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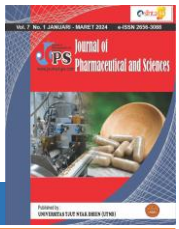

Cardiovascular Drug–Drug Interactions (DDIs) in Coronary Heart Disease Patients with Hypertension

Analisis Interaksi Obat-Obat Kardiovaskular pada Pasien Jantung Koroner dengan Riwayat Hipertensi

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Abstract

Coronary heart disease (CHD) accompanied by hypertension often necessitates the use of multiple cardiovascular agents. The concurrent use of multiple drugs increases the risk of drug-drug interactions (DDIs), which may alter drug metabolism, reduce therapeutic efficacy, or cause adverse effects. This study aimed to characterize the potential, mechanisms, and severity of drug interactions; to assess differences in the average number of drugs used per day in relation to the potential for drug interactions; and to assess the clinical profile based on DDI severity levels. A retrospective, analytic, observational method was applied, utilizing secondary data from hospital medical records. Statistical analysis included the Mann–Whitney test to compare the mean number of drugs per day between the interaction potential groups. A total of 52 patients met the inclusion criteria through purposive sampling. The results showed that most CHD patients with a history of hypertension were male (75%) and aged 18–64 years (73.1%). A total of 405 potential DDIs were identified. From these, 80 unique drug-pair interactions were selected for detailed analysis of their mechanisms and severity. Most were pharmacodynamic (77.5%), with aspirin–nitroglycerin the most frequent (7.6%). Among the 80 interactions analyzed in detail, those with moderate severity predominated (58.8%), followed by minor (35%) and major (6.2%). Polypharmacy (defined as the use of three or more medications) was observed in all patients who experienced DDIs. There was a significant difference in the average number of medications per day between patients with potential drug interactions and those without, $p = 0.023$ ($p < 0.05$).

***Keywords*: Hypertension, Coronary Heart Disease, Drug-drug Interaction, Cardiovascular Drugs.**

Abstrak

Pasien jantung koroner (PJK) dengan riwayat hipertensi memerlukan penggunaan berbagai agen kardiovaskular. Penggunaan beberapa obat secara bersamaan meningkatkan risiko terjadinya interaksi obat-obat yang dapat memengaruhi perjalanan obat dalam tubuh, efektivitas terapi maupun menimbulkan efek samping. Penelitian ini bertujuan untuk menggambarkan potensi, mekanisme, dan tingkat keparahan interaksi obat; menilai perbedaan jumlah rata-rata obat yang digunakan per hari terkait potensi interaksi dan profil klinis berdasarkan tingkat keparahan interaksi obat. Penelitian dilakukan dengan metode observasional analitik retrospektif menggunakan data sekunder dari rekam medis rumah sakit. Analisis data menggunakan uji Mann-Whitney untuk melihat perbedaan antara jumlah rata-rata obat perhari dengan potensi interaksi obat. Sebanyak 52 pasien memenuhi kriteria inklusi melalui metode purposive sampling. Hasil penelitian menunjukkan bahwa sebagian besar pasien laki-laki (75%) dan berusia 18–64 tahun (73,1%). Sebanyak 405 potensi interaksi obat telah diidentifikasi. Dari jumlah tersebut, 80 interaksi pasangan obat yang unik dipilih untuk analisis terperinci mengenai mekanisme dan tingkat keparahannya. Sebagian besar interaksi bersifat farmakodinamik (77,5%), dengan interaksi aspirin–nitrogliserin sebagai yang paling sering terjadi (7,6%).

Pada 80 interaksi yang dianalisis secara detail, interaksi dengan tingkat keparahan sedang mendominasi (58,8%), diikuti ringan (35%) dan berat (6,2%). Interaksi obat ditemukan pada pasien yang mengonsumsi ≥3 obat. Terdapat perbedaan signifikan dalam rata-rata jumlah obat per hari antara pasien yang memiliki potensi interaksi obat dan yang tidak p = 0,023 (p < 0,05).

Kata Kunci: Hipertensi, Penyakit Jantung Koroner, Interaksi Obat-obat, Obat Kardiovaskular.

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Introduction

Hypertension is a common condition defined as a persistent elevation of arterial blood pressure (BP) [1]. Globally, more than 1.28 billion adults aged 30–79 years suffer from hypertension, yet 46% remain unaware of their condition [2]. In Indonesia, the prevalence of hypertension in 2018 reached 34.11%, with a rate of 25.16% in West Sumatra [3].

Hypertension is one of the most prevalent chronic diseases and a major risk factor for coronary heart disease (CHD). CHD is the leading cause of death worldwide, accounting for 17.9 million deaths annually [4]. According to the 2018 RISKESDAS survey, the prevalence of CHD in Indonesia was 1.5% and 1.6% in West Sumatra, representing an increase compared to 2013 [3,5]. Patients with CHD and a history of hypertension generally require complex cardiovascular therapy, including the use of β-blockers, ACE inhibitors, angiotensin receptor blockers (ARBs), diuretics, and antiplatelet agents. [6].

The concurrent use of multiple drugs (polypharmacy) increases the risk of drug–drug interactions (DDIs), either through pharmacokinetic or pharmacodynamic mechanisms, which may reduce therapeutic effectiveness or cause adverse effects [7]. Previous studies have reported a high incidence of cardiovascular DDIs, reaching 98.51% and 93.65%, with moderate severity being the most frequently observed [6,8]. Common drug combinations associated with interactions include aspirin with clopidogrel, bisoprolol with furosemide, and candesartan with spironolactone [6,9].

Accordingly, this study aimed to characterize the patterns, mechanisms, and severity of DDIs among patients with coronary heart disease (CHD) and hypertension at Dr. M. Djamil Padang Hospital. The findings are expected to provide insights for optimizing drug therapy and establishing safer monitoring protocols within this setting.

Material and Methods

Research Design

This research was conducted in the medical records department of Dr. M. Djamil Hospital in Padang from March to June 2025. This study is an analytical observational study with retrospective data, involving the collection of data from patients' medical records in 2023 using a purposive sampling method.

Patient Criteria

Data were collected from patients receiving cardiovascular drug therapy who were aged ≥18 years. Inpatients diagnosed with coronary heart disease and a history of hypertension (ICD-10 codes I20.0, I20.9, I21.0, I21.1, I21.4, I25.1) at RSUP Dr. M. Djamil Padang in 2023. Data from medical records that were not found,

were unreadable, or had incomplete examination data were excluded from the study. All patients who met the inclusion criteria were analyzed for potential DDIs. We conducted a detailed analysis of all unique interactions (drug pairs) that occurred, comprising 80 of a total of 405 interaction events.

Data Analysis

Collected data included age, sex, admission date, medication list, blood pressure, and pulse rate. All eligible data were processed and analyzed using the Statistical Product and Service Solutions (SPSS) for Windows. The average number of cardiovascular drugs used per patient per day was calculated, along with a clinical profile based on the severity levels of DDIs. Potential drug–drug interactions, interaction mechanisms, and severity levels (minor, moderate, and major) were identified using Stockley's Drug Interactions (2010), Medscape (2025), the Drug Interaction Checker database (www.drugs.com) (2025), Drugbank online (2025), and Drug Interaction Facts (2009). Subsequently, the relationship between the average number of cardiovascular drugs per day and the potential for drug interactions was analyzed using the Mann–Whitney test.

Ethical Approval

This research received ethical approval from the Health Research Ethics Committee of Dr. M. Djamil Padang Hospital with approval No. DP.04.03/D.XVI.10.1/31/2025.

Results and Discussion

A total of 52 patients who met the inclusion criteria were identified. Patients included in this study were those diagnosed with one of the following conditions based on ICD-10 codes: subendocardial myocardial infarction (NSTEMI) (I21.4), acute transmural myocardial infarction (STEMI) (I21.0, I21.1), stable angina pectoris (I20.9), unstable angina pectoris (I20.0), or atherosclerotic heart disease (I25.1). Based on Table 1, most patients were aged 18-64 years (73.1%), with a mean age of 58.04 ± 9.387 years. This finding is consistent with the study conducted by Novriyanti (2014), which reported that the highest prevalence of coronary heart disease with hypertension occurred in the adult age group [10].

Table 1. Distribution of Patient Demographics

Patient Characteristics		Total Patient (n = 52)	Percentage(%)
Age	18-64 years	38	73.1
	≥65 years	14	26.9
Sex	Male	39	75
	Female	13	25

Based on sex, male patients were more frequently affected by coronary heart disease with a history of hypertension, totaling 39 patients (75%). This finding is consistent with the study conducted by Nurhikmawati (2024), which reported that hypertensive patients with cardiovascular complications, including coronary heart disease, were predominantly male (56.1%) compared to female patients (43.9%). This indicates that men are more likely to experience coronary heart complications resulting from hypertension [11]. Similarly, Shoufiah stated that the predominance of male patients is strongly associated with risk factors, particularly smoking, which contributes to elevated cholesterol levels [12].

Based on Table 2, coronary heart disease patients with a history of hypertension most frequently used aspirin, accounting for 51 patients (14.3%). According to the 2024 guideline of the Indonesian Heart Association (PERKI) on acute coronary syndrome (ACS), antithrombotic agents (antiplatelet and anticoagulant) play a crucial role in its management. Aspirin is the most widely used oral antiplatelet agent [13]. Aspirin acts as an acetylating agent, irreversibly inactivating cyclooxygenase (COX)-1 and suppressing the formation of prostaglandin H2, the precursor of thromboxane A2. Low-dose aspirin can completely inhibit COX-1 (with long-term effects) with daily dosing. To date, aspirin has been regarded as a drug that prevents arterial thrombosis by inhibiting COX-1. Current guidelines establish the role of aspirin in the primary prevention of cardiovascular events [14]. In clinical practice, aspirin can be combined with other oral antiplatelet agents, specifically ADP receptor inhibitors such as clopidogrel, ticagrelor, or prasugrel [13]. Accordingly, clopidogrel was used in 27 patients (7.6%) and ticagrelor in 37 patients (10.4%).

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Table 2. Profile of Cardiovascular Drug Usage

Class	Drug Name	Drug Usage	Percentage (%)
Diuretics	Furosemide (Lasix®)	8	2.2
	Spironolactone (Spirola™)	6	1.7
	Hydrochlorthiazide	2	0.6
Antihypertensives	Bisoprolol (Concor®)	33	9.3
	Candesartan	16	4.5
	Ramipril	27	7.6
	Amlodipine	18	5.1
	Nicardipine	2	0.6
	Imidapril (Tanapress®)	6	1.7
	Nifedipine (Adalat® Oros)	6	1.7
	Carvedilol (V-Bloc®)	5	1.4
	Valsartan	1	0.3
	Clonidine	1	0.3
	Diltiazem (Herbesser®)	1	0.3
Antianginal agents	Nitroglycerin (Nitrokaf)	40	11.2
	ISDN (Isosorbide Dinitrate)	1	0.3
Antiplatelets	Aspirin (Aspilets®, Aptor®, Miniaspi®)	51	14.3
	Clopidogrel	27	7.6
	Ticagrelor (Brilinta®)	37	10.4
Anticoagulants	Enoxaparin (Lovenox®)	17	4.8
Statins	Simvastatin	1	0.3
	Atorvastatin	50	14

In patients with coronary heart disease, β-blockers are the first-line therapy for the management of hypertension, particularly in those presenting with angina symptoms. Calcium channel blockers (CCBs) are used as adjunctive agents after β-blocker dosage optimization. The management of hypertension in patients with acute coronary syndrome (ACS) focuses on restoring the balance between myocardial oxygen supply and demand after the initiation of antiplatelet and anticoagulant therapy. In both NSTEMI and STEMI patients, the initial antihypertensive therapy after nitrates is β-blockers, particularly cardioselective agents such as bisoprolol. In this study, bisoprolol was administered to 33 patients (11.1%). For STEMI patients, therapy is further complemented by the addition of ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs). The ACEIs prescribed in this study were ramipril (7.6%) and imidapril (1.7%), while the ARBs included candesartan (4.5%) and valsartan (0.3%) [15].

Table 3. Potential Drug–Drug Interactions of Cardiovascular Drugs

Potential Interaction	Frequency (n=52)	Percentage (%)
Yes	50	96,2
No	2	3,8

According to the data in Table 3, the increase in drug interactions among patients may occur as a result of a higher number of drugs being taken concurrently, either due to multiple comorbidities requiring different therapies or due to more frequent drug use. This ultimately increases the likelihood of drug–drug interactions, which may reduce therapeutic effectiveness or cause adverse effects.

Hypertension contributes significantly to the risk of cardiovascular disease, as it places additional strain on the heart to pump blood and may also cause vascular damage. Persistent high blood pressure can damage the coronary arteries; as plaque accumulates along the vessel walls, the arteries may become hardened, thickened, and stiff, thereby reducing vascular elasticity [16]. A study conducted by Atika et al. (2021) at RSI Siti Rahmah Padang reported that among 51 patients with coronary heart disease, 52.9% also had hypertension. Elevated blood pressure increases cardiac workload, potentially leading to ventricular

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hypertrophy. If arterial pressure continues to rise, valvular narrowing may occur, and the ventricles must generate greater force to pump blood throughout the body [17].

Several important factors must be considered when prescribing medications to ensure treatment safety and effectiveness. These include assessing medical indications and potential risks, selecting appropriate drugs based on the patient's condition, adjusting dosages based on age, organ function, and medical history, and determining the optimal route of administration to achieve a safe and effective therapeutic effect. In this study, 50 of 52 patients (96.2%) experienced potential drug interactions, either among cardiovascular drugs prescribed for coronary heart disease with a history of hypertension or between cardiovascular and non-cardiovascular drugs for other conditions. Only two patients (3.8%) did not experience any potential drug interactions.

Table 4. List of Interaction Drug Pairs, Mechanisms, Severity, and Frequency of Occurrence

No.	Drugs that potentially have interactions		Mechanism	Severity level	Frequency of Occurrence
	Drug A	Drug B			(n= 405)
1	Amlodipine	Aspirin	FD[c]	Moderate[b]	5
2		Atorvastatin	FK[b]	Moderate[b]	3
3		Bisoprolol	FD[c]	Moderate[b]	10
4		Candesartan	FK[d]	Moderate[d]	4
5		Clopidogrel	FK[d]	Moderate[d]	6
6		Enoxaparin	FD[d]	Minor[d]	4
7		Furosemide	FD[d]	Minor[d]	2
8		Nifedipine	FK[c]	Major[c]	1
9		Nitroglycerin	FD[e]	Moderate[e,b]	11
10		Ramipril	FD[e]	Minor[e,b]	4
11		Spironolactone	FD[d]	Major[d]	5
12		Ticagrelor	FD[c]	Minor[b,c]	9
13	Aspirin	Bisoprolol	FD[c]	Minor[c]	6
14		Candesartan	FD[e]	Moderate[b,e]	11
15		Carvedilol	FD[e]	Minor[b,e]	2
16		Clopidogrel	FD[d]	Moderate[b,d]	13
17		Diltiazem	FD[c]	Minor[c]	1
18		Enoxaparin	FD[c]	Moderate[b]	11
19		Furosemide	FD[a,c]	Minor[b]	3
20		Hydrochlorotiazide	FD[b]	Moderate[b]	1
21		Nicardipine	FD[c]	Moderate[b]	1
22		Nifedipine	FD[e]	Moderate[b]	3
23		Nitroglycerin	FD[b]	Minor[b]	31
24		Ramipril	FD[b,e]	Moderate[b,e]	20
25		Spironolactone	FK[e]	Minor[b,e]	2
26		Ticagrelor	FD[b]	Moderate[b]	29
27		Valsartan	FD[a,c]	Moderate[b]	1
28	Atorvastatin	Candesartan	FK[b,d]	Moderate[d]	14
29		Clopidogrel	FK[b]	Moderate[b]	6
30		Nicardipine	FK[d]	Moderate[d]	1
31		Nifedipine	FK[b]	Moderate[b]	2
32		Ticagrelor	FK[b,d]	Moderate[d]	20
33		Valsartan	FK[d]	Minor[d]	1
34	Bisoprolol	Candesartan	FD[a,c]	Moderate[b]	2
35		Enoxaparin	FD[d]	Minor[d]	4
36		Nifedipine	FD[b]	Moderate[b]	3
37		Nitroglycerin	FD[d]	Minor[d]	20
38		Ramipril	FD[d]	Minor[d]	3

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39		Spironolactone	FD[e]	Moderate[e,b]	4
40		Ticagrelor	FD[d]	Minor[c]	15
41	Candesartan	Carvedilol	FD[d]	Minor[d]	3
42		Clopidogrel	FK[d]	Moderate[d]	3
43		Enoxaparin	FD[c]	Moderate[b]	3
44		Nicardipine	FK[d]	Major[d]	1
45		Nifedipine	FD[d]	Minor[d]	4
46		Nitroglycerin	FD[d]	Minor[d]	13
47		Ramipril	FD[d]	Moderate[d]	1
48		Spironolactone	FD[c,e]	Major[b,e]	1
49		Ticagrelor	FK[d]	Minor[b,d]	4
50	Carvedilol	Clopidogrel	FD[d]	Moderate[d]	3
51		Enoxaparin	FD[d]	Minor[d]	1
52		Nifedipine	FD[b]	Moderate[b]	4
53		Nitroglycerin	FD[d]	Moderate[d]	4
54		Ticagrelor	FD[d]	Moderate[d]	2
55	Clonidin	Nifedipine	FD[d]	Minor[d]	1
56		Nitroglycerin	FD[d]	Moderate[d]	1
57	Clopidogrel	Enoxaparin	FD[b]	Major[b]	7
58		Nicardipine	FD[d]	Moderate[d]	1
59		Nifedipine	FD[d]	Moderate[d]	3
60		Ticagrelor	FD[c]	Moderate[b]	1
61	Diltiazem	Nitroglycerin	FD[d]	Moderate[d]	1
62		Ticagrelor	FK[d]	Moderate[d]	1
63	Enoxaparin	Imidapril	FD[d]	Minor[d]	1
64		Nifedipine	FD[d]	Minor[d]	1
65		Ramipril	FD[b]	Moderate[b]	6
66		Spironolactone	FD[c]	Moderate[b]	1
67		Ticagrelor	FD[c]	Moderate[b]	3
68	Furosemide	Hydrochlorotiazide	FK[e]	Moderate[b,e]	1
69		Imidapril	FD[a]	Moderate[d]	1
70		Nitroglycerin	FD[d]	Minor[d]	5
71	Hydrochlorotiazide	Nifedipine	FD[d]	Minor[d]	1
72	Imidapril	Nitroglycerin	FD[d]	Minor[d]	5
73	ISDN	Nitroglycerin	FD[d]	Moderate[d]	1
74	Nicardipine	Nifedipine	FD[d]	Moderate[d]	1
75		Nitroglycerin	FD[e]	Moderate[e,b]	1
76	Nifedipine	Nitroglycerin	FD[e]	Moderate[e,b]	4
77		Ramipril	FD[b]	Minor[b]	1
78		Ticagrelor	FK[d]	Minor[d]	2
79	Nitroglycerin	Ramipril	FD[c]	Moderate[b]	12
80	Spironolactone	Ticagrelor	FD[c]	Moderate[b]	1

Description: a: Stockley's Drug Interaction (2009); b: Drugs.com (2025); c: Medscape (2025); d: Drug Bank Online (2025); and e: Drug Interaction Fact PD: Pharmacodynamic (77.5%); PK: Pharmacokinetic (22.5%); Major (6.25%); Moderate (58.75%); and Minor (35%)

A total of 405 drug interaction events occurred across 80 different drug pairs. Table 4 lists these 80 drug pairs and their frequency of occurrence. From these, 80 cases were selected for detailed analysis of interaction mechanisms and severity (Table 5). The analysis revealed that most were pharmacodynamic interactions, accounting for 62 cases (77.5%). This finding is consistent with Setyoningsih (2022), who also reported pharmacodynamic interactions as the most frequent type, occurring in 44 patients (58.7%) [18]. These results suggest that pharmacodynamic interactions are more common, particularly in chronic conditions such as coronary heart disease with hypertension, where patients are often prescribed multiple drugs with additive, synergistic, or antagonistic effects on shared receptor systems or physiological pathways.

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Pharmacodynamic interactions are drug interactions that act at the same receptor system, site of action, or physiological pathway, resulting in additive, synergistic, or antagonistic effects without altering plasma concentrations or other pharmacokinetic profiles [19]. Additive effects occur when two drugs with similar actions are combined, yielding a total effect equal to the sum of their individual effects. Synergistic effects arise when the combination produces a greater effect than the sum of each drug alone, whereas antagonistic effects occur when the combined effect is less than that of the individual drugs [20].

Table 5. Description of drugs that potentially have interactions, mechanisms, and the severity level of drug interaction.

Potential Interaction		Total Cases (n=80)	Percentage (%)
Mechanism	Pharmacodynamic	62	77.5
	Pharmacokinetic	18	22.5
Severity level	Major	5	6.25
	Moderate	47	58.75
	Minor	28	35

The most frequent pharmacodynamic interaction observed was between aspirin and nitroglycerin, which accounted for 31 cases (7.6%) of the 405 total interactions. This interaction is considered minor in severity. Although the concurrent use of aspirin and nitroglycerin generally does not interfere with each other's efficacy, higher doses of aspirin may modify the effects of nitroglycerin. Management strategies include dose adjustment and careful clinical monitoring to minimize potential adverse effects [21].

Other frequently observed interactions included aspirin with ticagrelor (29 cases, 7.1%), aspirin with ramipril (20 cases, 4.9%), and atorvastatin with ticagrelor (20 cases, 4.9%). All three were classified as moderate interactions. The interaction between aspirin and ticagrelor occurs through a pharmacodynamic mechanism, where aspirin doses above 100 mg may reduce the effectiveness of ticagrelor [21]. The interaction between aspirin and ramipril reduces the antihypertensive effect of ramipril when combined with high-dose aspirin, for which monitoring of blood pressure and hemodynamic parameters is recommended [21,22]. The atorvastatin–ticagrelor interaction, on the other hand, is pharmacokinetic, as atorvastatin concentrations may increase when co-administered with ticagrelor. Management involves monitoring lipid levels and prescribing the lowest effective statin dose [21,23].

Pharmacokinetic interactions occur when the co-administration of two or more drugs influences each other's pharmacokinetic processes. These interactions alter drug concentrations in the body by affecting absorption, distribution, metabolism, or elimination [24]. Pharmacokinetic interactions were identified in 18 cases (22.5%) of the total 80 interactions. One of the most frequent was between atorvastatin and candesartan. Since CYP2C8 metabolizes atorvastatin, its metabolism may be reduced when combined with candesartan, leading to elevated atorvastatin levels. Management includes periodic monitoring of drug concentrations [21,23].

In total, 405 potential drug–drug interactions (DDIs) were identified in the study population. The analysis showed that pharmacodynamic interactions were the most common, accounting for 62 of the 80 cases (77.5%). This predominance is consistent with the study by Setyoningsih (2022), which also reported pharmacodynamic interactions as the dominant type [18]. Notably, the most frequent pharmacodynamic interaction in the overall dataset was between aspirin and nitroglycerin, observed in 31 cases (7.6%) of the 405 interactions, and categorized as minor in severity.

In terms of severity, moderate interactions were the most frequent, accounting for 47 cases (58.75%), followed by minor interactions (28 cases, 35%) and major interactions (5 cases, 6.25%). These results are consistent with Oktaviani et al. (2023), who also reported moderate interactions as the most prevalent (309 cases, 63.7%), followed by minor (146 cases, 30.1%) and major (30 cases, 6.2%) [25]. Major interactions are clinically important because they may pose serious, potentially life-threatening risks or lead to permanent harm. In this study, the most frequently observed major interaction was between aspirin and spironolactone, found in 5 cases (1.2% of the 405 total interactions), which carries the risk of hyperkalemia. Preventive strategies include regular monitoring of potassium levels and dose adjustments where necessary [23].

Another major interaction observed was between clopidogrel and enoxaparin. When used concurrently, clopidogrel and enoxaparin (Lovenox®) may increase the risk of bleeding complications [23,26]. If co-administration is necessary, careful clinical and laboratory monitoring is required. Unless strongly indicated,

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the combination should be avoided due to the elevated risk of bleeding [21,26]. In contrast, moderate interactions may worsen the patient's clinical condition, necessitating additional medical management [22].

Minor interactions generally have mild effects that may be inconvenient or clinically insignificant, not altering therapeutic outcomes, and typically do not require additional intervention [22]. One example observed in this study was the interaction between bisoprolol and nitroglycerin. Bisoprolol can enhance the hypotensive effect of nitroglycerin, resulting in additive or synergistic reductions in blood pressure. Management involves regular monitoring of blood pressure [23].

Table 6. Differences in the Average Number of Drug Types per Day and the Potential for Drug Interactions

Potential Drug Interaction	n	Average daily use of cardiovascular drugs					*p-value**
		Mean ±SD	95% CI		Min	Max	
			Lower	Upper			
Yes	50	4.84 ± 1.184	4.503	5.177	3	7	0.023
No	2	2.5 ± 0.707	3.865	8.853	2	3	

*Mann–Whitney test

Table 6 summarizes the comparison of average daily drug use between patients with and without potential drug–drug interactions (DDIs). Among the 52 patients included, 50 (96.2%) experienced potential interactions, whereas only 2 (3.8%) did not. Patients with potential DDIs had a higher mean daily drug use of 4.84 ± 1.184 (range: 3–7 drugs), compared with 2.5 ± 0.707 (range: 2–3 drugs) in those without potential interactions. The difference between the two groups was statistically significant ($p < 0.023$). This finding is consistent with the results of Permatasari et al. (2024), who also reported a significant association between the average number of cardiovascular drugs prescribed per day and the likelihood of DDIs ($p = 0.021$, $p < 0.05$)[6]. Similarly, a strong positive correlation was observed, indicating that an increasing number of prescribed medications was associated with a higher probability of DDIs ($r = 0.728$, $p = 0.0001$) [27].

These findings demonstrate that the more drugs consumed by patients, the higher the likelihood of drug interactions. Statistically, it can be concluded that there is a significant association between the average daily use of cardiovascular drugs and the potential for drug interactions. Saputri (2023) further showed that an increased number and frequency of drugs prescribed contributed to a higher risk of interactions [28]. Patients prescribed polypharmacy were found to have 0–3 potential interactions in 10 patients (9.5%) and 4–7 potential interactions in 15 patients (14.3%), with a p-value of 0.000 [29].

Drug interactions may lead to reduced drug effectiveness, enhanced drug response, or even toxic effects. Risk factors that may increase the likelihood of drug interactions include advanced age, obesity, hypoproteinemia, polypharmacy, genetic polymorphisms, sepsis, and impaired renal and hepatic function [30].

Table 7. Clinical Profile Based on DDI's Severity Levels

Clinicalsymptoms	Severity levels	Status		
		Improvement (%)	Worsening (%)	No change (%)
Blood Pressure	Major	50	0	50
	Moderate & Minor	47.4	0	52.6
Pulse	Major	0	0	100
	Moderate & Minor	7.9	0	92.1

As shown in Table 7, among those with major interactions, 50% demonstrated improvement in blood pressure, while the remainder showed no change. In the moderate and minor interaction groups, 47.4% of patients experienced improvement, and 52.6% showed no change. A similar pattern was observed for pulse rate, with no improvement in the major interaction group and only 7.9% improvement in the moderate and minor groups. Assessment of clinical parameters is defined as improvement when blood pressure and pulse are abnormal, they change to normal, worsening when blood pressure and pulse go from normal to abnormal, and no change when they remain abnormal or remain normal.

The lack of significance may be attributed to the small number of major interaction cases, which reduced statistical power, as well as the influence of comorbidities (e.g., diabetes, pneumonia) that may have

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confounded the observed clinical outcomes. Clinical trial data cumulatively demonstrate that ACEI, CCB, or ARB-based antihypertensive therapy reduces CV events [1]. This study is further limited by its retrospective, single-center design, small sample size, reliance on secondary medical record data without adjustment for potential confounders, and use of purposive sampling, which may limit representativeness and generalizability.

Conclusions

This study demonstrated that most coronary heart disease (CHD) patients with hypertension were at risk of drug–drug interactions (DDIs), predominantly pharmacodynamic in nature, with moderate severity being the most common. A significant difference was observed between the average number of cardiovascular drugs used per day and the likelihood of DDIs ($p < 0.05$). The high prevalence of DDIs underscores the need for careful prescribing, regular medication reviews, and the use of DDI screening tools in hospital practice to improve patient safety. Future multicenter, prospective studies are recommended to validate these findings and support the development of standardized monitoring protocols.

Conflict of Interest

There is no conflict of interest from any of the authors.

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References

[1] Dipiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey LM. Pharmacoterapy A Phatophysiologic Approach. 12th ed. 2023.
[2] Shimizu Y. Hypertension WHO 2023. https://www.who.int/news-room/fact-sheets/detail/hypertension.
[3] Kemenkes. Laporan Riskesdas 2018 Nasional (2018 National Riskesdas Report). Lemb Penerbit Balitbangkes 2018:hal 156.
[4] Mattingly Q. Cardiovascular WHO 2024. https://www.who.int/health-topics/cardiovascular-diseases.
[5] Kemenkes. Laporan Riskesdas 2013 Nasional (2013 National Riskesdas Report) 2013. https://doi.org/10.1126/science.127.3309.1275.
[6] Permatasari D, Husna NA, Yosmar R. Potensial Drug-Drug Interaction of Cardiovascular Drugs Based on Literature in Geriatric Patients with Congestive Heart Failure at Dr. M. Djamil Padang Hospital. Int J Appl Pharm 2024;16:28–34. https://doi.org/10.22159/ijap.2024.v16s1.06.
[7] Maulia AN, Kumala MT, Rochmah NN. Kajian Potensi Interaksi Obat Pada Pasien Hipertensi Di Instalasi Rawat Jalan Rumah Sakit X Periode Agustus 2019 (Study of Potential Drug Interactions in Hypertensive Patients in the Outpatient Unit of Hospital X, August 2019). J Ilm JOPHUS J Pharm UMUS 2022;3:111–9. https://doi.org/10.46772/jophus.v3i02.506.
[8] Aisyah S, Andini MD, Saputra GH. Overview of Drug Interactions in Geriatric Heart Failure Patients with BPJS Insurance at the Heart Clinic of Jakarta Islamic Hospital Cempaka Putih for the Period October-December 2018. J Farm IKIFA 2021;1:74–80.
[9] Adondis J, Mongi J, Tiwow GAR, Palandi RR. Studi Potensi Interaksi Obat Pada Pasien Gagal Jantung Di Instalasi Rawat Inap Rumah Sakit Advent Manado (Study of Potential Drug Interactions in Heart Failure Patients at the Inpatient Unit of Manado Adventist Hospital). Biofarmasetikal Trop 2019;2:124–35. https://doi.org/10.55724/jbiofartrop.v2i2.125.

Electronic ISSN : 2656-3088
Homepage: https://www.journal-jps.com

[10] Novriyanti ID, Usnizar F, Irwan. The Effect of Duration of Hypertension on Coronary Heart Disease in the Cardiology Clinic of Dr. Mohammad Hoesin General Hospital Palembang 2012. J Kedokt Dan Kesehat 2014;1:55–60. https://doi.org/10.1002/em.20332.
[11] Nurhikmawati, Afiifah I, Syahruddin FI, Aspar A, Lestari I. Karakteristik Pasien Hipertensi dengan Gangguan Kardiovaskular (Characteristics of Hypertensive Patients with Cardiovascular Disorders). Fakumi Med J J Mhs Kedokt 2024;4:513–20. https://doi.org/10.33096/fmj.v4i7.479.
[12] Shoufiah R. Hubungan Faktor Resiko Dan Karakteristik Penderita Dengan Kejadian Penyakit Jantung Koroner (The Relationship Between Risk Factors and Patient Characteristics and the Incidence of Coronary Heart Disease). Mahakam Nurs J 2016;1:17–26.
[13] PERKI. Pedoman Tata Laksana Sindrom Koroner Akut 2024 (Acute Coronary Syndrome Management Guidelines 2024). vol. 5. 2024.
[14] Mekaj YH, Daci FT, Mekaj AY. New insights into the mechanisms of action of aspirin and its use in the prevention and treatment of arterial and venous thromboembolism. Ther Clin Risk Manag 2015;11:1449–56. https://doi.org/10.2147/TCRM.S92222.
[15] PERKI. Pedoman Tatalaksana Hipertensi Pada Penyakit Kardiovaskular (Guidelines for the Management of Hypertension in Cardiovascular Disease). Perhimpunan Dokter Spesialis Kardiovaskular Indonesia; 2015.
[16] Tampubolon LF, Ginting A, Turnip FES. Gambaran Faktor yang Mempengaruhi Kejadian Penyakit Jantung Koroner (PJK) di Pusat Jantung Terpadu (PJT) (Overview of Factors Influencing the Incidence of Coronary Heart Disease (CHD) at the Integrated Heart Center (IHC)) 2023;13:1043–52.
[17] Atika Y. Gambaran Faktor Risiko Kejadian Penyakit Jantung Koroner di Poliklinik Jantung RSI Siti Rahmah Padang Tahun 2017-2018 (Overview of Risk Factors for Coronary Heart Disease Events at the Heart Polyclinic of RSI Siti Rahmah Padang in 2017-2018) 2019:20–8.
[18] Setyoningsih H, Zaini F. Hubungan Interaksi Obat Terhadap Efektivitas Obat Antihipertensi di RSUD dr. R. Soetrasno Rembang (The Relationship between Drug Interactions and the Effectiveness of Antihypertensive Drugs at Dr. R. Soetrasno Regional General Hospital, Rembang). Cendekia J Pharm 2022;6:76–88. https://doi.org/10.31596/cjp.v6i1.186.
[19] Azizah LN, Anwar T, Nastiti AD, Muhalla HI, Zuhroidah I, Dwipayanti PI, et al. Buku Ajar Farmakologi Keperawatan (Nursing Pharmacology Textbook). PT. Sonpedia Publishing Indonesia; 2024.
[20] Nuryati. Farmakologi (Pharmacology). Kementerian Kesehatan RI; 2017.
[21] Drugs.com 2025. https://www.drugs.com/drug_interactions.html.
[22] Tatro, David. Drug Interaction Facts. United State of America: Wolters Kluwer Health; 2009.
[23] Drugbank. Drug Interaction Checker 2025. https://go.drugbank.com/drug-interaction-%0Achecker.
[24] Mashar HM, Ilyas M, Mulki MA, Haryani R, Angganawati RT, Ismail. Interaksi Obat (Drug Interactions). Eureka Media Aksara; 2023.
[25] Oktaviani I, Setiadi F, Oktovina MN. Potensi Interaksi Obat Pada Pasien Penyakit Jantung Koroner Akut Di Rawat Inap Rumah Sakit Fatmawati Tahun 2023 (Potential Drug Interactions in Patients with Acute Coronary Heart Disease Hospitalized at Fatmawati Hospital in 2023). J Farm Klin Base Pract 2024;3:56–70. https://doi.org/10.58815/jfklin.v3i2.54.
[26] Baxter K. Stockley's Drug Interactions. 9th ed. Pharmaceutical Press; 2010.
[27] Dasopang ES, Harahap U, Lindarto D. Polifarmasi dan Interaksi Obat Pasien Usia Lanjut Rawat Jalan dengan Penyakit Metabolik (Polypharmacy and Drug Interactions in Elderly Outpatients with Metabolic Diseases). J Farm Klin Indones 2015;4:235–41. https://doi.org/10.15416/ijcp.2015.4.4.235.
[28] Saputri M, Dewi SR. Potensi Interaksi Polifarmasi Pasien Jantung Koroner (PJK) di Rumah Sakit I.A. Moeis Samarinda (Potential Polypharmacy Interactions in Coronary Heart Disease (CHD) Patients at I.A. Moeis Hospital, Samarinda). J Sains Dan Kesehat 2023;5:109–14. https://doi.org/10.25026/jsk.v5i2.1709.
[29] Harahap NRA, Putri RA. The Relationship Between Polypharmacy and Potential Drug-Drug Interactions (DDIs) in Coronary Heart Disease (CHD) Patients at a Private Hospital in Bekasi. J Ris Kefarmasian Indones 2025;7:231–44.
[30] Abet MA, Gayatri A. Potensi Interaksi Obat Tersering pada Pasien Sakit Kritis (Potential Most Frequent Drug Interactions in Critically Ill Patients). J Indones Med Assoc 2023;73:206–12. https://doi.org/10.47830/jinma-vol.73.4-2023-1036.

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