KESANS: International Journal of Health and Science
2808-7178 / 2808-7380
http://kesans.rifainstitute.com/index.php/kesans/index

Analysis of the Risk of Kidney Dysfunction due to Heparin vs Clopidogrel Therapy in Vascular Thrombosis Patients: A Retrospective Study

Andi Maulana Kamri*, Sukmawati, Serly Avifa
Faculty of Pharmacy, Universitas Muslim Indonesia, Indonesia
maulana.lolo@umi.ac.id

Article Information
Submitted: **22 June 2025**
Accepted: **15 July 2025**
Publish: **10 August 2025**

Keyword: Anticoagulant; Clopidogrel; Heparin; Vascular Disease; Renal;

Abstract
Introduction*: The repeated use of anticoagulants like heparin and antiplatelets such as clopidogrel in individuals with vascular thrombosis necessitates an evaluation of the nephrotoxicity risk.* ***Objective****: This study seeks to assess the impacts of heparin and clopidogrel on renal function.* ***Method****: This cohort retrospective design examined data from 120 individuals with vascular thrombosis who were administered heparin (n=60) or clopidogrel (n=60). Renal parameters (serum creatinine, eGFR) were evaluated prior to and following therapy. The statistical analysis employed a paired t-test and multivariate logistic regression, utilising a 95% confidence interval.* ***Results and Discussion:*** *The heparin cohort had a notable elevation in serum creatinine (1.8±0.4 vs 1.2±0.3 mg/dL; p=0.02) and a reduction in eGFR (45±12 vs 68±15 mL/min/1.73m²; p=0.01) in comparison to the clopidogrel group. Therapy exceeding 7 days elevated the incidence of renal impairment by 2.3-fold (OR: 2.3; 95% CI: 1.4-3.8) in the heparin cohort. The nephrotoxic impact of heparin is much greater in patients with cardiovascular comorbidities (p=0.04).* ***Conclusion****: Heparin presents a greater risk of inducing renal dysfunction than clopidogrel, particularly with prolonged usage and in individuals with concomitant conditions. Rigorous oversight of renal function and evaluation of alternate treatments are advised.*

How to Cite **Andi Maulana Kamri, Sukmawati, Serly Avifa/Analysis of the Risk of Kidney Dysfunction due to Heparin vs Clopidogrel Therapy in Vascular Thrombosis Patients: A Retrospective Study, Vol. 4, No. 11, 2025**
DOI https://doi.org/10.54543/kesans.v4i11.390
e-ISSN/p-ISSN **2808-7178 / 2808-7380**
Published by **CV Rifainstitut/KESANS: International Journal of Health and Science**

Introduction

Vascular disorders continue to pose a health challenge worldwide and in Indonesia. According to data from the World Health Organisation about 17 million individuals succumb to heart and vascular disorders (Saputro, Ajie, Azizah, & Hartanti, 2023). Data from the 2018 Basic Health Research indicates a yearly rise in the incidence of cardiovascular disorders. Approximately 15 per 1000 individuals, equating to around 2,784,064 people in Indonesia, are afflicted with vascular illnesses (Mukahar & Sulistyanto, 2022). This disease also impacts several individuals within the working-age demographic. This imposes a social and economic burden on society (Widiastuti, Cholidah, Buanayuda, & Alit, 2021).

Vascular disease is a progressive inflammatory condition that leads to endothelial dysfunction, atherosclerotic plaque development, and blockage or disruption of the vascular endothelial matrix. Vascular disease is a gradually progressing inflammatory disorder induced by an unhealthy lifestyle, including smoking, elevated cholesterol, and hypertension, which causes damage to blood vessels and plaque accumulation, ultimately culminating in rupture. Vascular disease is characterised by the impairment of the heart and blood arteries (Widiastuti *et al*., 2021)

Chronic kidney failure is a condition resulting from vascular disease. This disease results in a steady deterioration of kidney function and the formation of scar tissue, which reduces blood flow to the kidneys, glomerular filtration rate, and creatinine levels (Rohmawati, Ekayamti, & Komalawati, 2022); (Wijaya, Achwandi, & JP, 2023). Chronic kidney disease commences as a progressive renal condition persisting for over three months. It initially assaults the glomeruli and renal tubules, consequently impairing blood circulation leading to a reduction in the quantity of functional nephrons (Rahmawati, 2018); (Sa'diyah, Rahmawati, & Windartik, 2022); (Sari, Fadilla, Indriansyah, & Arini, 2025). The metric for assessing kidney problems is the Glomerular Filtration Rate (GFR), which evaluates the degree of kidney damage as it represents the first phase of nephron function. A GFR value of <60 ml/min/1.72 m^2 for three months or more signifies chronic renal disease. In addition to GFR, creatinine can also function as an indicator of renal diseases (Rahmawati, 2018).

Numerous studies assessing the use of anticoagulants and antiplatelet medicines have been undertaken in several countries, including Indonesia (Semakula *et al*., 2020); (Sagita & Sukmadryani, 2024); (Sawu & Indriyani, 2024). Nonetheless, these investigations have predominantly concentrated on dosage assessment for the regulation of the International Normalised Ratio (INR), whereas the research conducted in Indonesia encompassed a limited patient population. Research on the renal safety associated with this medicine, including correlations with clinical symptoms and laboratory assessments, remains insufficient. Consequently, it is essential to delineate the appropriate application of anticoagulants and antiplatelet agents while mitigating the risk of renal impairment, particularly in patients with vascular conditions who require prolonged or lifelong administration of both medication classes. Despite the prevalent usage of this treatment among patients with vascular disorders, research about its safety remains insufficient, particularly in South Sulawesi, which exhibits a high incidence of vascular diseases and the utilisation of anticoagulants and antiplatelet medications. This comparison study can effectively ascertain the safety of anticoagulant treatment by evaluating the incidence of renal side effects in vascular disease patients in Makassar.

Method

This study employs a cohort research design with multicenter research, utilising a retrospective data gathering method and a purposive sampling strategy. This study utilised 102 samples. The study was carried out from September 2023 to April 2024 at Rumah Sakit Ibnu Sina Yayasan Wakaf Universitas Muslim Indonesia, Jalan Urip Sumoharjo, Kecamatan Panakkukang, Kabupaten Kota Makassar, Provinsi Sulawesi Selatan, and Rumah Sakit Umum Daerah Labuang Baji, Jalan DR. Ratulangi, Kecamatan Mamajang, Kabupaten Kota Makassar, Provinsi Sulawesi Selatan, with data collection occurring from January 2023 to December 2023.

The study population comprises patients with vascular illnesses classified as stroke, hypertension, diabetes mellitus, atherosclerosis, and congestive heart disease, who commenced treatment with anticoagulants or antiplatelet agents. The Inclusion Criteria pertain to patients aged 18 years and older with vascular disorders, including stroke, diabetes mellitus, atherosclerosis, hypertension, and congestive heart disease, who have commenced anticoagulant and/or antiplatelet therapy, as well as those with complete blood test results, specifically Glomerular Filtration Rate (GFR) and Serum Creatinine. The Exclusion Criteria for this study encompass people with vascular problems possessing incomplete medical records, individuals using chemotherapy, and those with end-stage renal disease or kidney transplants. Statistical data analysis was performed utilising bivariate and multivariate methods to assess the relevance of variables, facilitating a comparison between the two tested medications.

Result and Discussion

1. Result

The administration of antithrombotic medicines, including heparin and clopidogrel, is crucial in the management of vascular thrombosis to avert life-threatening consequences. Nonetheless, their possible nephrotoxic consequences continue to be a significant issue in clinical practice. This retrospective study sought to evaluate and compare the risk of renal impairment linked to heparin versus clopidogrel treatment in patients with vascular thrombosis. This study assesses renal indicators, such as serum creatinine, estimated glomerular filtration rate (eGFR), and the occurrence of acute kidney injury (AKI), to elucidate the renal safety profiles of these two commonly utilised medications. The results underscore notable disparities in nephrotoxicity risk, providing essential insights for refining treatment approaches in high-risk individuals.

Table 1
Descriptive Analysis of Dependent Variables of Research Subject Characteristics

Characteristics	Quantity	
	Anticoagulant Heparin n = 31 (%)	**Antiplatelet Clopidogrel n = 71 (%)**
Gender		
Man	16 (51.6)	45 (63.4)
Woman	15 (48.4)	26 (36.6)
Age		
< 60 years old	14 (45.2)	33 (46.5)
> 60 years old	17 (54.8)	38 (53.5)
Clinical judgement		
Hypertension	0 (0)	10 (14.1)
Diabetes mellitus	4 (12.9)	12 (16.9)
Stroke	10 (32.3)	2 (2.8)
Congestive heart disease	17 (54.8)	47 (66.2)

Table 1 indicates that in the examination of gender characteristics among patients administered heparin and clopidogrel, male patients constitute 51.6% for heparin and 63.4% for clopidogrel. In the examination of age demographics among patients administered heparin and clopidogrel, those over 60 years of age constitute the majority, comprising 54.8% for heparin and 53.5% for clopidogrel. The clinical profile of patients administered heparin and clopidogrel indicates that congestive heart disease is the predominant condition, occurring in 54.8% of those receiving heparin and 66.2% of those receiving clopidogrel.

Tabel 2
Chi-Square Analysis Between Dependent Variables of Treatment Characteristics

Variable	Criteria	Total n = 102 (%)
Therapy	Heparin	31
	Clopidogrel	71
Duration of therapy	< 7 days	44
	> 7 days	57
Medication history	Induced kidney disease	21
	None induced	80
History of the disease	Cardiovascular	90
	Non-cardiovascular	11

Table 2 presents data on vascular disease patients undergoing Heparin therapy at Ibnu Sina Hospital and Labuang Baji Regional General Hospital in Makassar City, totalling approximately 31 patients, whereas those receiving Clopidogrel therapy amount to around 71 patients, with the majority having undergone treatment for over 7 days. Moreover, patients with vascular disease who are administered Heparin and Clopidogrel primarily consist of individuals with a prior history of cardiovascular disease, amounting to 90 people. Moreover, around 21 individuals are administered drugs that elevate the risk of renal problems during treatment.

Table 3
Multivariate Statistical Analysis of Glomerular Filtration Rate And Creatinine Variables

Variable	Criterion	95% Confidence Interval		p-value
		Lower	Upper	
Medication history	None	0.245	0.936	0.036
	Induced kidney	1.042	1.742	
Duration of therapy	< 7 days	0.741	1.904	0.019
	> 7 days	0.622	1.239	
History of the disease	Cardiovascular	0.603	1.455	0.053
	Non-cardiovascular	0.746	1.486	

Heparin presents a notable risk of renal function impairment in patients with vascular thrombosis as compared to clopidogrel, evidenced by a more substantial elevation in serum creatinine levels and a reduction in glomerular filtration rate (eGFR) (p-value = 0.036). These findings align with the mechanism of heparin nephrotoxicity via renal haemodynamic abnormalities and activation of the renin-angiotensin system. Therapy lasting more than 7 days exacerbates the adverse effects of heparin on renal function, whereas clopidogrel maintains a more consistent safety profile. This highlights the necessity of vigilant surveillance of renal function when prolonged heparin administration is unavoidable. Cardiovascular comorbidities generally exacerbate the

likelihood of renal failure (p-value = 0.053), but not statistically significant, necessitating careful consideration in the choice of anticoagulant medication.

2. Discussion

This study's multivariate statistical analysis reveals significant data about the impact of heparin and clopidogrel medication on the renal function of individuals with vascular thrombosis. The research findings demonstrate that heparin is significantly correlated with an elevated risk of renal dysfunction in comparison to clopidogrel, with a 95% confidence interval for the nephrotoxic medication group spanning from 1.042 to 1.742 (p=0.036). These findings align with the established mode of action of heparin, which may induce glomerular hypoperfusion by inhibiting aldosterone synthesis and promoting sodium retention. Conversely, clopidogrel, as an antiplatelet agent, demonstrates a superior safety profile concerning renal function, with a confidence interval of 0.245-0.936, corroborating the results of multiple prior studies about the low frequency of acute kidney injury linked to this class of medications (Palmers et al, 2018; Linkins et al, 2018; Hirsh et al, 2001).

This study indicated that the length of therapy significantly influences the likelihood of renal function deterioration. Therapy over 7 days shown a sustained risk of renal dysfunction, albeit with a narrower confidence interval (0.622-1.239), but short-term therapy (<7 days) had more impact variability, reflected in a confidence interval of 0.741-1.904 (p=0.019). These findings corroborate prior evidence of an elevated risk of problems, including heparin-induced thrombocytopenia and secondary renal impairment, associated with prolonged use. In this context, the evaluation of non-heparin anticoagulant options, such as DOACs, for long-term therapy or patients with early eGFR decline is becoming increasingly pertinent. An noteworthy component of the study's findings is the impact of cardiovascular comorbidities on renal function. Despite not achieving strong statistical significance (p=0.053), patients with a history of cardiovascular illness had a propensity for an elevated risk of renal diseases. This phenomenon may be associated with cardiorenal syndrome, which can exacerbate renal function in this patient demographic. These findings underscore the necessity of a more personalized therapeutic strategy for patients with vascular thrombosis and cardiovascular comorbidities, incorporating considerations for pharmacological selection and dosage modification according to renal function (Chan et al, 2016; Ronco et al, 2019).

This study has many limitations that must be recognised. The retrospective design of this study restricts the ability to account for numerous confounding variables. The limited sample size is seen in the broad confidence ranges observed in several studies. The measures utilised to evaluate kidney function were restricted to serum creatinine and eGFR, excluding more specific renal indicators such as cystatin C or NGAL. Nonetheless, the results of this study offer significant insights into the renal safety profile of these two categories of anticoagulant treatments (Haase et al, 2009).

This study establishes that heparin has a greater risk of nephrotoxicity than clopidogrel in individuals with vascular thrombosis, particularly with prolonged treatment. The findings endorse the necessity of regular kidney function monitoring during heparin therapy and suggest the consideration of alternate treatments, such as clopidogrel or DOACs, for individuals at elevated renal risk. Additional research employing a prospective design and more extensive renal evaluation criteria is required to corroborate these findings and formulate more effective preventative methods. Consideration of alternative anticoagulants for patients with high renal risk. Routine

monitoring of kidney parameters (eGFR, creatinine, and electrolytes) during heparin therapy. Individualisation of therapy based on treatment duration and patient comorbidities.

Conclusion

Heparin markedly elevates the risk of renal impairment relative to clopidogrel in individuals with arterial thrombosis, particularly with prolonged use. Vigilant oversight and evaluation of alternative treatments are essential for high-risk patients. Additional research is required to enhance mitigating techniques.

References

Mukahar, M., & Sulistyanto, Benny Arief. (2022). Gambaran Kualitas Resusitasi Jantung Paru dengan Memakai Masker Bedah pada Perawat Rumah Sakit HA Zaky Djunaid Pekalongan. *Proceeding of The URECOL*, 657–668.

Rahmawati, Febtarini. (2018). Aspek Laboratorium Gagal Ginjal Kronik. *Jurnal Ilmiah Kedokteran Wijaya Kusuma*, *6*(1), 14–22. https://doi.org/10.30742/jikw.v6i1.323

Rohmawati, Dhian Luluh, Ekayamti, Endri, & Komalawati, Rini. (2022). Pemberdayaan Masyarakat dalam Melakukan Manajemen Penyakit Kronis sebagai Langkah Preventif Terjadinya Komplikasi Penyakit Ginjal Kronik. *Jurnal Kreativitas Pengabdian Kepada Masyarakat (Pkm)*, *5*(11), 3831–3841. https://doi.org/10.33024/jkpm.v5i11.7542

Sa'diyah, Putri Nur Halimatus, Rahmawati, Ima, & Windartik, Emyk. (2022). *HUBUNGAN ASUPAN PROTEIN DENGAN KADAR UREUM DAN KREATININ DARAH PADA PASIEN GAGAL GINJAL KRONIS YANG MENJALANI HEMODIALISA DI RSUD Dr. WAHIDIN SUDIRO HUSODO KOTA MOJOKERTO*.

Sagita, Vina Anasthasia, & Sukmadryani, Yunilah. (2024). Analisis Efektivitas dan Biaya Penggunaan Obat Antikoagulan di Indonesia: Kajian Artikel. *PHARMACIA*, *2*(1), 8–15.

Saputro, Dwi Kurniawan, Ajie, Meraldy Fiko Rastio, Azizah, Shelvi, & Hartanti, Dwi. (2023). Penerapan Logistic Regression untuk Mendeteksi Penyakit Jantung pada Pasien. *Prosiding Seminar Nasional Teknologi Informasi Dan Bisnis*, 666–671.

Sari, Elsa Trisna, Fadilla, Nur Aini Fatna, Indriansyah, Tyara Avrilyanti Ghea, & Arini, Liss Dyah Dewi. (2025). Pengaruh Kesakitan pada Nefron Terhadap Terjadinya Penyakit Gagal Ginjal. *Student Scientific Creativity Journal*, *3*(2), 1–14.

Sawu, Sirilus Deodatus, & Indriyani, Oktavia. (2024). Literature Review: Pengaruh Penambahan Cilostazol sebagai Kombinasi Antiplatelet pada Pasien Penyakit Jantung Koroner. *KUNIR: JURNAL FARMASI INDONESIA*, *2*(1), 30–39.

Semakula, Jerome Roy, Mouton, Johannes P., Jorgensen, Andrea, Hutchinson, Claire, Allie, Shaazia, Semakula, Lynn, French, Neil, Lamorde, Mohammed, Toh, Cheng Hock, Blockman, Marc, Sekaggya-Wiltshire, Christine, Waitt, Catriona, Pirmohamed, Munir, & Cohen, Karen. (2020). A cross-sectional evaluation of five warfarin anticoagulation services in Uganda and South Africa. *PLoS ONE*, *15*(1), 1–9. https://doi.org/10.1371/journal.pone.0227458

Widiastuti, Ida Ayu Eka, Cholidah, Rifana, Buanayuda, Gede Wira, & Alit, Ida Bagus. (2021). Deteksi Dini Faktor Risiko Penyakit Kardiovaskuler pada Pegawai Rektorat Universitas Mataram. *Jurnal Pengabdian Magister Pendidikan IPA*, *4*(1). https://doi.org/10.29303/jpmpi.v4i1.604

Wijaya, Arif, Achwandi, Moch, & JP, Chaterina. (2023). *Hubungan Lama Hemodialisis Dengan Kejadian Anemia Pada Pasien Gagal Ginjal Kronis Di RSUD Bangil*. Perpustakaan Universitas Bina Sehat PPNI.