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A Review on Cardiovascular Diseases: Advances and Challenges in Prevention and Treatment

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ABSTRACT

Cardiovascular disease (CVD) remains the leading cause of global mortality, accounting for 17.9 million deaths annually. This review synthesizes current knowledge on CVD epidemiology, etiology, risk factors, pharmacological interventions, and adverse drug reactions (ADRs). The global burden of CVD has risen, with 20.5 million cases reported in 2021, disproportionately affecting low- and middle-income countries. Modifiable risk factors, including smoking, dyslipidemia, hypertension, diabetes, and psychosocial stress, drive the majority of cases, while non-modifiable factors like age and genetics also play significant roles. Advances in antiplatelet and anticoagulant therapies, such as dual antiplatelet therapy and direct oral anticoagulants, have improved outcomes, but challenges persist, including bleeding risks and access disparities. Drug utilization reviews enhance treatment safety and efficacy, yet ADRs, ranging from dose-related bleeding to idiosyncratic reactions, complicate management. This paper highlights progress in CVD prevention and treatment, identifies gaps in equitable healthcare delivery, and underscores the need for personalized approaches and public health interventions to address this global epidemic.

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INTRODUCTION

Cardiovascular disease (CVD) encompasses a range of disorders affecting the heart or blood vessels, including coronary artery diseases (CAD) such as angina and myocardial infarction (heart attack). Other CVDs include stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, cardiac arrhythmia, congenital heart disease, valvular heart disease, aortic aneurysms, peripheral artery disease, and venous thrombosis (1). Globally, CVD is the leading cause of mortality, responsible for approximately 17.9 million deaths annually (1). According to the World Heart Federation (WHF), CVD cases increased from 12.1 million in 1990 to 20.5 million in 2021, with four out of five deaths occurring in low- and middle-income countries (LMICs) (2). While CVD mortality has declined in developed nations since the 1970s due to improved healthcare, preventive measures, and public health campaigns, it is rising in developing regions due to lifestyle changes, urbanization, and limited access to healthcare (3,4). Coronary heart disease and stroke account for 80% of CVD deaths in men and 75% in women, predominantly affecting older populations (1). In the United States, CVD prevalence increases with age: 11% in ages 20–40, 37% in 40–60, 71% in 60–80, and 85% in those over 80 (5). The average age of CVD-related death is approximately 80 years in developed countries and 68 years in developing nations, with men typically affected 7–10 years earlier than women (4,6). This gender disparity is attributed to hormonal differences and variations in risk factor exposure (6).

Table 1: Global CVD Statistics (1990 vs. 2021)

Year	Total CVD Cases (Millions)	Proportion of Deaths in LMICs
1990	12.1	Not specified
2021	20.5	4 out of 5

Source: World Heart Federation (2)

MYOCARDIAL INFARCTION

Myocardial infarction (MI), commonly known as a heart attack, occurs when a portion of the myocardium receives inadequate blood flow, leading to oxygen deprivation (7). Prolonged ischemia can cause necrosis and cell death, potentially resulting in hemodynamic collapse or sudden death (7,8). MI may be asymptomatic ("silent") or present with symptoms such as chest pain or pressure radiating to the jaw, arm, neck, or shoulder, accompanied by shortness of breath, sweating, or nausea (7). Diagnosis involves clinical examination, patient history, electrocardiogram (ECG) changes, and elevated cardiac biomarkers such as troponins (9,10). Acute myocardial infarction (AMI) is a leading cause of death in developed countries, with approximately 3 million cases annually in the U.S., resulting in over 1 million deaths (11). AMI is classified into ST-segment elevation myocardial infarction (STEMI), caused by complete coronary artery occlusion, and non-ST-segment elevation myocardial infarction (NSTEMI), distinguished from unstable angina by cardiac biomarkers (11,12,13). STEMI typically results from a coronary artery

dissection, erosion, or rupture leading to an obstructive thrombus, while NSTEMI may involve partial occlusion or microembolization (14).

Risk Factors for Myocardial Infarction

The INTERHEART study identified key modifiable risk factors for MI, including smoking, abnormal lipid profiles (elevated ApoB/ApoA1 ratio), hypertension, diabetes, abdominal obesity (waist/hip ratio >0.9 for men, >0.85 for women), psychosocial stress, inadequate fruit/vegetable intake, physical inactivity, and moderate alcohol consumption (protective) (15,16,17). Smoking and abnormal lipid profiles were the strongest predictors, with women showing a higher risk from diabetes and hypertension but greater benefits from exercise and moderate alcohol consumption (15). Elevated plasma homocysteine is an independent risk factor, treatable with vitamins B6, B12, and folic acid (18). Non-modifiable risk factors include advanced age, male gender, and a family history of early cardiovascular events (before age 50) (16,19). Ongoing research continues to explore genetic loci associated with increased MI risk (20,21).

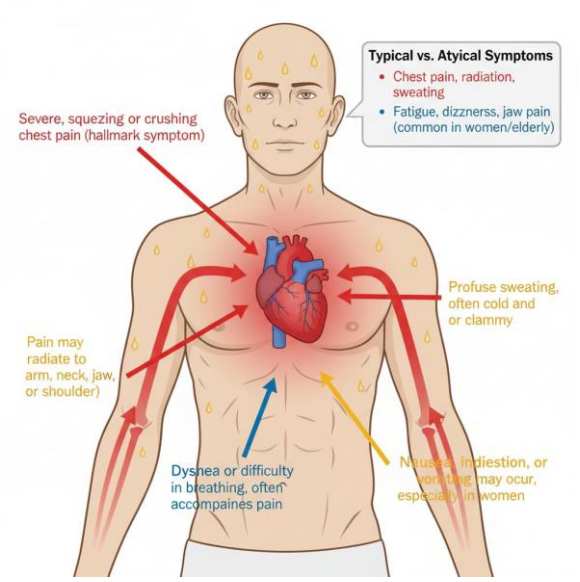

Figure 1: Common Symptoms of Myocardial Infarction

Table 2: Modifiable Risk Factors for Myocardial Infarction

Risk Factor	Description	Relative Risk (INTERHEART Study)
Smoking	Strongest predictor of MI	High
Abnormal Lipid Profile	Elevated ApoB/ApoA1 ratio	High
Hypertension	Higher risk in women	Moderate
Diabetes	Stronger risk in women	Moderate
Abdominal Obesity	Waist/hip ratio >0.9 (men), >0.85 (women)	Moderate
Psychosocial Stress	Includes depression, financial stress, life events	Moderate
Inadequate Diet	Low fruit/vegetable intake	Moderate
Physical Inactivity	Lack of regular exercise	Moderate
Alcohol Consumption	Moderate intake may be protective	Low (protective)

Source: INTERHEART Study (15)

ETIOLOGY

The etiology of coronary artery disease and myocardial infarction is multifactorial, involving both modifiable and non-modifiable risk factors. The INTERHEART study highlighted the following modifiable risk factors (15,16,17):

- **Tobacco Use**: The strongest risk factor, significantly increasing MI risk.
- **Abnormal Lipid Profile**: Elevated ApoB/ApoA1 ratio, indicative of dyslipidemia.
- **Hypertension**: More pronounced in women, contributing to arterial damage.
- **Type II Diabetes**: Increases vascular inflammation and atherosclerosis risk.
- **Abdominal Obesity**: Measured by waist/hip ratio, linked to metabolic syndrome.
- **Psychosocial Factors**: Stress, depression, and life events (e.g., divorce, job loss).
- **Inadequate Diet**: Low intake of fruits and vegetables.
- **Physical Inactivity**: Contributes to obesity and poor cardiovascular health.
- **Alcohol Consumption**: Moderate intake has a weak protective effect.

Non-modifiable risk factors include advanced age, male gender, and a family history of early cardiovascular events (16,19). Elevated plasma homocysteine is an independent risk factor, manageable with vitamin B6, B12, and folic acid supplementation (18). Genetic studies continue to identify loci that increase MI susceptibility, particularly in younger individuals (20,21).

Environmental factors, such as air pollution, also contribute to CVD risk by promoting inflammation and oxidative stress (22).

EPIDEMIOLOGY

Coronary artery disease is the leading cause of mortality and disability worldwide (23). According to the National Health Interview Survey (NHIS-CDC) in 2015, MI mortality was 114,023, with MI mentioned as a contributing factor in 151,863 deaths (24). Data from the National Health and Nutrition Examination Survey (NHANES-CDC) from 2011–2014 estimated that 16.5 million Americans over 20 have coronary artery disease, with higher prevalence in men than women across all age groups (16). The total prevalence of MI in U.S. adults over 20 is 3.0% (16). The Atherosclerosis Risk in Communities (ARIC) study (2005–2014) reported an annual incidence of 605,000 new MIs and 200,000 recurrent MIs (25). The average age at first MI is 65.6 years for men and 72.0 years for women (25). Recent decades have shown a decline in MI prevalence in the U.S. due to improved risk factor management and medical interventions (25).

Table 3: MI Epidemiology in the U.S. (2011–2014)

Metric	Value
Total CAD Prevalence (>20 years)	16.5 million
MI Prevalence (>20 years)	3.0%
Annual New MI Cases	605,000
Annual Recurrent MI Cases	200,000
Average Age at First MI (Men)	65.6 years
Average Age at First MI (Women)	72.0 years

Source: NHANES and ARIC Studies (16,25)

RISK FACTORS

CVD risk factors include both modifiable and non-modifiable elements. Modifiable risk factors include tobacco use, excessive alcohol consumption, physical inactivity, poor diet, obesity, hypertension, hyperlipidemia, diabetes mellitus, air pollution, psychosocial factors, low educational attainment, and poverty (15,26,27,28,29). Non-modifiable factors include age, gender, and family history of cardiovascular disease (16,19). While the relative contributions of these risk factors vary across cultures and ethnic groups, their overall impact is consistent (30). Modifiable risk factors can be addressed through lifestyle changes, social interventions, and medical treatments such as antihypertensive, lipid-lowering, and antidiabetic therapies (26).

ANTIPLATELET DRUGS

Antiplatelet drugs are prescribed post-myocardial infarction to prevent further cardiovascular events and are used in patients with established arterial plaque or irregular cardiac rhythms like atrial fibrillation (31). They are categorized into oral and parenteral types, with oral medications further divided by mechanism of action (32). Aspirin, a cyclooxygenase inhibitor, is the cornerstone of antiplatelet therapy. Other oral agents include thienopyridines (clopidogrel, ticagrelor, prasugrel) and miscellaneous drugs (dipyridamole, cilostazol). Parenteral glycoprotein IIb/IIIa inhibitors (tirofiban, eptifibatide) are used in acute coronary syndrome (ACS) (33).

Mechanism of Action

Antiplatelet drugs are classified by their mechanism (34,35):

- **Platelet Aggregation Inhibitors**: Aspirin (cyclooxygenase inhibitor), clopidogrel, ticagrelor, ticlopidine, prasugrel (thienopyridines).
- **Glycoprotein Platelet Inhibitors**: Abciximab, eptifibatide, tirofiban.
- **Protease-Activated Receptor-1 Antagonists**: Vorapaxar.
- **Miscellaneous**: Dipyridamole (nucleoside transport inhibitor and PDE3 inhibitor), cilostazol (PDE3 inhibitor).

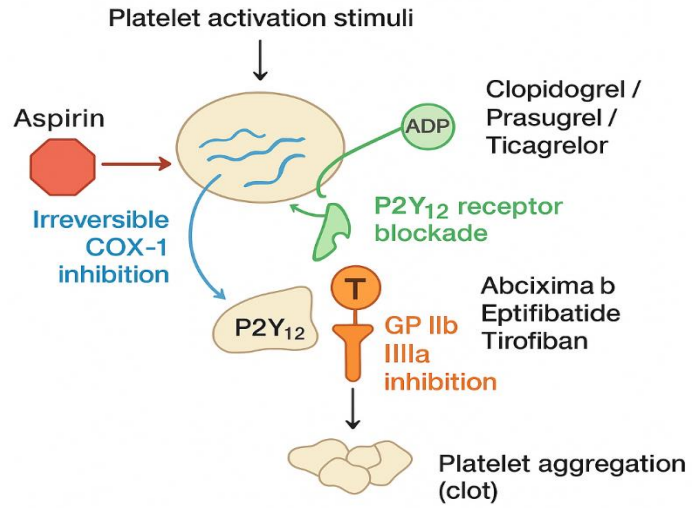

Figure 2: Mechanism of Antiplatelet Drugs

ANTICOAGULANT DRUGS

Coronary artery disease can lead to plaque formation, which may cause blood clots that obstruct cardiac vessels, potentially resulting in MI, pulmonary embolism, or stroke (31). Anticoagulants prevent clot formation but cannot dissolve existing clots (31). They are critical in managing conditions like atrial fibrillation, post-heart valve replacement, and venous thromboembolism (36).

Physiology

Anticoagulants interfere with the coagulation cascade by inhibiting specific enzymes, binding to antithrombin, or blocking vitamin K-dependent factor synthesis (37).

Available Anticoagulants

Unfractionated Heparin (UFH)

Inactivates coagulation factors via antithrombin 3 complexes, with a rapid onset and short half-life, monitored by activated partial thromboplastin time (aPTT) targeting 1.5–2.2 times the baseline (37).

Low Molecular Weight Heparin (LMWH)

Includes enoxaparin, dalteparin, tinzaparin, and nadroparin, with longer half-lives and anti-factor Xa activity; monitoring is typically unnecessary except in renal failure or pregnancy (37).

Vitamin K Antagonists (VKA)

Warfarin inhibits vitamin K epoxide reductase, preventing gamma-carboxylation of factors II, VII, IX, X, and proteins C and S. It requires frequent monitoring via the international normalized ratio (INR) due to dietary and drug interactions (38).

Direct Thrombin Inhibitors

Dabigatran, argatroban, and bivalirudin prevent thrombin from cleaving fibrinogen into fibrin, metabolized renally (39).

Direct Factor Xa Inhibitors

Include apixaban, rivaroxaban, edoxaban, and betrixaban, inhibiting prothrombin conversion to thrombin, administered orally (39). Direct oral anticoagulants (DOACs) are preferred for their ease of dosing and lower bleeding risk (40,41).

Indications

Anticoagulants are indicated for atrial fibrillation, post-heart valve replacement, and venous thromboembolism, selected based on patient history, risk assessment, and preferences (36,42,43).

DRUG UTILIZATION REVIEW (DUR)

Drug Utilization Review (DUR) is a structured process to ensure safe, effective, and appropriate medication use, improving patient outcomes and reducing healthcare costs (44). DUR compares patient or population data against evidence-based standards, identifying deviations that may necessitate therapy changes (45,46).

Prospective DUR

Involves reviewing prescriptions for potential drug-related issues before dispensing, preventing adverse events (47,48).

Concurrent DUR

Assesses prescriptions during treatment, adjusting therapy based on ongoing diagnostic and laboratory results (47,48).

Retrospective DUR

Analyzes practice patterns to identify costly drugs, compare drug classes across providers, and ensure adherence to treatment guidelines (47,48,49).

ADVERSE DRUG REACTIONS (ADRS)

Adverse drug reactions (ADRs) are noxious, unintended responses to medications at standard doses used for prophylaxis, diagnosis, or treatment (50). Serious ADRs, as defined by Laurence, exclude minor side effects and focus on harmful or potentially hazardous reactions requiring dose reduction or drug withdrawal (51).

Classification

ADRs are classified into (52,53):

- **Type A (Augmented)**: Dose-related reactions.
- **Type B (Bizarre)**: Non-dose-related, idiosyncratic reactions.
- **Type C**: Dose- and time-related reactions.
- **Type D**: Delayed reactions.
- **Type E**: Withdrawal reactions.
- **Type F**: Unexpected therapeutic failure (proposed) (54).

ADR Prevention
Many ADRs are preventable through evidence-based prescribing and monitoring. Avoidable ADRs result from deviations from guidelines or impractical treatment plans (55). Strategies include regular monitoring, patient education, and adherence to clinical protocols (56).

CONTRAINDICATIONS
A contraindication is a condition that prohibits the use of a medication, procedure, or surgery due to potential harm (57).

Relative Contraindications
Require cautious use, weighing benefits against risks, e.g., combining warfarin with aspirin (57).

Absolute Contraindications
Prohibit use due to life-threatening risks, e.g., isotretinoin in pregnancy due to teratogenic effects (57).

DRUG INTERACTIONS
Drug interactions can enhance, reduce, or cause unexpected effects of medications, sometimes posing significant risks (58).

Drug-Drug Interactions
Occur when drugs interact, e.g., sedatives and antihistamines causing slowed reactions (58).

Drug-Food/Beverage Interactions
Involve interactions with food or drink, e.g., alcohol enhancing sedative effects of certain drugs (58).

Drug-Condition Interactions
Arise when a medical condition makes a drug unsafe, e.g., nasal decongestants in hypertension (58).
Reading over-the-counter (OTC) medication labels is crucial to identify potential interactions and ensure safe use (58).

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