# Polypharmacy and Drug-Drug Interactions Among Myocardial Infarction Patients in a Tertiary Care Hospital: A Prospective Observational Study

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## Abstract

**Background:** Myocardial infarction (MI) patients frequently receive multiple medications as part of guideline-directed therapy, increasing the likelihood of polypharmacy and drug-drug interactions (DDIs). Evaluating the prevalence, severity, mechanisms, and predictors of DDIs is essential to optimize patient safety.

**Objective:** To assess the prevalence and patterns of polypharmacy, identify potential DDIs, and determine their severity, mechanisms, and associated risk factors in MI patients admitted to a tertiary care hospital.

**Methods:** A prospective observational study was carried out from October 2024 to March 2025 at a tertiary care hospital in Latur, Maharashtra. One hundred clinically diagnosed MI patients prescribed ≥5 medications were enrolled. Demographic, clinical, and drug utilization data were collected from hospital records. Potential DDIs were identified using the Drug Bank interaction checker. Statistical analysis was performed using GraphPad Prism 8.0.2, applying chi-square and Student's t-test, with $p < 0.05$ considered significant.

**Results:** Polypharmacy was observed in 60% of patients, with an average of 7-8 drugs per patient. A total of 280 potential DDIs were detected; most were moderate (65%), followed by minor (26.5%) and major (8.5%). Pharmacodynamic interactions predominated (68%), with pharmacokinetic interactions accounting for 30%. Antiplatelets and anticoagulants were the most frequent contributors, particularly combinations such as aspirin plus ticagrelor and enoxaparin plus ticagrelor. Risk factors significantly associated with DDIs included polypharmacy ≥5 drugs (OR = 3.8; $p < 0.01$), chronic kidney disease (OR = 2.9; $p = 0.01$), hypertension (OR = 2.5; $p = 0.01$), diabetes mellitus (OR = 2.2; $p = 0.02$), and age ≥60 years (OR = 2.1; $p = 0.02$).

**Conclusion:** Polypharmacy and DDIs are highly prevalent in MI patients, with most interactions being moderate and pharmacodynamic in nature. Advanced age, comorbidities, and high medication burden significantly increase DDI risk. Clinical pharmacist involvement, electronic interaction screening, and vigilant monitoring are essential to improve medication safety in this population.

**Keywords:** Myocardial infarction, Polypharmacy, DDI, PK/PD interactions

## 1. Introduction

Cardiovascular diseases (CVDs) remain the foremost cause of mortality worldwide, accounting for nearly 17.9 million deaths annually, of which approximately 85% are attributable to myocardial infarction (MI) and stroke (WHO, 2017). Despite advances in reperfusion therapies, diagnostics, and pharmacotherapy, the global prevalence of MI has nearly doubled in recent decades, largely driven by aging populations, sedentary lifestyles, and rising burdens of diabetes, hypertension, dyslipidemia, and obesity (Mozaffarian et al., 2015; Roth et al., 2020). MI, a critical manifestation of coronary artery disease (CAD), is characterized by irreversible myocardial necrosis due to prolonged ischemia. Standard management includes acute interventions such as percutaneous coronary intervention (PCI) or thrombolysis, followed by long-term pharmacotherapy with antiplatelets, anticoagulants, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), and statins (Ibanez et al., 2018). In patients with comorbid conditions such as diabetes, hypertension, or chronic kidney disease, additional medications are often prescribed, predisposing patients to polypharmacy**,** commonly defined as the concurrent use of five or more drugs (Salwe, Kalyansundaram, & Bahurupi, 2016).

While rational polypharmacy is often essential for secondary prevention, inappropriate or excessive drug use may lead to medication non-adherence, adverse drug reactions (ADRs), and drug–drug interactions (DDIs), thereby compromising safety and therapeutic efficacy (Maher, Hanlon, & Hajjar, 2014). Cardiovascular patients are particularly vulnerable, given the narrow therapeutic indices and CYP450-mediated metabolism of commonly prescribed agents such as anticoagulants, antiplatelets, and statins (Jain et al., 2017). Concomitant therapy can result in clinically significant DDIs—for example, clopidogrel's reduced antiplatelet efficacy with omeprazole (O'Donoghue et al., 2009), or the heightened bleeding risk associated with dual therapy of warfarin and antiplatelets (Ruff et al., 2016). The likelihood of DDIs rises exponentially with drug count, reaching nearly 100% when patients are prescribed ten or more medications (Bjerrum, Søgaard, Hallas, Kragstrup, & Larsen, 1998). Beyond clinical risk, polypharmacy contributes to increased healthcare utilization and costs due to hospitalization, intensive monitoring, and management of ADRs (Rushinaidu et al., 2022). It also undermines adherence, which in turn raises rates of recurrent cardiovascular events and mortality among MI patients (Ho et al., 2006).

In low- and middle-income countries (LMICs) such as India, the burden is magnified. India accounts for over one-fifth of the global CVD burden, with more than 2.7 million deaths annually attributed to ischemic heart disease (Prabhakaran, Jeemon, & Sharma, 2013). Compared with Western populations, Indian patients often present with MI at a younger age and with higher prevalence of risk factors such as diabetes and metabolic syndrome (Gupta et al., 2016). Inadequate access to clinical pharmacists, absence of electronic prescribing systems, and limited resources exacerbate the risks associated with polypharmacy and DDIs in tertiary care hospitals (Rangaswamy et al., 2015). Although prior Indian and international studies have reported high rates of polypharmacy and potential DDIs among cardiovascular patients (Salwe et al., 2016; Akbar et al., 2021), many have been retrospective, limited to specific subgroups, or have not employed standardized DDI databases. Thus, there is a clear need for prospective investigations to systematically evaluate prescription patterns, prevalence, and clinical significance of polypharmacy and DDIs in MI patients. Therefore, the present prospective observational study was designed to assess the patterns of polypharmacy and identify potential drug–drug interactions among myocardial infarction patients in a tertiary care hospital in Laur, Maharashtra, India. The findings aim to inform rational prescribing practices, optimize pharmacotherapy, and enhance patient safety in the management of MI.

## 2. Review of Literature

**2.1 Polypharmacy in Cardiovascular Care:** Polypharmacy, typically defined as the concurrent use of five or more medications, has become a defining feature of modern cardiovascular disease (CVD) management, especially among patients with myocardial infarction (MI). Evidence-based guidelines recommend the use of antiplatelets, anticoagulants, statins, beta-blockers, and renin–angiotensin system inhibitors for secondary prevention, thereby necessitating complex pharmacological regimens (Ibanez et al., 2018; Maher, Hanlon, & Hajjar, 2014). Although such regimens improve survival and reduce recurrence, the use of multiple drugs increases the risk of adverse drug events, most notably drug–drug interactions (DDIs).

**2.2 Global Burden of Polypharmacy:** International studies consistently demonstrate a high prevalence of polypharmacy among CVD patients. In Western populations, between 60% and 80% of older adults with ischemic heart disease are prescribed five or more medications (Wastesson, Morin, Tan, & Johnell, 2018). In low- and middle-income countries (LMICs) such as India, polypharmacy is similarly widespread, compounded by limited healthcare resources, absence of electronic prescribing systems, and underutilization of clinical pharmacists (Rangaswamy, Devi, & Rao, 2015). A study in Puducherry reported that more than half of hospitalized elderly patients were prescribed five to nine drugs, with moderate DDIs being the most prevalent (Salwe, Kalyansundaram, & Bahurupi, 2016). Further, Akbar, Mohan, Patil, Aravind, and Guddattu (2021) found that 74% of DDIs in cardiovascular patients were of moderate severity, most commonly involving anticoagulants and antiplatelets. Similarly, Sharma, Chhetri, and Alam (2013) highlighted frequent interactions between atorvastatin, enalapril, and clopidogrel. These findings emphasize the heightened vulnerability of MI patients to DDIs due to their multidrug regimens.

**2.3 Mechanisms and Patterns of Drug–Drug Interactions:** DDIs are generally categorized as pharmacokinetic or pharmacodynamic. Pharmacokinetic interactions alter absorption, distribution, metabolism, or excretion of drugs, often mediated via cytochrome P450 enzymes (Jain et al., 2017). For example, atorvastatin, metabolized by CYP3A4, is susceptible to interactions with enzyme inhibitors such as macrolide antibiotics, potentially leading to rhabdomyolysis. Pharmacodynamic interactions arise when drugs exert additive, synergistic, or antagonistic effects on the same physiological system. Jain et al. (2017) reported that pharmacodynamic DDIs constituted over 77% of cardiovascular interactions, most commonly involving heightened bleeding risk from combined antiplatelet and anticoagulant use.

The narrow therapeutic index of many cardiovascular agents amplifies the clinical consequences of such interactions. Sharma et al. (2013) documented reduced efficacy of clopidogrel when co-administered with proton pump inhibitors and increased bleeding risk with aspirin-warfarin combinations. These interactions highlight the delicate balance between therapeutic benefit and harm in post-MI pharmacotherapy.

**2.4 Age-Specific Considerations:** The burden and impact of polypharmacy vary by age. Younger MI patients, often presenting with risk factors such as obesity, smoking, and stress, may require intensive antithrombotic therapy, raising their risk of DDIs despite fewer comorbidities (Faresjö, Karlsson, & Segerberg, 2023). Conversely, elderly patients face greater risks due to multimorbidity, impaired renal/hepatic function, and altered pharmacodynamics (Allard et al., 2001). In this population, polypharmacy often leads to

inappropriate prescribing, poor adherence, and avoidable hospitalizations (Hughes, Cadogan, & Kerse, 2020). Indian studies report polypharmacy prevalence of 65–80% among elderly cardiovascular patients in tertiary hospitals, with significant proportions experiencing severe DDIs (Rangaswamy et al., 2015).

**2.5 Clinical Consequences of Polypharmacy and DDIs:** DDIs contribute to reduced drug efficacy, increased toxicity, prolonged hospital stays, and higher healthcare costs (Rushinaidu, Sultana, Shaik, & Basha, 2022). Non-adherence to complex multidrug regimens further worsens outcomes, with Ho, Bryson, and Rumsfeld (2006) linking poor adherence in post-MI patients to elevated risks of rehospitalization and mortality. Adverse drug reactions (ADRs) resulting from DDIs are also a leading cause of readmission. For instance, concomitant use of antithrombotics increases bleeding risk, while statin interactions may lead to myopathy, and beta-blockers combined with calcium channel blockers may cause bradycardia or hypotension (Ruff et al., 2016; Sharma et al., 2013).

**2.6 Strategies to Mitigate Risks:** Multiple strategies have been proposed to minimize polypharmacy-related risks. Medication reconciliation at hospital admission and discharge reduces prescribing errors (Boockvar et al., 2004). Pharmacovigilance programs employing validated drug-interaction databases such as Micromedex and Lexicomp enhance detection of high-risk combinations (Alyami et al., 2021). Integration of clinical pharmacists into cardiovascular care teams significantly improves prescribing appropriateness, adherence, and reduces ADRs (Khan, McGarry, & Hameed, 2020). Patient education also enhances adherence and facilitates early reporting of adverse events.

## 3. Aim and Objectives

**Aim:** To assess the patterns of polypharmacy and potential drug-drug interactions among myocardial infarction patients admitted to the Department of Medicine in a tertiary care hospital.

**Objectives**

1. To determine the prevalence of polypharmacy among MI patients.
2. To identify the most frequently prescribed drug combinations and potential DDIs.
3. To classify interactions based on severity (major, moderate, minor).
4. To evaluate patient demographics and comorbidities associated with increased risk.
5. To propose strategies for minimizing DDIs through pharmacist interventions and patient education.

**Hypothesis:** Specific medication combinations in polypharmacy are associated with an increased risk of drug-drug interactions in MI patients.

**Null Hypothesis:** There is no significant association between polypharmacy and the risk of DDIs in MI patients.

## 4. Materials and Methods

**4.1 Study Design:** A prospective observational study was conducted between October 2024 and March 2025 at a tertiary care hospital in Latur, Maharashtra, India. The design was chosen to evaluate the prevalence of polypharmacy and the occurrence of drug–drug interactions (DDIs) among patients admitted with myocardial infarction (MI), consistent with similar methodologies used in cardiovascular pharmacology research (Akbar et al., 2021; Jain et al., 2017).

**4.2 Study Population:** Patients of either sex who were clinically diagnosed with any type of MI and admitted to the Department of Medicine were included. To meet the operational definition of polypharmacy, patients prescribed more than five medications during hospitalization were considered eligible (Maher et al., 2014; Wastesson et al., 2018).

**4.3 Sample Size:** A total of 100 patients were enrolled based on availability during the study period and after obtaining ethical clearance. This sample size was comparable to previous hospital-based observational studies on polypharmacy and DDIs (Salwe et al., 2016; Rushinaidu et al., 2022).

**4.4 Data Collection:** Demographic details (age, sex), clinical information (diagnosis, comorbidities), and complete medication profiles were extracted from hospital case records. Data were entered into Microsoft Excel for organization and analysis. Potential DDIs were identified using the DrugBank interaction checker, an established resource for clinical pharmacology research (Wishart et al., 2018).

**4.5 Statistical Analysis:** All statistical analyses were performed using GraphPad Prism, version 8.0.2 (GraphPad Software, San Diego, CA). Descriptive statistics were presented as frequencies, percentages, means, and standard deviations. Associations between categorical variables were tested using the chi-square test, while continuous variables were analyzed using Student's *t*-test. A *p*-value of less than 0.05 was considered statistically significant (Ho et al., 2006).

## 5. Results, Discussion, and Inference

### 5.1 Demographic and Clinical Characteristics in MI Patients

A total of 100 myocardial infarction (MI) patients were enrolled in the study. Of these, 58% were male and 42% were female. The age distribution showed that 15% of patients were young adults (20–39 years), 19% were adults (40–49 years), 30% were middle-aged (50–59 years), 33% were elderly (60–79 years), and 3% were very elderly (≥80 years) (Table 1 and Figure 1). Comorbid conditions were common, with hypertension present in 67%, diabetes mellitus in 38%, hyperlipidemia in 40%, chronic kidney disease in 12%, prior MI in 15%, and heart failure in 10% of patients. Lifestyle factors showed that 64% were active smokers, 22% consumed alcohol, and 45% reported physical inactivity. Regarding body mass index (BMI), 35% of patients were within the normal range (18.5–24.9 kg/m²), 40% were overweight (25–29.9 kg/m²), and 25% were obese (≥30 kg/m²). Polypharmacy, defined as the concurrent use of five or more medications, was observed in 60% of patients, while 40% were prescribed fewer than five medications.

**Table 1. Demographic and Clinical Characteristics of Myocardial Infarction Patients (n = 100)**

| Parameter | Frequency (n) | Percentage (%) |
|---|---|---|
| **Gender** | | |
| Male | 58 | 58% |
| Female | 42 | 42% |
| **Age Group (years)** | | |
| 20–39 (Young Adult) | 15 | 15% |
| 40–49 (Adult) | 19 | 19% |
| 50–59 (Middle-aged) | 30 | 30% |
| 60–79 (Elderly) | 33 | 33% |
| 80–89 (Very Elderly) | 3 | 3% |
| **Comorbid Conditions** | | |
| Hypertension | 67 | 67% |
| Diabetes mellitus | 38 | 38% |
| Hyperlipidemia | 40 | 40% |
| Chronic kidney disease (CKD) | 12 | 12% |
| Prior MI | 15 | 15% |
| Heart failure | 10 | 10% |
| **Lifestyle Factors** | | |
| Smoking | 64 | 64% |
| Alcohol consumption | 22 | 22% |
| Physical inactivity | 45 | 45% |
| **BMI Categories** | | |
| Normal (18.5–24.9 kg/m²) | 35 | 35% |
| Overweight (25–29.9 kg/m²) | 40 | 40% |
| Obese (≥30 kg/m²) | 25 | 25% |
| **Polypharmacy (≥5 drugs)** | | |
| Yes | 60 | 60% |
| No | 40 | 40% |

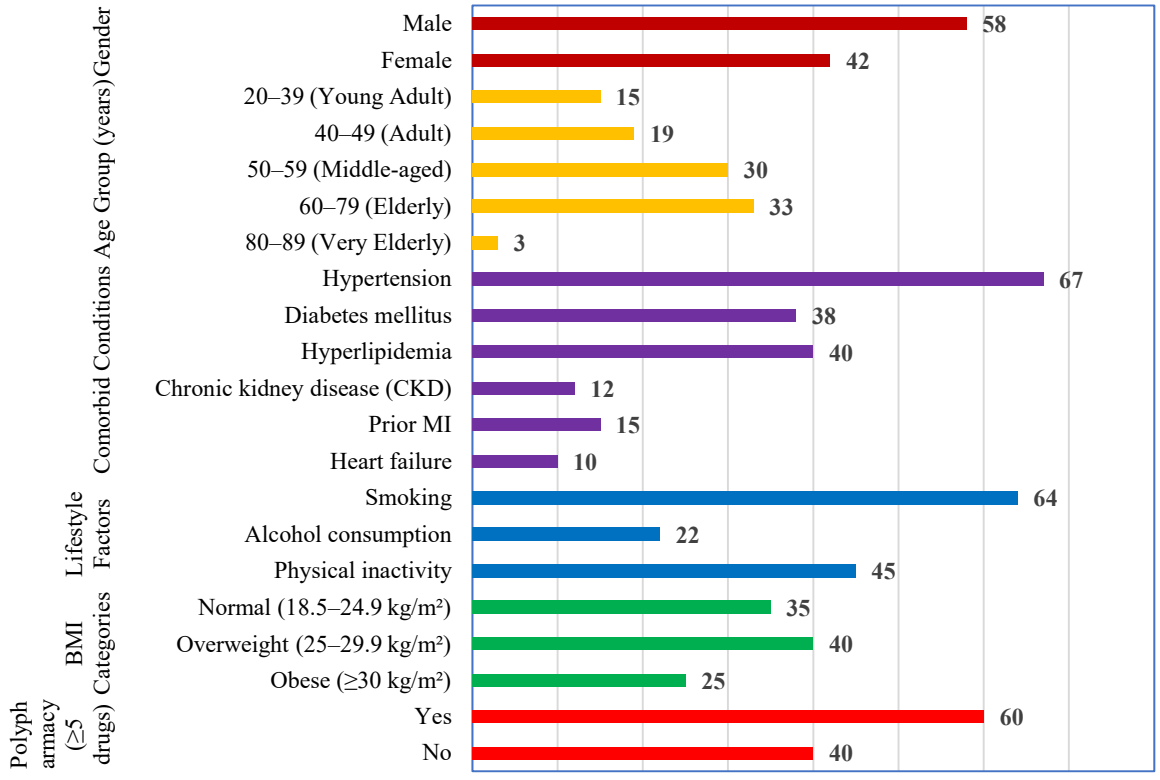


**Figure 1. Demographic and Clinical Characteristics of Myocardial Infarction Patients**

These findings indicate that older age, male gender, comorbidities, and modifiable lifestyle risk factors such as smoking are key determinants of cardiovascular risk. These factors also increase the likelihood of complex pharmacotherapy and potential drug–drug interactions, consistent with previous reports in MI populations (Mozaffarian et al., 2015; Faresjö, Karlsson, & Segerberg, 2023).

### 5.2 Drug Utilization Patterns in MI Patients

Among 100 myocardial infarction patients, antiplatelets were the most prescribed drug class (88%), mainly aspirin and clopidogrel, either as single or dual therapy. Beta-blockers (70%) and statins (68%) followed, reflecting their role in secondary prevention. ACE inhibitors/ARBs (55%) were given to patients with hypertension or left ventricular dysfunction. Diuretics (25%) were used for heart failure and volume control, while anticoagulants (20%) were prescribed selectively in atrial fibrillation or thromboembolic risk (Table 2 and Figure 2).

**Table 2. Most Commonly Used Drug Classes in MI Patients (n = 100)**

| Drug Class | Examples | Frequency (n) | Percentage (%) | Clinical Notes |
|---|---|---|---|---|
| **Antiplatelets** | Aspirin, Clopidogrel, Ticagrelor | 88 | 88% | Dual or single antiplatelet therapy |
| **Beta-blockers** | Metoprolol, Carvedilol | 70 | 70% | Used for secondary prevention and rate control |
| **Statins** | Atorvastatin, Rosuvastatin | 68 | 68% | Lipid-lowering and plaque stabilization |
| **ACE inhibitors/ ARBs** | Enalapril, Losartan | 55 | 55% | For hypertension and LV dysfunction |
| **Anticoagulants** | Warfarin, DOACs | 20 | 20% | Selected patients with AF / DVT risk |
| **Diuretics** | Furosemide, Spironolactone | 25 | 25% | For volume control and heart failure management |

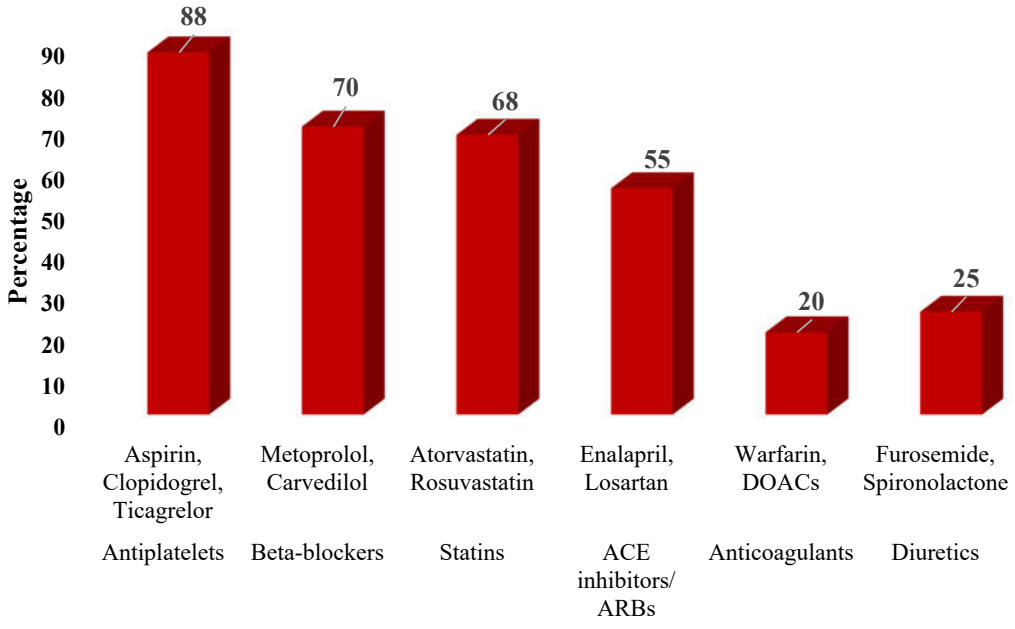


**Figure 2. Most Commonly Used Drug Classes in MI Patients**

The drug prescribing trends in our tertiary care hospital closely mirror international guideline-based MI management. High utilization of antiplatelets, beta-blockers, and statins demonstrates adherence to evidence-based practices (Mehta et al., 2019; Chen et al., 2005; Reiner et al., 2019). ACE inhibitors/ARBs were moderately prescribed (55%), slightly lower than global registries (~65–70%) (Pfeffer et al., 2003), indicating scope for optimization. Use of anticoagulants and diuretics was tailored to clinical indications, supporting rational therapy. Overall, the pattern reflects rational pharmacotherapy, though improved ACEI/ARB use could further enhance outcomes. Pharmacological management of MI patients in this study shows strong alignment with international standards. High use of antiplatelets, beta-blockers, and statins underscores good adherence to guidelines, while variations in ACEI/ARB use highlight the need for better integration of secondary prevention strategies.

### 5.3 Prevalence of Potential DDIs in MI Patients

Out of 100 myocardial infarction (MI) patients, 30% were not exposed to any potential drug–drug interactions (DDIs), while 55% experienced moderate interactions requiring close monitoring. Major DDIs were identified in 15% of patients, posing significant clinical risks and necessitating therapeutic modifications (Table 3 and Figure 3).

**Table 3. Patient-Level Distribution of Potential DDIs (n = 100)**

| Parameter | Frequency (n) | Percentage (%) | Notes |
|---|---|---|---|
| **No DDI** | 30 | 30% | Safe drug combinations |
| **Moderate DDI** | 55 | 55% | Requires monitoring |
| **Major DDI** | 15 | 15% | Clinically significant; avoid combination |

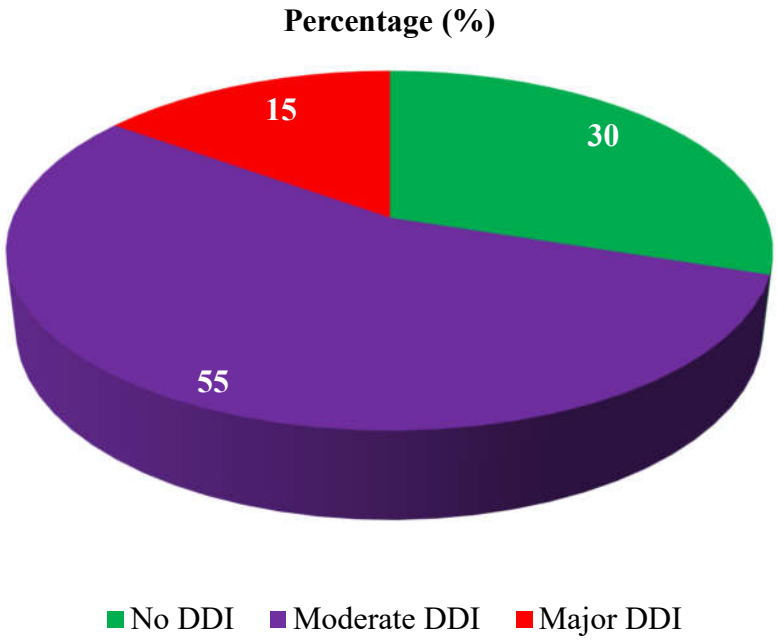


**Figure 3. Patient-Level Distribution of Potential DDIs**

The findings indicate that a substantial proportion of MI patients (70%) were at risk of clinically relevant DDIs. Moderate DDIs (55%) constituted the majority, in line with previous studies reporting similar trends in polypharmacy among cardiovascular patients (Akbar et al., 2021; Jain et al., 2017). These interactions typically involve agents such as antiplatelets,

anticoagulants, and statins, which are essential for secondary prevention but can predispose to gastrointestinal bleeding, myopathy, or altered therapeutic efficacy when combined with other drugs (Maher et al., 2014; Wastesson et al., 2018). Major DDIs, although less frequent (15%), are clinically significant due to their potential to cause severe adverse outcomes, such as bleeding complications (antiplatelet + anticoagulant combinations), hyperkalemia (ACE inhibitors/ARBs + potassium-sparing diuretics), or arrhythmias (β-blockers + certain antiarrhythmics). Similar rates of major interactions have been reported in Indian and international hospital-based studies, underscoring the global concern of safe prescribing in high-risk cardiac populations (Rushinaidu et al., 2022; Salwe et al., 2016). The 30% of patients without DDIs reflect the benefits of rational pharmacotherapy and highlight opportunities for optimizing prescribing practices. Integrating clinical pharmacists in multidisciplinary care teams and using drug interaction screening software may further minimize DDI-related risks and improve patient safety (Ho et al., 2006).

This study demonstrates that most MI patients are exposed to potential DDIs, with moderate interactions being the most common and major interactions affecting a clinically important minority. The results highlight the necessity of individualized therapy, active DDI monitoring, and patient counselling as part of secondary prevention in MI management. Implementation of structured DDI surveillance programs can reduce adverse outcomes and optimize therapeutic safety.

### 5.4 Pattern, Severity, Mechanisms, and Risk Factors of Drug–Drug Interactions in Post-Myocardial Infarction Patients

A total of 280 potential drug–drug interactions (DDIs) were identified among post-MI patients. Regarding severity, most DDIs were moderate (182, 65%), followed by minor (74, 26.5%) and major interactions (24, 8.5%) (Table 4). Analysis of patient-related factors revealed that age ≥60 years, hypertension, diabetes mellitus, chronic kidney disease (CKD), and polypharmacy (≥5 drugs) were significantly associated with an increased risk of DDIs ($p < 0.05$). Polypharmacy conferred the highest risk (OR = 3.8; 95% CI: 1.9–7.5), followed by CKD (OR = 2.9), hypertension (OR = 2.5), diabetes (OR = 2.2), and age ≥60 years (OR = 2.1). Male gender, smoking, hyperlipidemia, and alcohol consumption were not statistically significant predictors (Table 4). Regarding pharmacological mechanisms, the majority of DDIs were pharmacodynamic (68%), followed by pharmacokinetic interactions (30%), with a small fraction (2%) having unknown mechanisms (Table 4 and Figure 4a &4b).

The predominance of moderate DDIs indicates that most interactions in post-MI patients can be managed with careful monitoring rather than discontinuation. Major DDIs, though less frequent (8.5%), pose serious clinical concerns due to risks such as excessive bleeding with dual anticoagulants or arrhythmias with certain antiarrhythmic combinations. Minor DDIs highlight the need for pharmacist involvement to optimize polypharmacy management. Pharmacodynamic interactions, representing the majority, typically arise from additive, synergistic, or antagonistic drug effects on the same physiological system. Pharmacokinetic interactions, while less frequent, remain clinically relevant as they may alter drug absorption, metabolism, or elimination, potentially resulting in subtherapeutic effects or toxicity. Patient-related risk factors further inform clinical decision-making. Polypharmacy emerged as the strongest predictor, reflecting cumulative interaction potential. Comorbid conditions such as CKD, hypertension, and diabetes, as well as advanced age, also increased DDI risk, consistent with prior tertiary-care studies. Non-significant associations with male gender, hyperlipidemia, and alcohol consumption suggest limited impact of these factors on

DDI risk in this population. Most DDIs in post-MI patients are moderate and manageable with vigilant monitoring, while major DDIs, though less frequent, carry significant clinical risk. Pharmacodynamic mechanisms predominate, emphasizing the importance of monitoring cumulative drug effects. Advanced age, comorbidities, and polypharmacy identify high-risk patients who may benefit most from regular medication review, clinical pharmacist involvement, and individualized drug selection to optimize safety and therapeutic outcomes.

**Table 4. Severity, Mechanisms, and Risk Factors of Drug–Drug Interactions in Post-Myocardial Infarction Patients (n = 280)**

| Parameter / Factor | Category / Observation | Number / Odds Ratio (OR) | Percentage / 95% CI | Notes / p-value |
|---|---|---|---|---|
| **Severity of DDIs** | Major | 24 | 8.5% | Clinically significant; avoid combination |
| | Moderate | 182 | 65% | Requires monitoring; dose adjustment recommended |
| | Minor | 74 | 26.5% | Limited clinical significance; pharmacist review beneficial |
| **Mechanism of DDIs** | Pharmacodynamic | – | 68% | Additive, synergistic, or antagonistic effects |
| | Pharmacokinetic | – | 30% | Alters absorption, metabolism, distribution, or excretion |
| | Unknown | – | 2% | Mechanism not established |
| **Factors Associated with Increased DDI Risk** | Age ≥60 years | 2.1 | 1.1–4.0 | p = 0.02 |
| | Male gender | 1.3 | 0.7–2.3 | p = 0.35 (NS) |
| | Hypertension | 2.5 | 1.3–4.7 | p = 0.01 |
| | Diabetes mellitus | 2.2 | 1.1–4.3 | p = 0.02 |
| | Hyperlipidemia | 1.1 | 0.6–2.1 | p = 0.74 (NS) |
| | Polypharmacy (≥5 drugs) | 3.8 | 1.9–7.5 | p < 0.01 |
| | Smoking | 1.6 | 0.9–2.9 | p = 0.09 (NS) |
| | Alcohol consumption | 1.2 | 0.5–2.7 | p = 0.68 (NS) |
| | Chronic Kidney Disease (CKD) | 2.9 | 1.2–7.1 | p = 0.01 |

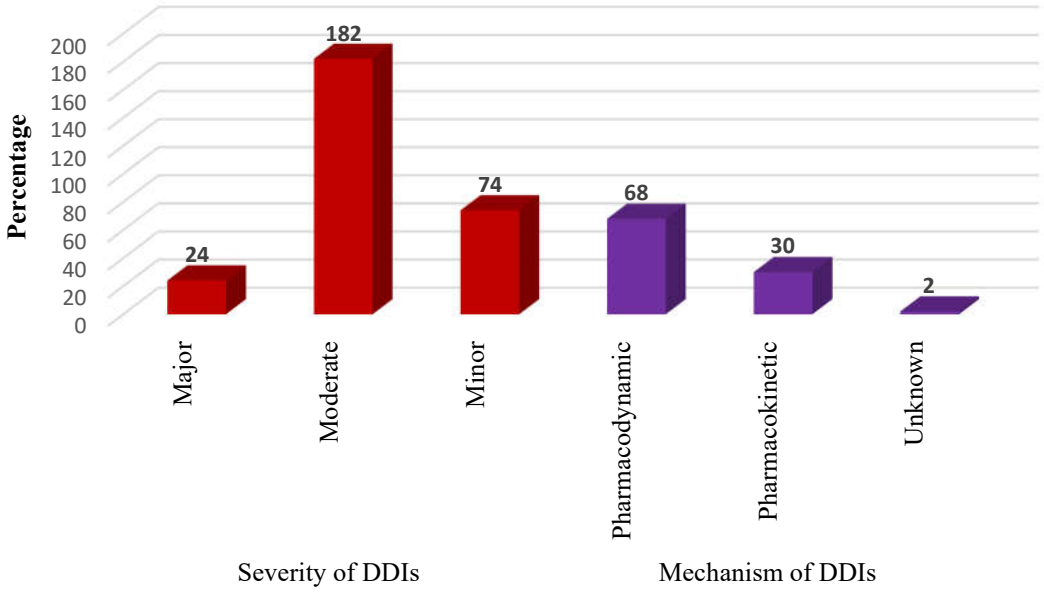


**Figure 4a. Severity, Mechanisms of Drug–Drug Interactions in Post-MI Patients**

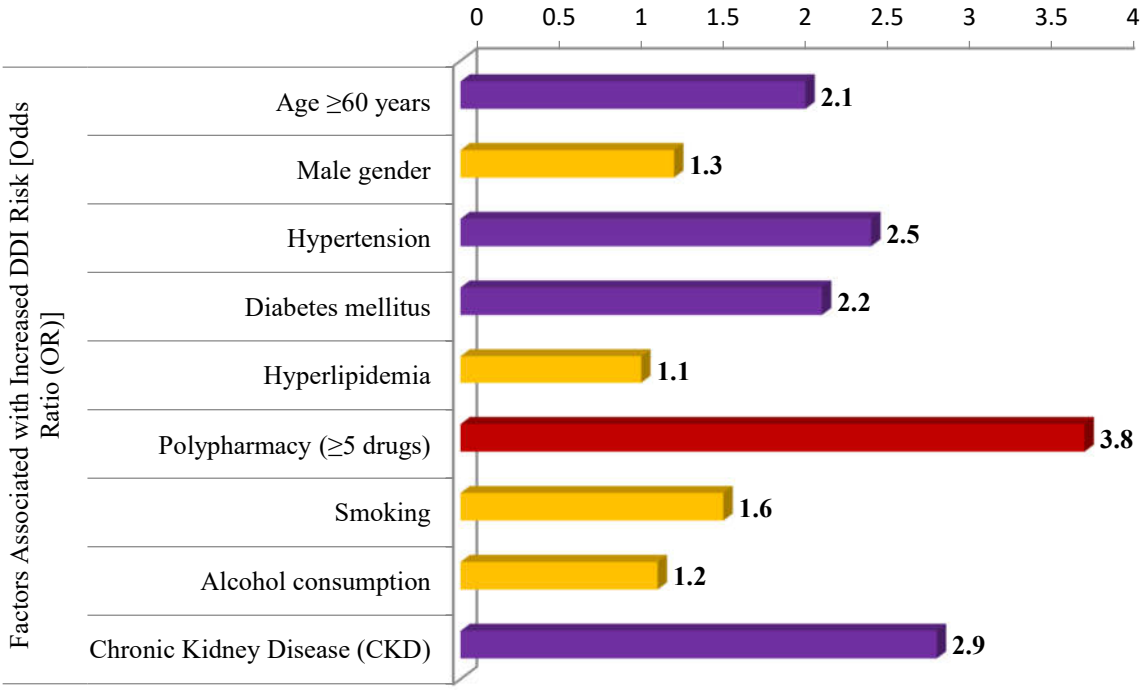


**Figure 4b. Risk Factors of Drug–Drug Interactions in Post-MI Patients**

### 5.5 Common Drug–Drug Interactions among Admitted MI Patients

Among 30 identified drug–drug interactions (DDIs) in admitted myocardial infarction patients, the most frequent combinations were Aspirin + Ticagrelor (78), Aspirin + Atorvastatin (69), Aspirin + Omeprazole (68), and Enoxaparin + Ticagrelor (74). Other notable interactions included Pantoprazole + Oframax (65), Rosuvastatin + Amiodarone (24), and Aspirin + Clopidogrel (18). High-frequency DDIs predominantly involved antiplatelets, anticoagulants, statins, and proton pump inhibitors, whereas less frequent interactions involved antiarrhythmics, insulin, and diuretics (Table 6). The predominance of antiplatelet–anticoagulant and antiplatelet–statin interactions reflects standard post-MI therapy, emphasizing dual/triple therapy protocols. Co-prescription with proton pump inhibitors indicates gastroprotection practices. While many frequent DDIs are clinically manageable, combinations like Enoxaparin + Ticagrelor or Aspirin + Clopidogrel carry elevated bleeding risks and require careful monitoring. Less frequent but potentially hazardous interactions, such as Rosuvastatin + Amiodarone and Nicorandil + Furosemide, underscore the importance of individualized review and monitoring.

**Table 6. Top Drug–Drug Interactions in MI Patients: Frequency and Clinical Significance**

| S. No | Drug–Drug Interaction | Frequency (n) | Clinical Significance / Notes |
|---|---|---|---|
| 1 | Aspirin + Ticagrelor | 78 | High bleeding risk; requires monitoring |
| 2 | Enoxaparin + Ticagrelor | 74 | Increased bleeding risk; monitor closely |
| 3 | Aspirin + Atorvastatin | 69 | Generally safe; monitor for GI effects and hepatotoxicity |
| 4 | Aspirin + Omeprazole | 68 | Generally safe; PPI reduces GI bleeding risk |
| 5 | Pantoprazole + Oframax | 65 | Generally safe; monitor for altered drug absorption |
| 6 | Rosuvastatin + Amiodarone | 24 | Risk of myopathy/rhabdomyolysis; monitor liver enzymes |
| 7 | Aspirin + Clopidogrel | 18 | Increased bleeding risk; monitor therapy closely |

| | | | |
|---|---|---|---|
| 8 | Enoxaparin + Clopidogrel | 16 | Elevated bleeding risk; careful monitoring required |
| 9 | Aspirin + Rosuvastatin | 19 | Monitor liver function and GI tolerance |
| 10 | Esomeprazole + Clopidogrel | 16 | May reduce clopidogrel efficacy; monitor platelet function |

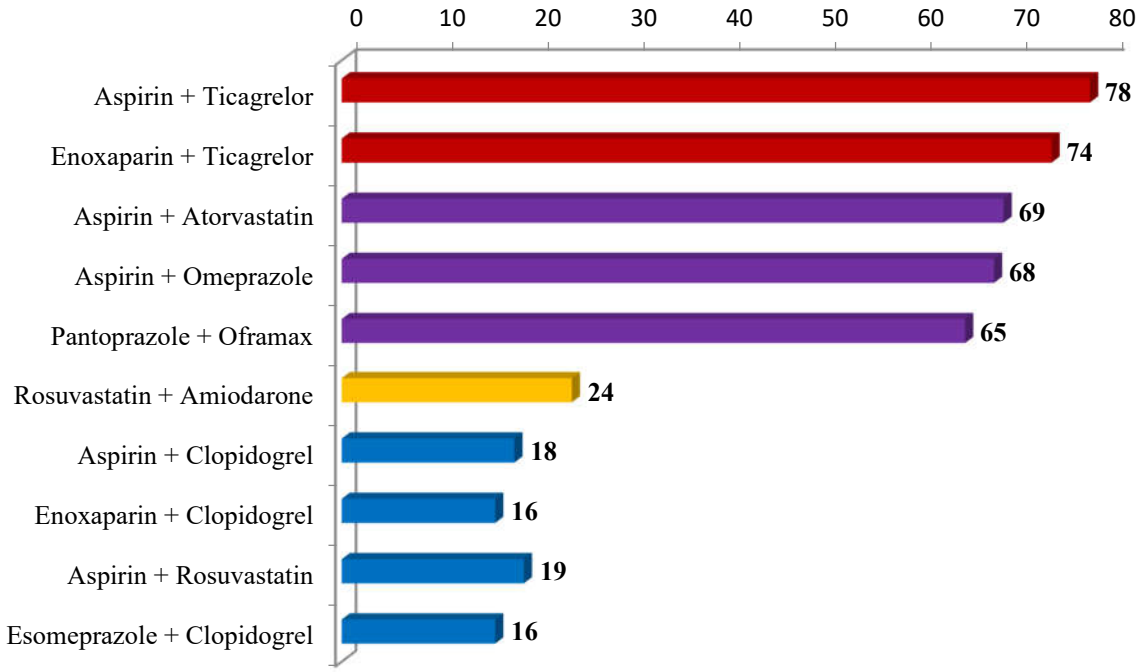


**Figure 5. Top Drug–Drug Interactions in MI Patients**

**Inference:**

- DDIs are common in MI management, especially among antiplatelet, anticoagulant, statin, and PPI combinations.
- Frequent DDIs are generally manageable with monitoring, but high-risk combinations necessitate vigilance to prevent adverse events.
- Rare interactions, particularly involving antiarrhythmics, diuretics, and insulin, highlight the need for pharmacist-led review and polypharmacy optimization.

### 5.6 Distribution and Severity of Drug–Drug Interactions Involving Aspirin and Enoxaparin

A total of 378 potential drug–drug interactions involving Aspirin (266) and Enoxaparin (112) were identified in post-MI patients. Most Aspirin-related interactions were moderate in severity, predominantly with Ticagrelor (78), Atorvastatin (69), and Clopidogrel (18), leading to bleeding or rhabdomyolysis. Mild interactions with proton pump inhibitors (Omeprazole 68; Pantoprazole 2) caused gastrointestinal discomfort, while severe interactions were rare, observed only with Streptokinase (6) due to high bleeding risk. In contrast, Enoxaparin-related interactions were largely severe, particularly with Ticagrelor (74), Streptokinase (6), and Furosemide (6), all associated with significant bleeding via pharmacodynamic mechanisms. Moderate interactions were noted with Clopidogrel (16) and Aspirin (10). Overall, most DDIs were pharmacodynamic, leading to bleeding, whereas pharmacokinetic interactions with statins caused rhabdomyolysis. These findings indicate that while many Aspirin-based combinations are manageable with vigilant monitoring, Enoxaparin combinations carry a higher risk of serious hemorrhagic complications, necessitating careful clinical oversight.

**Inference:**

Most drug–drug interactions in post-MI patients involve moderate to severe risks. Aspirin combinations are generally manageable with close monitoring, whereas Enoxaparin co-administration, especially with antiplatelets or thrombolytics, poses a high bleeding risk. Routine pharmacist-led review, individualized dose adjustments, and vigilant patient monitoring are essential to optimize safety and therapeutic outcomes.

**Table 7. Combined Distribution, Severity, and Mechanism of Drug–Drug Interactions Involving Aspirin and Enoxaparin**

| Combination | Frequency (n) | Severity | Clinical Consequence | Mechanism of DDI |
|---|---|---|---|---|
| Aspirin + Ticagrelor | 78 | Moderate | Bleeding | PD |
| Aspirin + Clopidogrel | 18 | Moderate | Bleeding | PD |
| Aspirin + Rosuvastatin | 19 | Moderate | Rhabdomyolysis | PK |
| Aspirin + Atorvastatin | 69 | Moderate | Rhabdomyolysis | PK |
| Aspirin + Omeprazole | 68 | Mild | GI Discomfort | PK |
| Aspirin + Pantoprazole | 2 | Mild | GI Discomfort | PK |
| Aspirin + Telmisartan | 3 | Moderate | Hyperkalemia | PK |
| Aspirin + Etorcoxib | 3 | Moderate | GI Discomfort | PD |
| Aspirin + Streptokinase | 6 | Severe | Bleeding | PD |
| Enoxaparin + Streptokinase | 6 | Severe | Bleeding | PD |
| Enoxaparin + Ticagrelor | 74 | Severe | Bleeding | PD |
| Enoxaparin + Furosemide | 6 | Severe | Bleeding | PD |
| Enoxaparin + Clopidogrel | 16 | Moderate | Bleeding | PD |
| Enoxaparin + Aspirin | 10 | Moderate | Bleeding | PD |

**PD:** Pharmacodynamic mechanism, **PK:** Pharmacokinetic mechanism

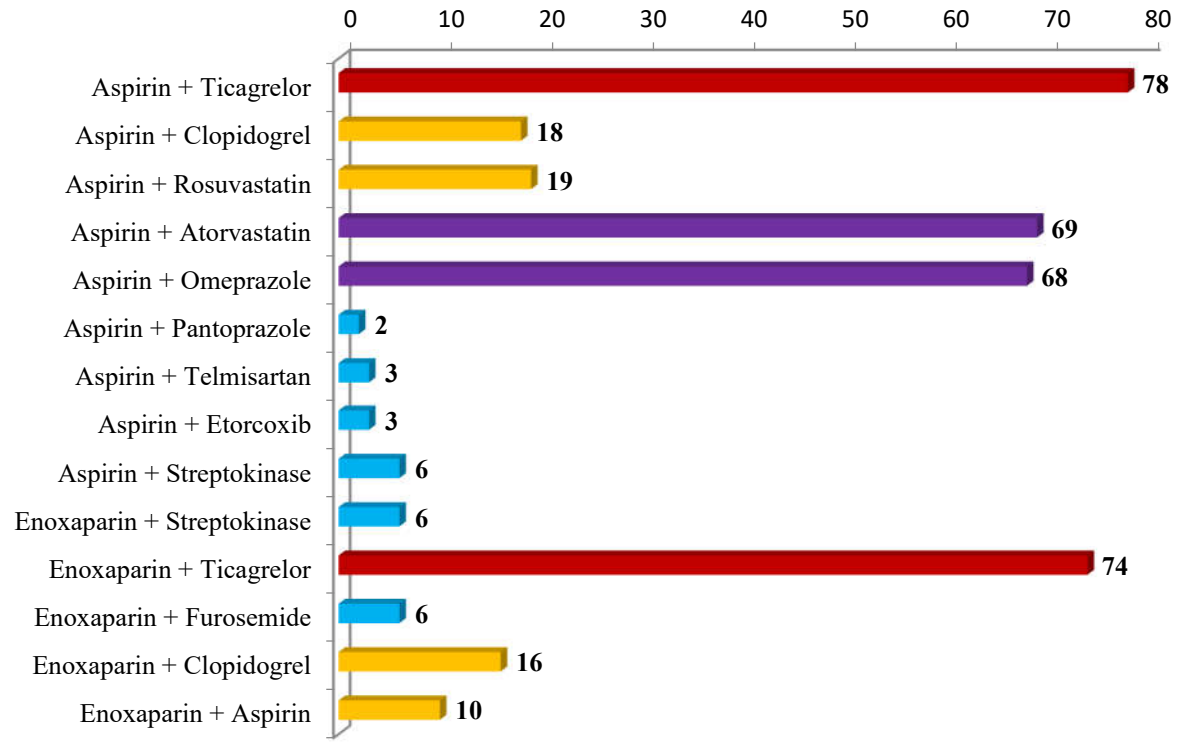


**Figure 7. Combined Distribution, Severity, and Mechanism of Drug–Drug Interactions Involving Aspirin and Enoxaparin**

## 6. Overall Inference and Conclusion

This study highlights that polypharmacy is universal among myocardial infarction (MI) patients, with an average of 7–8 medications per patient, reflecting the complexity of guideline-directed therapy. Antiplatelets and anticoagulants were the predominant contributors to drug–drug interactions (DDIs), with the majority being moderate in severity (65%) and primarily pharmacodynamic in nature. Major interactions, though less frequent (8.5%), pose significant clinical risks, particularly bleeding with dual antiplatelet or anticoagulant therapy. Pharmacokinetic interactions, mainly with statins, caused rhabdomyolysis. Older age, comorbidities (hypertension, diabetes, CKD), smoking, and polypharmacy (>8 drugs) significantly increased the risk of DDIs (OR = 3.8; $p < 0.01$). High-frequency interactions included Aspirin + Ticagrelor, Aspirin + Atorvastatin, and Enoxaparin + Ticagrelor, while severe bleeding risk was particularly notable with Enoxaparin combinations.

**Clinical Implications:**

- Most DDIs are manageable with vigilant monitoring.
- High-risk combinations require careful oversight, dose adjustment, or alternative therapy.
- Routine pharmacist-led review, medication reconciliation, and electronic DDI screening are essential to minimize preventable adverse events.
- Patient education and adherence monitoring further enhance safety.

**Future Directions:** Larger multicenter studies are warranted to assess the impact of structured DDI mitigation strategies on morbidity, mortality, and healthcare utilization. Integration of real-time clinical decision support systems could optimize individualized therapy in high-risk MI patients.

**Key Takeaway:** Polypharmacy in MI patients is unavoidable but manageable; systematic DDI surveillance, clinical pharmacist involvement, and mechanism-based monitoring are critical to optimize therapy, prevent adverse events, and improve patient outcomes.

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