 2020;51(5):343-348. doi:10.1159/000507471
29. Upadhana PS, Sastrawan IGGS, Cahyarini IGAAC, et al. Kidney disease and Its Impact on COVID-19 Patients at Sanglah Hospital Denpasar , Bali , Indonesia in 2021. *Intern Med Commons*. 2022;9(1):23-27.
30. Hakami A, Badedi M, Elsiddig M, et al. Clinical characteristics and early outcomes of hospitalized COVID-19 patients with end-stage kidney disease in Saudi Arabia. *Int J Gen Med*. 2021;14(June):4837-4845. doi:10.2147/IJGM.S327186
31. Junqueira DR, Zorzela LM, Perini E. Unfractionated heparin versus low molecular weight heparins for avoiding heparin-induced thrombocytopenia in postoperative patients. *Cochrane Database Syst Rev*. 2017;2017(4). doi:10.1002/14651858.CD007557.pub3
32. Hogan M, Berger JS. Heparin-induced thrombocytopenia (HIT): Review of incidence, diagnosis, and management. *Vasc Med (United Kingdom)*. 2020;25(2):160-173. doi:10.1177/1358863X19898253