# Drug-Induced Cardiotoxicity in Chinese Population: Current Status and Future Perspectives (Postprint)

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## Abstract

Drug-induced cardiotoxicity is a common and relatively serious adverse drug reaction in clinical practice, and also represents an important risk factor for the occurrence and progression of cardiovascular diseases. Nevertheless, current clinical practice still lacks early predictive indicators with high specificity and sensitivity, as well as effective preventive and therapeutic agents. Understanding the current status of drug-induced cardiotoxicity in China, exploring clinical evaluation indicators for early detection, and summarizing measures to reduce toxicity while enhancing efficacy are of great significance for ameliorating cardiac injury and improving drug safety. This article aims to systematically summarize the clinical status of drug-induced cardiotoxicity in China, enumerate in detail drugs with confirmed or potential cardiotoxicity, and explore the underlying mechanisms of their toxicity. Simultaneously, it focuses on early monitoring and early warning of drug-induced cardiotoxicity, summarizes preventive and therapeutic measures from both Chinese and Western medicine, and provides valuable references for its early detection and intervention.

## Full Text

## Drug-Induced Cardiotoxicity in the Chinese Population: Current Analysis and Considerations

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**Abstract**

Drug-induced cardiotoxicity represents a common and relatively severe adverse drug reaction in clinical practice, as well as a significant risk factor for the development and progression of cardiovascular disease. Nevertheless, current clinical practice still lacks highly specific and sensitive early predictive indicators and effective preventive or therapeutic agents. Understanding the current status of drug-induced cardiotoxicity in China, exploring clinical evaluation metrics for early detection, and summarizing measures to reduce toxicity while enhancing efficacy are of great significance for improving cardiac injury and enhancing drug safety. This article systematically summarizes the clinical status of drug-induced cardiotoxicity in China, enumerates in detail the drugs with established or potential cardiotoxicity, and explores the mechanisms underlying their toxic effects. Simultaneously, it focuses on early monitoring and warning of drug-induced cardiotoxicity, summarizes prevention and treatment measures in both Chinese and Western medicine, and provides valuable references for early detection and intervention.

**Keywords:** Drug-related side effects and adverse reactions; Cardiotoxicity; Drug-induced cardiotoxicity; Drug safety; China

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Drug-induced cardiotoxicity refers to pharmacodynamic responses where drugs and their metabolites affect or impair normal cardiac physiological function [1-2]. The pathological process typically begins with myocardial injury and alterations in myocardial tension, followed by progressive decline in left ventricular ejection fraction (LVEF), eventually leading to symptomatic heart failure [3]. Drug-induced cardiotoxicity is the most prevalent and severe type of adverse drug reaction. Nearly 2,000 drugs are associated with cardiovascular adverse reactions, with an incidence rate of 15%-35% among marketed drugs, causing substantial losses to public health and medical resources [4]. Moreover, drug-induced cardiotoxicity constitutes an important risk factor that contributes to and exacerbates cardiovascular burden [5], making its prevention and control key measures for reducing cardiovascular disease burden. To prevent irreversible serious consequences from progressive drug-induced cardiotoxicity, early identification and intervention are particularly crucial.

Enhancing healthcare professionals' understanding of drug-induced cardiotoxicity in Chinese populations and comprehending its occurrence patterns, composition of cardiotoxic drugs, and preventive and therapeutic measures holds significant importance. Through database searches, this article collected clinical case reports, experimental studies, and trial reports related to drug-induced cardiotoxicity in Chinese populations, summarizing the clinical status, monitoring and early warning strategies, and prevention and treatment measures

for drug-induced cardiotoxicity in China, with the aim of providing valuable references for early detection, intervention, and prognosis improvement.

## 1. Clinical Status of Drug-Induced Cardiotoxicity

Drug-induced cardiotoxicity is influenced by multiple factors including drug characteristics, patient populations, and clinical treatment regimens [6], which can independently or interactively contribute to cardiac toxic reactions. Currently, drugs with potential cardiotoxicity in Chinese populations include antineoplastic agents, antibiotics, antipsychotics, and certain traditional Chinese medicines. Drug-induced cardiotoxicity can manifest as various clinical symptoms, encompassing arrhythmias, cardiac insufficiency, myocarditis, sudden cardiac death, and heart failure (Table 1 ). While some patients may experience gradual recovery of cardiac function after discontinuing the offending drugs, others may develop irreversible cardiac dysfunction. Recovery is influenced by multiple factors, including drug type, dosage, treatment duration, and individual variations [7]. Therefore, strict control of drug dosage and treatment course, close monitoring of cardiac effects during medication, and cardiac function assessment when necessary are essential.

## 2. Mechanisms of Drug-Induced Cardiotoxicity

The pathological process of drug-induced cardiotoxicity involves several key factors and mechanisms, primarily including ion channel blockade, oxidative stress, and mitochondrial damage (Table 2 ) [8-21]. Drugs may act on ion channels in cardiomyocyte membranes, such as sodium, potassium, and calcium channels, thereby inducing abnormal changes in cardiac electrophysiological activity. The most common clinical manifestation, QT interval prolongation, is fundamentally mediated by drug blockade of hERG potassium channels that disrupts cardiac electrical activity. Oxidative stress plays a crucial role in drug-induced cardiotoxicity. Imbalance between reactive oxygen species (ROS), reactive nitrogen species (RNS), and antioxidants leads to modification of biological macromolecules including DNA and proteins, causing myocardial oxidative stress injury [22]. Mitochondrial damage represents a primary mechanism of drug-induced cardiotoxicity, manifesting mainly through excessive ROS release and reduced adenosine triphosphate (ATP) generation [23], which results in insufficient cardiac energy supply and subsequent cardiac dysfunction.

**Table 1. Clinical Manifestations and Related Drugs of Drug-Induced Cardiotoxicity**

| Clinical Manifestation | Related Drugs |
|---|---|
| QT interval prolongation | Anthracyclines, TKIs, ICIs, antiarrhythmic drugs, $\beta$-lactams, calcium channel blockers, quinolones, macrolides, typical antipsychotics, atypical antipsychotics, polypeptides, terpenoids |
| Torsades de pointes | Anthracyclines, antiarrhythmic drugs, $\beta$-lactams, macrolides, quinolones, $\beta$-blockers |
| Supraventricular tachycardia | Anthracyclines, antimicrotubule agents, antimetabolites, $\beta$-lactams, fluoroquinolones, macrolides, typical antipsychotics, atypical antipsychotics, alkaloids, terpenoids |
| Ventricular tachycardia | Anthracyclines, TKIs, ICIs, alkylating agents, antimicrotubule agents, platinum compounds, antimetabolites, antiarrhythmic drugs, $\beta$-lactams, fluoroquinolones, macrolides, atypical antipsychotics, alkaloids, terpenoids |
| Myocardial ischemia | Anthracyclines, TKIs, antimicrotubule agents, platinum compounds, macrolides, quinolones, digitalis, alkaloids |
| Cardiac insufficiency | Anthracyclines, HER2-targeted drugs, TKIs, antimicrotubule agents, platinum compounds, $\beta$-blockers |
| Myocarditis | Anthracyclines, ICIs, antipsychotics (clozapine), terpenoids |
| Myocardial infarction | Anthracyclines, TKIs, antimetabolites, $\beta$-lactams |

| Clinical Manifestation | Related Drugs |
|---|---|
| Heart failure | Anthracyclines, HER2-targeted drugs, TKIs, alkylating agents, ICIs, platinum compounds, antimetabolites, ARBs, $\beta$-lactams, diuretics, antiarrhythmic drugs, ACEIs, nitrates, alkaloids, polypeptides |
| Cardiogenic shock | Anthracyclines, ICIs, platinum compounds, antimetabolites, ARBs, $\beta$-lactams, ACEIs, nitrates |
| | Antimetabolites, $\beta$-blockers, alkaloids, terpenoids, polypeptides |

*Note: TKIs = tyrosine kinase inhibitors, ICIs = immune checkpoint inhibitors, HER2 = human epidermal growth factor receptor 2, ARB = angiotensin receptor blocker, ACEI = angiotensin-converting enzyme inhibitor.*

## 3. Monitoring and Early Warning of Drug-Induced Cardiotoxicity

### 3.1 Electrocardiogram

Electrocardiogram (ECG) is a widely used, simple, and non-invasive examination method that can effectively monitor potential functional or structural myocardial problems [24]. In clinical practice, ECG is considered a routine test for diagnosing acute myocardial injury, acute myocardial infarction, or acute myocarditis. Studies have shown that ECG changes in drug-induced cardiotoxicity mainly include QT interval prolongation, low QRS voltage, flattened T waves, and ST-T changes [25-26]. Relevant guidelines recommend ECG monitoring for patients before and during treatment with potentially cardiotoxic drugs [1].

### 3.2 Echocardiography

Echocardiography is a non-invasive, radiation-free, and inexpensive technique with broad clinical applicability that can accurately assess cardiac structure and hemodynamics [27]. Consequently, echocardiography serves as the first-line imaging modality for screening, diagnosing, and monitoring drug-induced cardiotoxicity. LVEF is currently an important reference indicator for monitoring drug-induced cardiotoxicity; however, this parameter is susceptible to influences from cardiac loading conditions [28-29], limiting early detection of cardiotoxicity.

The Tei index is also a common indicator for evaluating overall cardiac function, positively correlating with the degree of cardiac dysfunction. Notably, the Tei index is not affected by heart rate, atrioventricular structural morphology, or cardiac preload and afterload, providing a reliable basis for comprehensive assessment of cardiac systolic and diastolic function. However, the Tei index is not suitable for patients with irregular heart rates [30]. Left ventricular global longitudinal strain (GLS) reflects changes in global long-axis systolic function, directly tracking myocardial activity and accurately assessing myocardial function based on two-dimensional speckle tracking imaging. Research suggests that a $ $15% decrease in GLS from baseline indicates subclinical cardiotoxicity or left ventricular dysfunction [31]. These new technologies address the limitations of conventional echocardiography, improving its sensitivity and accuracy in evaluating cardiac function and enabling early and precise assessment of drug-induced cardiotoxicity [32].

### 3.3 Cardiac Magnetic Resonance Imaging (CMR)

CMR can obtain comprehensive information including left and right ventricular function, ventricular and atrial volumes, deformation, myocardial mass, pericardial disease, myocardial fibrosis, myocardial edema, and inflammatory responses, providing evidence for chronic or permanent damage from drug-induced cardiotoxicity [33-34]. CMR feature tracking (CMR-FT), as an emerging technique based on conventional cine sequences, enables quantitative assessment of myocardial motion and deformation capacity by deriving global strain, strain rate, torsion angle, and dyssynchrony. Clinical studies have demonstrated that myocardial strain parameters obtained through CMR-FT technology exhibit higher sensitivity compared to traditional cardiac function evaluation indices, enabling earlier identification of subclinical myocardial injury and helping prevent more severe myocardial damage [35]. However, CMR is expensive and contraindicated in patients with pacemakers, metallic implants, severe heart failure, or those unable to remain still, collectively limiting its widespread clinical application [36].

### 3.4 Biomarkers

Troponin and natriuretic peptides are the most commonly used biomarkers for early detection of cardiotoxicity and subsequent follow-up studies, offering high sensitivity, accuracy, and reproducibility [37-38]. Cardiac troponin T (cTnT) and cardiac troponin I (cTnI) can identify early myocardial injury with high sensitivity and specificity for diagnosing myocardial infarction. B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are considered the preferred biomarkers for heart failure diagnosis, differential diagnosis, condition assessment, and prognosis prediction. Evaluating baseline levels of troponin and natriuretic peptides before administering high-risk cardiotoxic drugs is particularly crucial, as this helps clarify patients' cardiovascular risk status at treatment initiation for appropriate risk stratification. When

patients have concurrent cardiovascular disease, baseline levels may be elevated, assisting clinicians in determining whether patients have pre-existing cardiovascular conditions or develop new myocardial injury during subsequent treatment [39]. Monitoring changes in these biomarkers can effectively assess the severity of myocardial injury and provide important guidance for developing personalized monitoring strategies [40]. Pre-treatment biomarker testing serves not only as an important baseline reference but also as a basis for evaluating cardiovascular risk after treatment [35,41]. While the effectiveness of traditional biomarkers in predicting drug-induced cardiotoxicity and cardiovascular events has been confirmed, research on their specificity and optimal timing remains insufficient. Novel biomarkers may offer alternative monitoring approaches, including galectin-3 (GAL3), heart-type fatty acid binding protein (H-FABP), and glycogen phosphorylase BB (GPBB) [42]. MicroRNAs also show great potential in early monitoring of drug-induced cardiotoxicity [43]. Identifying optimal biomarkers, determining detection timing, and exploring combined multimarker panels represent important areas for future research.

### 3.5 Endomyocardial Biopsy

Endomyocardial biopsy allows direct observation of cardiomyocyte structural changes and is considered the "gold standard" for monitoring drug-induced cardiotoxicity due to its high specificity and sensitivity [44]. However, because it is an invasive procedure requiring high technical expertise, it cannot be used as a routine examination for drug-induced cardiotoxicity.

## 4. Prevention and Treatment Measures for Drug-Induced Cardiotoxicity

### 4.1 Dexrazoxane

Dexrazoxane is currently the most commonly used cardioprotective agent in clinical practice, effectively reducing the risk of cardiac events induced by anthracycline chemotherapy. Its mechanism involves competitive binding with free iron ions, thereby effectively preventing drug-induced cardiotoxicity. Clinical studies have demonstrated that dexrazoxane significantly reduces the incidence of cardiac adverse reactions, decreases levels of myocardial injury markers such as cTnI and BNP, and improves LVEF, confirming its efficacy against anthracycline-induced cardiotoxicity [45]. Additionally, dexrazoxane has a relatively short half-life, rapid metabolism, minimal adverse effects such as hepatotoxicity and nephrotoxicity, and does not negatively impact the therapeutic efficacy of the primary drug [46], demonstrating high safety and feasibility in clinical application.

### 4.2 Neurohormonal Agents

Angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), aldosterone receptor antagonists (AAs), and $\beta$-blockers (BBs)

can effectively prevent and treat drug-induced cardiotoxicity by modulating the neurohumoral system [47-48]. ACEIs/ARBs act on the renin-angiotensin-aldosterone system (RAAS), reducing angiotensin-converting enzyme activity in the heart, dilating peripheral vessels, and decreasing myocardial oxygen consumption and afterload to achieve myocardial protection. Multiple studies have confirmed that timely administration of ACEI/ARB drugs after detecting LVEF decline helps promote cardiac function recovery [49-50]. However, other studies suggest that prophylactic use of ACEIs/ARBs has limited protective effects against drug-induced cardiovascular injury, with no statistically significant difference compared to control groups [26,51]. Therefore, the definitive efficacy of neurohormonal agents in treating drug-induced cardiotoxicity requires further validation through additional, longer-term clinical trials.

### 4.3 Statins

Statins are commonly used in clinical practice for cardiovascular diseases, possessing anti-inflammatory, antioxidant, and lipid-lowering effects [52]. They can maintain stable LVEF, alleviate myocardial injury, and reduce the risk of acute heart failure by inhibiting cellular immune responses and oxidative stress reactions [53-54]. Guidelines recommend using traditional cardioprotective drugs such as ACEIs and ARBs as primary prevention for high-risk and very high-risk patients undergoing drug therapy [55]. A meta-analysis showed that statin therapy can maintain LVEF to some extent and reduce the risk of drug-induced cardiotoxicity, with this protective effect likely related to modulation of left ventricular dysfunction, myocardial fibrosis, and apoptosis [56-57].

### 4.4 Traditional Chinese Medicine Formulas

Zhigancao Decoction, originating from *Shanghan Zabing Lun*, has the effects of replenishing qi and blood, nourishing yin, and restoring pulse [58]. Modern pharmacological studies have found that Zhigancao Decoction prevents and treats drug-induced cardiotoxicity by regulating the phosphatidylinositol 3-kinase (PI3K)/serine-threonine kinase (Akt), hypoxia-inducible factor 1 (HIF-1), tumor necrosis factor (TNF), and Toll-like receptor (TLR) signaling pathways [59]. Relevant randomized controlled trials have shown that adding Zhigancao Decoction to conventional chemotherapy can improve cardiac function and reduce the incidence of drug-induced cardiotoxicity in malignant tumor patients [60-61]. Zhang [62] found that combined treatment with Zhigancao Decoction could alleviate chemotherapy-induced cardiotoxicity and reduce cardiomyocyte injury. Shengmai Yin, composed of Red Ginseng, Ophiopogon, and Schisandra [63], has been shown in preliminary studies to prevent and treat doxorubicin-induced cardiotoxicity, possibly through increasing ROS activity and reducing myocardial oxidative damage [64-65]. Sini Decoction, consisting of Aconite, Ginger, and Licorice, functions to restore yang and rescue from collapse, treating heart-kidney yang deficiency with cold extremities. Modern pharmacological research has demonstrated that Sini Decoction can improve cardiac function,

combat oxidative stress, prevent myocardial fibrosis, improve hemodynamics, prevent atherosclerosis, and enhance immune response [66]. Xu [67] observed the efficacy of Sini Decoction in breast cancer patients receiving anthracycline therapy, with results showing it could effectively slow cardiotoxic reactions and improve the degree of myocardial damage. The cardioprotective effects of Yiqi Huoxue Formula [68], Shenqi Xianbu Decoction, and Hongjingtian Decoction [69] have also been validated in relevant trials.

### 4.5 Traditional Chinese Medicine Monomers

Numerous studies have demonstrated that single herbs or monomeric components can prevent and treat drug-induced cardiotoxicity and reduce cardiac injury [70]. Single herbs or monomeric components alleviate drug-induced cardiotoxicity through multiple mechanisms, including antioxidant stress, reducing autophagy-induced oxidative damage, protecting mitochondrial structure and function, anti-inflammatory effects, and inhibiting apoptosis [71]. Literature research indicates that the core therapeutic principles for preventing and treating antineoplastic drug-induced cardiotoxicity with traditional Chinese medicine are replenishing qi and nourishing yin, and activating blood to unblock collaterals, with frequently used herbs including Astragalus, Ophiopogon, Salvia, Ginseng, and Licorice [72]. Astragaloside can reverse drug-induced cardiotoxicity by acting on the nuclear factor E2-related factor 2 (Nrf-2)/heme oxygenase-1 (HO-1) signaling pathway to effectively inhibit the NLRP3-mediated pyroptosis process [73]. Tanshinone I possesses anti-inflammatory, antitumor, and antioxidant effects, providing excellent protection against cardiovascular diseases [74]. Experimental studies have shown that tanshinone I intervention can alleviate doxorubicin-induced cardiotoxicity by upregulating the Akt-Nrf2 pathway and inhibiting oxidative stress [75]. Ginsenoside Rb1 pretreatment can improve doxorubicin-induced apoptosis in primary rat cardiomyocytes and downregulate aryl hydrocarbon receptor-regulated CYP1A1 and CYP1A2 gene expression [76]. Ginsenoside Rg2 pretreatment can reduce trastuzumab-induced apoptosis in primary human cardiomyocytes while regulating the expression levels of autophagy regulatory proteins such as Beclin1 and autophagy-related gene 7, thereby activating autophagy to protect damaged cardiomyocytes [77]. Additionally, traditional Chinese medicine monomers such as resveratrol [78], berberine [79], cardamonin [80], and quercetin [81] all exhibit favorable preventive and therapeutic effects on drug-induced cardiotoxicity.

### 4.6 Traditional Chinese Patent Medicines

Tongmai Yangxin Pill, derived from modifications of Zhigancao Decoction and Shengmai Powder, has the effects of replenishing qi and nourishing yin, unblocking vessels and relieving pain, and has long been used to treat arrhythmias, coronary heart disease, angina pectoris, and heart failure [82]. Lü et al. [83-85] found that Tongmai Yangxin Pill can effectively reduce the toxic reactions of doxorubicin on myocardial tissue and significantly alleviate acute

and chronic cardiotoxicity symptoms. Its mechanism involves regulating insulin signaling pathway and P53 signaling pathway-related proteins, reducing mitochondrial outer membrane damage in cardiomyocytes, and decreasing cardiomyocyte apoptosis to achieve cardioprotection. Shenfu Injection, made from extracts of Ginseng and Aconite and based on the classic formula Shenfu Decoction, has the effects of replenishing qi to prevent collapse, supporting healthy qi, and restoring yang to rescue from collapse. Modern pharmacological studies have shown that the main active components of Shenfu Injection include ginsenosides Rg1, Rg2, Re, Rb1, and aconitine, hypaconitine, etc., which can inhibit cardiomyocyte autophagy and apoptosis and regulate myocardial energy metabolism to exert cardioprotective effects [86]. In vitro experiments have shown that Shenfu Injection may alleviate cardiotoxicity by inhibiting cardiomyocyte ferroptosis through the JAK2-STAT3 signaling pathway [87]. Shenmai Injection, primarily containing Red Ginseng and Ophiopogon, has the effects of replenishing qi to prevent collapse and nourishing yin to generate fluid. Clinical studies have confirmed its significant efficacy and reliable safety in preventing and treating cardiovascular diseases [88]. Meta-analysis results suggest that Shenmai Injection can simultaneously regulate oxidative stress indicators such as superoxide dismutase (SOD), glutathione (GSH), and malondialdehyde (MDA), improve cardiac function indicators including LVEF, cTnI, and creatine kinase-MB (CK-MB), reduce blood viscosity, improve microcirculation, increase blood fluidity, and effectively alleviate cardiotoxicity [89]. Shenmai Injection can block doxorubicin-induced apoptosis by regulating the c-Jun N-terminal kinase (JNK) signaling pathway, maintaining cardiomyocyte homeostasis and thereby exerting cardiovascular protective effects [90]. Xinmailong Injection, extracted from the traditional Chinese medicine *Periplaneta americana* (cockroach), has the effects of replenishing qi and nourishing blood, removing blood stasis and breaking accumulations, with active components including polypeptides, compound amino acids, and nucleosides [91]. Meta-analysis results show that Xinmailong Injection has cardioprotective effects in patients receiving anthracycline chemotherapy, can improve resulting cardiotoxicity, and has almost no adverse reactions [92]. In vitro experimental results indicate that Xinmailong Injection exerts its anti-cardiotoxicity and cardioprotective effects by regulating lysosomes and autophagy through HO-1 [93]. Aikeqing Granules, Shengmai Injection, Shenqi Fuzheng Injection, Astragalus Injection, Compound Kushen Injection, Yiqi Fumai Injection for injection, Huachansu Injection, and Xingda 莫 Injection also demonstrate favorable preventive and therapeutic effects on drug-induced cardiotoxicity [11,94-96].

### 4.7 Non-Pharmacological Interventions

Healthy lifestyle modifications significantly benefit the reduction of drug-induced cardiotoxicity risk [97]. Clinical trial results show that multimodal exercise interventions during chemotherapy can alleviate drug-induced cardiotoxicity, specifically by preventing resting heart rate increase, improving tachycardia, and restoring impaired heart rate [98]. Traditional exercises such

as Wuqinxi, Tai Chi, and Baduanjin embody the dialectical unity principle of combining hardness and softness with alternating urgency and slowness. These practices are beneficial for promoting heart vitality and smooth blood flow, playing an important role in cardiac rehabilitation [99-100]. The Mediterranean diet pattern can improve cardiac diastolic and systolic function, while diets rich in olive oil or reduced sugar intake also help prevent cardiotoxicity [101]. Psychological intervention may have potential positive effects in alleviating drug-induced cardiotoxicity. One study found that combining psychological intervention with conventional treatment could further curb myocardial injury in breast cancer patients, playing an important role in preventing drug-induced adverse reactions [102].

## 5. Research Prospects

### 5.1 Improving the Evaluation System for Drug-Induced Cardiotoxicity

The evaluation system for drug-induced cardiotoxicity remains in the exploratory stage. Establishing a scientific and comprehensive evaluation system and elucidating the causal relationship between drugs and cardiotoxicity will facilitate assessment and control of drug-induced cardiotoxicity. The International Council for Harmonisation (ICH) guidelines S7B [103] and E14 [104] are universal guidelines for cardiac safety evaluation during drug development. While drawing on this system, we should establish standardized and feasible non-clinical evaluation norms for cardiac safety that align with the characteristics of Chinese populations, scientifically assess the risk of drug-induced cardiotoxicity, guide rational clinical medication use, and ensure patient safety [105]. We must construct an evidence base for drug cardiac safety evaluation. Early evidence evaluation systems considered randomized controlled trials as the highest level of evidence; however, randomized controlled trials have limitations for evaluating drug cardiac safety [106]. Therefore, different types of research evidence should be selected based on the characteristics of drug-induced cardiotoxicity research questions, establishing safety evaluation evidence grading standards distinct from drug efficacy evaluation, systematically and comprehensively integrating existing research evidence to obtain an evidence evaluation framework.

### 5.2 Conducting High-Quality Studies Based on Chinese Population Characteristics

Currently, high-quality clinical research on drug-induced cardiotoxicity is lacking in China, with domestic guidelines primarily based on foreign studies or low-level evidence-based medical research, reducing credibility. Future efforts should focus on conducting large-sample, prospective, long-term observational studies based on Chinese populations [107], starting from clinical needs, performing long-term registration and follow-up of patients with drug-induced cardiotoxicity exposed to specific drugs, and employing comprehensive multi-indicator

evaluation. This is crucial for comprehensively assessing drug safety, accurately quantifying the incidence of drug-induced cardiotoxicity, identifying potential high-risk factors, and improving patient prognosis. Simultaneously, we should extensively collect and integrate real-world data including adverse drug reaction monitoring data, electronic health records, medical insurance claims data, and social media data, leveraging artificial intelligence and deep learning algorithms to comprehensively identify and deeply analyze drug-induced cardiotoxicity from multiple perspectives and models [108]. Systematic evaluation of drug cardiac safety is time-sensitive and of significant contemporary importance.

We should actively conduct centralized clinical safety monitoring of drugs. Centralized clinical safety monitoring refers to a research method that, within a certain time period and scope (one or several hospitals in one or several regions), uses patients or drugs as clues, targets inpatient and/or outpatient populations, and records detailed information on adverse events/reactions and drug usage to study the patterns of adverse event/reaction occurrence [109]. Actively conducting centralized clinical safety monitoring helps understand drug safety profiles, promotes rational clinical medication use, and serves as an important approach for identifying safety risk signals, analyzing drug safety risks, and implementing targeted risk management [110].

### 5.3 Deeply Exploring Traditional Chinese Medicine Characteristics

Traditional Chinese medicine has a long history and proven efficacy, standing the test of evidence-based medicine [111], and demonstrates potential advantages in preventing and treating drug-induced cardiotoxicity. We should deeply explore the theoretical essence and clinical practice advantages of traditional Chinese medicine to provide new research perspectives for addressing drug-induced cardiotoxicity. Future efforts may establish a theoretical system of traditional Chinese medicine cognition for drug-induced cardiotoxicity, integrate evidence-based medicine concepts, and construct a drug safety assessment framework that meets international standards while highlighting traditional Chinese medicine characteristics [112-113]. Using advanced systems biology approaches such as transcriptomics, metabolomics, and network pharmacology, we should deeply investigate the specific targets and mechanisms of traditional Chinese medicine interventions in drug-induced cardiotoxicity, providing new research perspectives for traditional Chinese medicine applications in this field [100]. Furthermore, we should integrate diverse traditional Chinese medicine evidence including research data, theoretical foundations, and clinical application experience to form a complementary and distinctive collaborative evidence base that supports and optimizes evidence-based decision-making for traditional Chinese medicine interventions in drug-induced cardiotoxicity [114].

## Conclusion

Drug-induced cardiotoxicity exhibits characteristics of multiple sources, high incidence, occult onset, susceptibility in special populations, diverse clinical symp-

toms, and complex pathogenic mechanisms [7], impairing patients' quality of life and severely affecting disease prognosis. Clinically, arrhythmias associated with anticancer drugs are most common; additionally, circulatory system drugs, antibiotics, antipsychotics, and some traditional Chinese medicines also carry cardiotoxicity risks. Different drugs cause varying degrees of cardiac damage, and cardiotoxicity episodes are often accompanied by multiple complex factors. Age, sex, and underlying diseases may be relevant risk factors for the occurrence and development of drug-induced cardiotoxicity [115-116]. The pathogenesis encompasses multiple aspects including oxidative stress, ferroptosis, mitochondrial damage, inflammatory responses, and immune reactions. Detection methods include ECG monitoring, echocardiography, cardiac CMR, and serum biomarker measurement, with endomyocardial biopsy being the recognized diagnostic gold standard. Additionally, various multi-angle and multi-modal detection markers and methods have been proposed and applied clinically. The effectiveness of traditional cardioprotective drugs has been further validated, while the efficacy and safety of novel cardioprotective agents and traditional Chinese medicine interventions require further verification. Exploring evaluation systems and early monitoring methods for drug-induced cardiotoxicity, identifying susceptibility factors in Chinese populations, and constructing and continuously optimizing clinical practice guidelines for drug-induced cardiotoxicity applicable to Chinese populations are urgent issues requiring resolution. Healthcare professionals need to continuously strengthen drug supervision, carefully select drugs that may induce cardiotoxicity, and implement early interventions for patients who have already developed drug-induced cardiotoxicity.

The pathogenesis of drug-induced cardiotoxicity has not been fully elucidated, requiring continued in-depth research. Discovering new key factors and pathways in traditional pathways will not only enhance understanding of drug-induced cardiotoxicity processes but also provide precise targets for effective prevention and monitoring [48]. Additionally, pharmacogenomic studies exploring the genetic basis of inter-individual differences in drug responses hold promise for guiding precision therapy and reducing the risk of drug-induced cardiotoxicity. Traditional Chinese medicine is a treasure of Chinese civilization, and relevant researchers should deeply explore this valuable resource to find new ideas and methods for solving these challenges.

**Author Contributions:** Zhong Lanfang was responsible for conceptualization, design, manuscript writing, and revision; Yu Xinyu and Pi Zheyu were responsible for data collection and organization; Li Bin was responsible for quality control, review, overall responsibility, and supervision.

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