

Evaluation of Drug Interactions in Polypharmacy: A Case Study of Patients with Heart Failure Hospitalized at Tangerang District Hospital

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ABSTRACT

Heart failure is a condition in which the heart is unable to pump enough blood to meet the body's metabolic needs. It is a clinical syndrome with signs and symptoms caused by abnormalities in the structure and/or function of the heart. Heart failure occurs when the heart can't pump enough blood to meet the body's needs. It is caused by problems with the structure or function of the heart. This can lead to polypharmacy, where several medications are often taken by patients with heart failure to manage their condition. This study aims to identify patient characteristics, treatment accuracy based on Indonesian Heart Association (PERKI) 2023 guidelines, and the relationship between drug interactions and polypharmacy in adult patients diagnosed with heart failure with or without comorbidities at Tangerang Regency Hospital in 2023. The research was conducted descriptively using a cross-sectional study design. A total of 78 samples specimens met the inclusion criteria, with a male majority of 37 (52.86%) patients. The most common age group was 56-65 years old with 25 (35.71%) patients. The most common length of stay was 1-5 days with 48 (68.57%) patients. Evaluation of the treatment accuracy showed that the appropriate drug class was achieved in 78 (100%) patients, the appropriate dose in 55 (70.51%) patients and the appropriate frequency in 45 (57.69%) patients. Statistical tests showed a correlation between polypharmacy and drug-drug interactions with p-value <0.05. Accordingly, it is important to enhance monitoring and assessment of drug interactions in heart failure patients to optimize treatment management and prevent the risk of complications.

INTRODUCTION

Heart failure is a condition in which the heart is unable to pump blood in sufficient quantities to meet the body's metabolic needs (Nurkhalis and Adista, 2020; Sulistiyowatiningsih *et al.*, 2016). The incidence of heart failure worldwide continues to rise each year. Annually in Indonesia, heart failure due to cardiovascular diseases causes over 650,000 deaths (Nurkhalis and Adista, 2020). Over the past 20 years, heart failure has become a leading cause of death worldwide. According to data from the Global Health Data Exchange (GHDx) in 2020, the number of cases of diagnosed congestive heart failure reached 64.34 million worldwide,

resulting in 9.91 million deaths (Praha and Fauzi, 2021).

It is estimated that over 15 million new cases of heart failure emerge worldwide every year. Approximately 50% of heart failure patients will die within five years of diagnosis. The primary cause of congestive heart failure is a weakening of the heart muscle walls, leading to the heart's failure to pump and meet the body's blood needs. Congestive heart failure is the second leading cause of death in Indonesia after stroke. According to the 2018 Basic Health Research data, diagnosed cases of congestive heart failure in Indonesia reached 1.5%, or around 1,017,290 individuals (Imaligy, 2014)

Classification according to the New York Heart Association (NYHA) can help determine therapy options for patients and predict the duration of hospitalization, quality of life, and mortality rates in patients with congestive heart failure. Besides NYHA functionality in determining therapy for patients with congestive heart failure, the presence of comorbidities or concurrent diseases is crucial in management. Comorbidities in patients with cardiovascular disorders can affect the treatment of cardiovascular disorders by exacerbating side effects and cardiovascular conditions (Mathers *et al.*, 2017). Medical conditions commonly experienced by patients with cardiovascular problems include angina, hypertension, diabetes, hyperlipidemia, kidney failure, and cardiorenal disorders (Ministry of Health Indonesia, 2018).

Considering the number of patients with cardiovascular disorders in the Banten Region amounted to 7,267 individuals, this number is approximately 0.09% of the total population in the Banten Region, and based on medical records, around 214 individuals suffer from congestive cardiovascular disease. Based on Tangerang District Hospital data in 2022, cardiovascular disorders are the third most prevalent disease in the inpatient ward (Cowie *et al.*, 2014). Heart failure patients with comorbidities are at risk for polypharmacy, or taking five or more medications simultaneously. The specific number of drugs used to define polypharmacy varies, but it generally starts with the use of a minimum of five appropriate drugs. The simultaneous use of several drugs allows for the possibility of interactions, both between drugs and between drugs and diseases, which can negatively affect patient treatment outcomes (Ferdinand and Widyantari, 2023). Polypharmacy can increase the likelihood of drug interactions because the more drugs used, the greater the likelihood of drug interactions (Alhumaidi *et al.*, 2023).

Changes in therapeutic effects can be caused by drug interactions (Puspitasari and Angeline, 2019). These interactions occur when one drug affects the effects of another drug consumed simultaneously. The combination of several drugs potentially causes harmful pharmacodynamic or pharmacokinetic interactions. Analysis of drug interactions is crucial in the medical field to minimize the likelihood of such interactions occurring. As many as 52% of drug interaction categories involve cardiovascular drugs. The high incidence of drug interactions in patients diagnosed with

heart failure poses a problem that requires a collective solution (Saputri and Dewi, 2023).

Accordingly, this study aims to evaluate the potential drug interactions in heart failure patients with or without comorbidities in the hospitalized of Tangerang District Hospital. This research is expected to elucidate the potential drug interactions in the inpatient ward and enhance healthcare professionals' knowledge and understanding to prevent adverse treatment responses, decrease therapy effectiveness, and drug toxicity in the hospital.

METHODS

Materials

This study utilized various materials and tools to support the data collection and analysis process. The primary materials used were patients' medical records and prescription archives, which provided detailed information about patients' health conditions and the medications they consumed. Additionally, the tools used included research permits required to access patient data, as well as data collection forms designed to systematically record relevant information. A laptop equipped with SPSS 25 (IBM Corp., Chicago, Ill.) and Excel (Microsoft Corp., Redmond, Wash.) was used to analyze the data enabling statistical processing and creating tables and graphs. The 2023 heart failure guidelines and management protocols were also employed as references in evaluating the appropriateness of treatment provided to patients. Internet sites providing drug interaction checking services, such as drugs.com and Medscape, were utilized to examine potential interactions among the medications consumed by patients. Furthermore, drug interaction checker software and the standard drug interaction reference book "Stockley's Drug Interaction", first published by Penerbit, Pharmaceutical Press in 2002, were used to ensure the validity and accuracy of drug interaction examinations. The combination of various materials and tools ensured that the research was conducted using systematic and evidence-based methods.

Methods

This study was conducted with the establishment of criteria and groups of patients to be evaluated. Inclusion criteria included adult patients aged 17 and above diagnosed with heart failure with or without comorbidities admitted to the hospitalized of Tangerang District Hospital during the period 2023. Additionally, patients receiving polypharmacy with the same diagnosis

were also included in the inclusion criteria. Exclusion criteria included heart failure patients treated outside the hospitalized, deceased patients, transferred patients, and unreadable or incomplete medical records. The study design of this research was descriptive analysis with a retrospective study, analyzing the medications used by patients based on specific criteria whose therapy periods had ended. Data were collected from prescription archives and medical records of adult patients with heart failure, both with and without comorbidities, who were admitted to the hospitalized of Tangerang District Hospital during the specified period. The types of data collected included medical record numbers, patient identities, disease diagnoses, and medications used (drug types, totals, dose regimens, and durations of administration). Establishment of drug use criteria was based on pharmacokinetic and pharmacodynamic interactions. Pharmacokinetic interactions included transformations in the absorption, distribution, metabolism, and excretion stages of drugs that could result in increases or decreases in drug concentrations in the blood. Pharmacodynamic interactions included interactions at the same drug (receptor) workplace, drugs affecting the same physiological system, and fluid and electrolyte disturbances that produce synergistic or antagonistic effects.

Data organization was performed to determine patient demographics, the quantity,

types, and classes of drugs used, patterns of polypharmacy, and the potential for drug interactions, both pharmacokinetic and pharmacodynamic. Data were analyzed using references from literature and electronic sources such as Tatro's Drug Interaction Facts, Stockley's Drug Interactions, and online tools such as Drugs.com Interaction Checker and Medscape. The analysis of the relationship between the duration of therapy and the number of drugs used and the potential occurrence of drug interactions was conducted using SPSS Statistics 25 and Microsoft Excel 2019 with the Spearman's rank test.

RESULTS AND DISCUSSION

Demographic Characteristics

Population and sample in this study consisted of heart failure patients with or without comorbidities admitted to the hospitalized of Tangerang District Hospital during the period of 2023. The population size in this study was 78 patients, and all of them met the inclusion criteria. Medical records contain various types of patient data, ranging from identities to clinical data. Data collection from medical records aims to determine the profile of heart failure patients with or without comorbidities at Tangerang District Hospital during the period of 2023. The data demographic characteristics of the included patients are presented in Table 1.

Table 1. Demographic characteristics

| Patient Characteristics | Patients (n= 78) | |
|-------------------------|------------------|-------|
| | n | % |
| Gender | | |
| Male | 40 | 51.28 |
| Female | 38 | 48.71 |
| Age (Years) | | |
| 17-25 | 3 | 2.86 |
| 26-35 | 4 | 5.71 |
| 36-45 | 2 | 2.86 |
| 46-55 | 23 | 28.57 |
| 56-65 | 29 | 35.71 |
| > 65 | 17 | 24.29 |
| Length of Stay (Days) | | |
| 1-5 | 48 | 68.57 |
| 6-10 | 24 | 30.77 |
| 11-15 | 6 | 7.69 |
| Comorbidity | | |
| Cardiovascular | 67 | 26.69 |
| Respiratory | 34 | 13.54 |
| Diabetes Mellitus | 30 | 11.95 |

This study describes findings relevant to the characteristics of heart failure patients, consistent with previous research identifying common patterns related to this disease. One study highlighted the predominance of men in the heart failure patient population at RS PKU Muhammadiyah Yogyakarta, in line with theories linking the risk of heart failure in men to genetic factors and unhealthy lifestyles. (Fadilah *et al.*, 2023; Hamzah and Widaryati, 2017). These findings are consistent with research by Utami (2021) which identified the role of hormones in influencing the occurrence of cardiovascular disease between men and women. Hormonal factors such as estrogen in women are associated with a protective effect against oxidative stress, while men's higher risk of cardiovascular disease is due to unhealthy lifestyles. However, increased low density lipoprotein (LDL) cholesterol also poses a significant risk for women (Utami, 2021).

From the data of heart failure patients at Tangerang District Hospital, it is known that patients also have comorbidities accompanying the diagnosis of heart failure. There were 246 cases of comorbidities in the 78 patients studied. If ranked, the most common comorbid group was cardiovascular with 66 cases (26.72%), respiratory with 34 cases (13.76%), and diabetes mellitus with 29 cases (11.74%). Based on the number of patients from the 78 medical records available, a total of 50 patients (64.10%) had cardiovascular comorbidities, 31 patients (39.74%) had respiratory comorbidities, and 29 patients (37.18%) had diabetes mellitus comorbidities. With the increasing elderly population, there is an increase in age-related chronic diseases, especially heart failure. The complex interactions of cardiovascular aging processes (excessive oxidative stress, low-grade chronic inflammation, limited endogenous regenerative capacity in response to injury, and the aging process itself with underlying risk factors such as obesity, hypertension, atherosclerosis, heart conditions); heart diseases (permanent atrial fibrillation, hypertension); comorbidities such as anemia, chronic kidney disease, diabetes, sarcopenia; as well as gender and genetic factors as disease modifiers can contribute to the development of heart failure phenotypes and outcomes (Triposkiadis *et al.*, 2019).

The pattern of hospitalization for heart failure patients at Tangerang District Hospital, which was mostly between 1 and 5 days, is consistent with previous findings from Ningrum, indicating that congestive heart failure patients

are hospitalized for an average of 3 days with high treatment efficacy. In this context, the primary goal of heart failure patient care is to reduce symptoms and improve health-related quality of life. It is known that poor quality of life is a common feature observed in hospitalized heart failure patients (Ningrum *et al.*, 2022).

Overall, these findings indicate that the length of hospital stays for heart failure patients at Tangerang district hospital aligns with common medical practices aimed at managing symptoms and improving patient quality of life. Additionally, these findings highlight the importance of efficiency in heart failure patient care, with relatively short hospital stays reflecting the effectiveness of the therapy provided. Accordingly, efforts to continuously improve care efficiency and therapy effectiveness need to be continued to ensure that patients receive optimal care and better quality of life (Ningrum *et al.*, 2022). According to research conducted on heart failure patients with comorbidities at Ulin Banjarmasin hospital, uncontrolled hypertension leads to heart failure complications, which also become comorbidities of heart failure itself. Previous studies have shown that one-quarter of heart failure cases are caused by hypertension. Blood pressure can increase the incidence of heart failure by 50-60% (Amelia *et al.*, 2023). Additionally, research conducted by Sulistiyowatiningsih *et al.* stated that heart failure is often accompanied by pathological conditions mostly dominated by cardiovascular system disorders, with 54 cases out of 70 patients studied (Sulistiyowatiningsih *et al.*, 2016).

Starting from atrial fibrillation, myocardial infarction, hypertension, deep vein thrombosis, ischemic heart disease, atherosclerotic heart disease, pulmonary hypertension, unstable angina pectoris, tricuspid regurgitation, nonrheumatic mitral, aortic, and valve disorders. Hypertension is the most common comorbidity in these cases. Increased systemic blood pressure increases resistance to blood flow from the left ventricle, leading to ventricular hypertrophy to increase contractile strength. This compensatory condition leads to increased oxygen demand in the myocardium. As a result, the workload of the heart increases, which can lead to angina and myocardial infarction (Boyette and Manna, 2023).

Treatment Accuracy

Analysis of medication accuracy, dosage, and frequency in heart failure patients with or

without comorbidities at Tangerang district hospital was based on the 2023 heart failure management guidelines. Table 2 shows data concerning treatment accuracy according to the PERKI 2023.

Drug Class

Based on the case data of heart failure hospitalized at Tangerang district hospital, the medications used consist of various therapeutic classes that are in line with the available management of heart disease. These medications include ACE-Inhibitors, ARNI, ARB, Beta-Blockers, Aldosterone Antagonists, SGLT2 Inhibitors, Loop Diuretics, as well as additional medications for low ejection fraction such as Digoxin and Ivabradine. Based on their classes, Table 3 shows the obtained data as follows.

Dosage

Based on the data of heart failure patients at Tangerang district hospital, out of 78 available medical records, several discrepancies were found in the dosage compared to the

recommended therapy management by PERKI 2023. In detail, there were 25 cases of dosage discrepancies, with the distribution as follows: spironolactone (10 cases), empagliflozin (6 cases), bisoprolol (3 cases), sacubitril-valsartan (2 cases), candesartan (1 case), valsartan (1 case), digoxin (1 case), and ramipril (1 case). Among all the reviewed medical records, 55 patients (70.51%) received the correct dosage per single administration. However, 12 patients (15.38%) received insufficient dosages, and 11 patients (14.10%) received excessive dosages in a single administration. Thus, 55 patients (70.51%) received appropriate dosages, while 23 patients (29.49%) experienced dosage discrepancies.

When considering daily dosages, there were several discrepancies in dosage per single usage compared to the heart disease therapy management in PERKI 2023. A total of 33 patients (42.31%) experienced discrepancies in daily dosage administration for one or several drugs, while 45 patients (57.69%) received appropriate daily dosages for all drugs.

Table 2. Treatment accuracy based on PERKI 2023 Guidelines

| Treatment Accuracy | n | % |
|--------------------|----|-------|
| Category | | |
| Correct | 78 | 100 |
| Incorrect | - | - |
| Dosage | | |
| Correct | 55 | 70.51 |
| Incorrect | 23 | 29.4 |
| Frequency | | |
| Correct | 45 | 57.69 |
| Incorrect | 33 | 42.31 |

Table 3. Medication use in heart failure patients based on PERKI 2023

| Drug Categories | n | % |
|---|----|-------|
| ACE-Inhibitor (Ramipril) | 34 | 43.59 |
| ARNI (Sacubitril-Valsartan) | 16 | 20.51 |
| ARB (Candesartan, Valsartan) | 17 | 21.79 |
| Beta-Blocker (Bisoprolol, Carvedilol) | 53 | 67.95 |
| Aldosterone Antagonist (Spironolactone) | 59 | 75.64 |
| SGLT2 Inhibitor (Empagliflozin) | 6 | 7.69 |
| Diuretic Loop (Furosemide) | 72 | 92.31 |
| Digoxin | 12 | 15.38 |
| Ivabradine | 16 | 20.51 |

The breakdown is as follows: 45 patients (57.69%) received appropriate daily dosages for all drugs, 6 patients (7.69%) received insufficient daily dosages for one drug, 23 patients (29.49%) received excessive daily dosages for one or several types of drugs, and 4 patients (5.13%) received both excessive and insufficient daily dosages for more than one drug. The detailed cases of daily dosage discrepancies based on drug types are as follows: ivabradine (8 cases), spironolactone (8 cases), sacubitril-valsartan (6 cases), ramipril (8 cases), empagliflozin (5 cases), and bisoprolol (3 cases).

Frequency

Based on the case data of heart failure patients at Tangerang district hospital, out of 78 available medical records, there were 33 patients (42.31%) who experienced issues with medication frequency, while 45 patients (57.69%) did not have any problems with medication frequency. Inappropriateness in medication frequency can lead to daily dosages that do not comply with the applicable therapy management, either below the minimum limit or above the maximum limit. Differences in medication frequency were found for several types of drugs, namely spironolactone, digoxin, ramipril, ivabradine, empagliflozin, sacubitril-valsartan, and bisoprolol. Meanwhile, other medications showed minimal errors in dosing frequency.

The results of this study are also consistent with research reviewed by Adondis *et al.*, where in the therapy algorithm for patients with heart failure, the first-line therapy for these patients is from the diuretic class (Adondis *et al.*, 2019). A total of 37 inpatient heart failure patients at Advent Manado Hospital received diuretics, with 15 of them receiving furosemide and 12 receiving spironolactone. Similar research was also conducted by Wulandari *et al.* (2018), where in congestive heart failure inpatients at Sultan Syafi Mohamad Alkadrie Pontianak Hospital, out of 31 existing patients, the most commonly used drugs were diuretics with a percentage of 62.5%, with the most commonly used first-line drug being furosemide with a percentage of 37.5% (Wulandari *et al.*, 2018).

Diuretics increase urine flow and sodium excretion to balance body fluid composition, including in heart failure conditions. In heart failure, increased volume is caused by reduced cardiac output, inhibiting blood flow to the kidneys. This condition causes the synthesis of

angiotensin II and aldosterone, which cause sodium and water retention. This sodium and water retention will cause swelling or congestion. Diuretics are used to address these clinical conditions (Adondis *et al.*, 2019). In single therapy for patients with heart failure, those who receive combination drugs range from 2 combinations to 7 combinations of drugs. This can occur due to adjustments to the patient's clinical condition so that everyone receives a different combination of drugs. Comorbidities can also be a factor in drug combination administration. Based on the research results, several inconsistencies were found in the use of drug doses in patients with heart failure compared to the therapeutic management recommended by PERKI 2023. These drug dose inconsistencies can have serious consequences for therapy effectiveness and patient safety. For example, excessive doses can increase the risk of harmful side effects, while doses that are too low may not provide optimal benefits in controlling heart failure. Accordingly, it is important for healthcare practitioners to adhere to recommended dosage guidelines and make appropriate adjustments based on individual patient characteristics and clinical conditions. This can help ensure that patients receive optimal and safe therapy (Khairani *et al.*, 2023)

This research found that some heart failure patients also experience issues with the frequency of medication. Inappropriateness in medication frequency can have serious implications for treatment effectiveness and patient well-being. For instance, if the medication frequency is incorrect, the daily doses administered may not align with the recommended therapeutic management guidelines, potentially resulting in doses being below the minimum or above the maximum recommended limits. The issues in medication frequency are likely attributable to several factors, including insufficient knowledge among medical staff regarding the administration of cardiovascular drugs to patients, as well as errors in the documentation of dosage and frequency in patients' medical records. Therefore, efforts should be made to enhance the understanding and awareness among medical staff regarding the importance of adherence to the appropriate medication frequency as per existing guidelines, along with expanded efforts to ensure accurate and comprehensive documentation in patients' medical records (Khairani *et al.*, 2023). According to the results of the study, there were 1019 types of interactions

of 1093 types of drugs or the average patient gets 14 types of drugs. The more medication given will affect the length of hospital stay and require intensive care. This is crucial for minimizing the risks of medication errors and enhancing the quality of care for heart failure patients at Tangerang District Hospital.

Incidence of Potential Drug Interactions

Analysis of potential drug interactions was conducted using drug interaction checking websites such as drugs.com and tertiary literature such as Stockley's Drug Interactions. Based on the case data of heart failure patients at Tangerang district hospital, there were 1,020 cases of drug interactions. These data indicate that each patient received two or more drugs that potentially interacted. Table 4 shows the potential drug interactions in heart failure patients with or without comorbidities at Tangerang district hospital for the period 2023:

Based on the case data of patients with heart failure at the district hospital, there were 1,023 cases of drug interactions, indicating that one patient among the 78 received two or more interacting drugs. A total of 381 cases (37.46%) exhibited pharmacokinetic interactions. Based on the Absorption, Distribution, Metabolism, and Excretion/Elimination (ADME) principles, the most common group of pharmacokinetic drug interactions was at the metabolism level, totaling 144 cases (37.89%), followed by elimination with a total of 106 cases (27.89%), and absorption and distribution with a total of 65 cases each (17.11%). Furthermore, based on the case data of heart failure patients at the hospital, there were 1,023 cases of drug interactions, with 638 of them being pharmacodynamic interactions. These cases of drug interactions were dominantly at the pharmacodynamic level (synergistic) with a total of 396 cases (62.07%), followed by pharmacodynamic (antagonistic) cases with a total of 242 cases (37.93%). In the context of the degree of drug interactions, based on the case data of heart failure patients at the hospital, there were 1,023 cases of drug interactions, with 132 cases being major/severe, 786 cases moderate, and 101 cases minor. Most drug interaction degrees occurred at the moderate level, accounting for 77.13%, followed by the major level at 12.95%, and the minor level at 9.91%.

According to previous research optimal liver perfusion under normal physiological

conditions is predominantly governed by the blood flow from the portal vein and hepatic artery. Consequently, the liver is protected from ischemic attacks during brief periods of hypotension. However, several cardiovascular conditions can increase the risk of injury and predispose individuals to changes in drug metabolism. Heart disease, which impedes blood flow to the liver, can disrupt the disposition of drugs whose metabolism is influenced by blood flow. Indeed, ischemic hepatitis has been detected in 22% of all intensive cardiovascular care with reduced cardiac output, with this occurrence being more frequent in elderly patients. Dysfunction of the liver resulting from cardiovascular disease significantly impacts the pharmacokinetics of cardiovascular drugs by slowing down first-pass metabolism. The first-pass elimination process, where the liver plays a vital role in drug metabolism and excretion into bile, can reduce drug bioavailability (Jain *et al.*, 2017).

Factors that may contribute to the dominance of drug interactions at the pharmacodynamic level include the complexity of the body's response to drug interventions, individual variability in response to drugs, and the complex interactions among various biological mechanisms in the body. Additionally, the potential for combinations of drugs given to patients with pharmacodynamic profiles that either enhance or inhibit each other may also contribute to drug interactions at this level. For example, combinations of drugs that target the same receptors or affect similar biological pathways in the body can lead to synergistic or antagonistic interactions, depending on the mechanisms of action of each drug. Furthermore, patient characteristics such as overall health status, metabolic status, and genetic factors can also influence drug response and the potential for drug interactions at the pharmacodynamic level (Palleria *et al.*, 2013)

Based on the case data of patients with heart failure at the hospital, the majority of drug interactions occur at the moderate level, followed by major and minor levels. The dominance of drug interactions at the moderate level may be attributed to the complexity of patients' medical conditions, which often require the concurrent use of multiple medications to manage symptoms and complications related to heart failure. This can increase the risk of drug

interactions due to the potential for increased or decreased drug effects resulting from these interactions. Additionally, common patterns of medication use in heart failure patients, such as diuretics, beta-blockers, and ACE inhibitors, may also contribute to drug interactions. Other factors that may influence this include a lack of coordination among the medical team in managing patient medications, as well as a lack of understanding or awareness of the potential for drug interactions among healthcare professionals. Therefore, it is important to enhance monitoring and assessment of drug interactions in heart failure patients to optimize treatment management and prevent the risk of complications. (Sapna *et al.*, 2023)

Correlation Evaluation

Based on the results of the Spearman's statistical test shown in Table 5, a significance value of 0.000 ($p < 0.05$) was obtained. This finding indicates that there is a significant relationship between drug interactions and polypharmacy in patients with heart disease. Additionally, a correlation coefficient of 0.540 indicates a strong relationship between these two variables. The positive value of the correlation coefficient indicates that the relationship between drug interactions and polypharmacy is positive, meaning that as the

complexity of drug administration increases, the likelihood of drug interactions also increases, and vice versa.

The explanation regarding the significant relationship between drug interactions and polypharmacy in patients with heart disease can be attributed to the complexity of patients' health conditions and the potential interactions between drugs that may occur. Polypharmacy, or the concurrent use of multiple drugs, is often necessary in the treatment of heart disease to manage various symptoms and related complications. However, the more drugs that are administered, the higher the likelihood of drug interactions (Sheikh-Taha and Asmar, 2021)

This factor can be influenced by various elements, such as the pharmacological mechanisms of each drug, drug metabolism in the body, and individual sensitivity to specific drugs. Additionally, patients with heart disease often have other comorbidities that require additional treatment, which can increase the complexity of polypharmacy and the risk of drug interactions.

This situation is exacerbated by the lack of understanding or awareness among healthcare professionals regarding potential drug interactions and the lack of coordination among healthcare providers in managing patient medications. Therefore, it is crucial to enhance

Table 4. Potential drug interactions by interaction type

| Incidence of Potential Drug Interactions | n | % |
|--|-----|-------|
| Interaction Type | | |
| Pharmacokinetic | 381 | 37.46 |
| Pharmacodynamic | 636 | 62.53 |
| Degree of Interaction | | |
| Major | 130 | 12.78 |
| Moderate | 786 | 77.28 |
| Minor | 101 | 9.93 |

Table 5. Correlation evaluation

| | | Correlation | | |
|----------------|-------------------|-------------------------|-------|-------|
| Spearman's rho | Polypharmacy | Correlation Coefficient | 1.000 | 0.540 |
| | | Sig(2-tailed) | | 0.00* |
| | | n | 78 | 78 |
| | Drug Interactions | Correlation Coefficient | 0.540 | 1.000 |
| | | Sig(2-tailed) | 0.00* | |
| | | n | 78 | 78 |

* Significant correlation at the 0.05 level (2-tailed).

understanding and awareness of the risks of drug interactions in polypharmacy patients and strengthen coordinated monitoring and management systems to reduce the risk of undesired drug interactions in patients with heart disease (Rojas-Ocaña *et al.*, 2023)

CONCLUSIONS

Among several interesting findings, there was a significant relationship found between the potential drug interactions and polypharmacy in patients with heart failure, with a p-value of 0.000 and a correlation coefficient of 0.540. This result indicates a strong association between polypharmacy and the potential for drug interactions, suggesting that the more complex the use of drugs by patients, the higher the likelihood of drug interactions that can affect the effectiveness of therapy and clinical outcomes for patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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