

REVIEW ARTICLE

Cardiovascular Implications of Platinum-Based Chemotherapy: Mechanisms, Clinical Manifestations, and Management

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Abstract

Platinum-based chemotherapeutic agents, including cisplatin, carboplatin, and oxaliplatin, are widely used in the treatment of solid malignancies but may cause clinically important cardiovascular complications. Platinum-induced cardiotoxicity is multifactorial and involves oxidative stress, endothelial dysfunction, inflammation, mitochondrial injury, and treatment-related electrolyte disturbances. Cardiovascular manifestations may occur acutely during or shortly after chemotherapy or may develop months to years after treatment, including arrhythmias, hypertension, coronary artery disease, thromboembolic events, and heart failure. The risk is increased by advanced age, pre-existing cardiovascular disease, high cumulative chemotherapy doses, combination treatment, renal dysfunction, and lifestyle-related factors. Baseline cardiovascular assessment, regular monitoring of electrocardiography, echocardiography, biomarkers, renal function, and electrolytes, together with appropriate lifestyle and pharmacological interventions, may reduce cardiovascular risk. Management should be individualized and may require correction of reversible factors, treatment of specific cardiovascular complications, and modification of the chemotherapy regimen. Close collaboration between oncology and cardiology teams is essential for early detection, prevention, and long-term management of platinum-associated cardiotoxicity.

Keywords: Platinum-based chemotherapy; cardiotoxicity; cisplatin; carboplatin; oxaliplatin; cardiovascular complications; oxidative stress; endothelial dysfunction; cardio-oncology; cancer survivors.

Introduction

Platinum-based chemotherapeutic agents, including cisplatin, carboplatin, and oxaliplatin, are widely used in the treatment of various solid malignancies such as lung, colorectal, ovarian, and testicular cancers [1–4]. These agents exert their antitumor effects primarily through the formation of DNA crosslinks, leading to inhibition of DNA replication and transcription, ultimately resulting in cancer cell apoptosis. Despite their proven efficacy and central role in many standard treatment protocols, their toxicity profile remains a significant clinical concern.

While their antitumor efficacy is well established, increasing evidence highlights their association with cardiovascular toxicity, which may manifest both in the acute phase and long after the completion of therapy [2,3,5]. Reported cardiovascular complications include endothelial dysfunction, hypertension, thromboembolic events, arrhythmias, and, in some cases, ischemic heart disease. Cisplatin, in particular, has been strongly linked

to vascular toxicity due to its ability to induce oxidative stress, inflammation, and direct endothelial injury, thereby accelerating atherosclerosis and promoting a prothrombotic state.

With improved cancer survival rates, largely due to advances in early detection and more effective systemic therapies, long-term complications such as cardiotoxicity have become increasingly relevant in clinical practice. As the population of cancer survivors continues to grow, there is a parallel rise in treatment-related comorbidities that can significantly impact quality of life and overall survival. In this context, cardiovascular disease has emerged as one of the leading non-cancer causes of morbidity and mortality among cancer survivors.

Understanding the cardiovascular risks associated with platinum-based chemotherapy is therefore critical for optimizing both oncological and cardiac outcomes. Early identification of high-risk patients, implementation of preventive strategies, and close multidisciplinary

collaboration between oncologists and cardiologists are essential components of modern cancer care. Furthermore, ongoing research into biomarkers and imaging techniques for early detection of cardiotoxicity may help to personalize treatment approaches and reduce the burden of long-term cardiovascular complications.

Mechanisms of Cardiotoxicity

The mechanisms of platinum-induced cardiotoxicity are complex and multifactorial, involving a combination of direct cellular injury and systemic vascular effects. Oxidative stress plays a central role in this process, as platinum compounds stimulate the excessive production of reactive oxygen species (ROS), overwhelming the antioxidant defense systems and leading to lipid peroxidation, protein modification, and DNA damage within cardiomyocytes [6,7]. This oxidative imbalance contributes not only to structural damage but also to functional impairment of cardiac cells.

Additionally, endothelial dysfunction represents a key mechanism underlying vascular toxicity. Platinum agents disrupt endothelial integrity by reducing nitric oxide (NO) bioavailability, increasing oxidative stress, and promoting vasoconstriction [7]. This results in impaired vasodilation, increased vascular stiffness, and a prothrombotic state. Inflammatory pathways are also activated, with elevated levels of cytokines and adhesion molecules further aggravating vascular injury and contributing to the progression of atherosclerosis.

Mitochondrial dysfunction further exacerbates cardiac damage, as platinum compounds interfere with mitochondrial DNA and impair oxidative phosphorylation, leading to reduced ATP production and increased apoptosis of cardiomyocytes. Moreover, electrolyte disturbances—particularly hypomagnesemia and hypokalemia—are commonly observed during platinum-based therapy due to renal tubular toxicity. These imbalances can significantly affect cardiac electrophysiology and predispose patients to various arrhythmias, including potentially life-threatening ventricular arrhythmias.

Clinical Manifestations

Clinical manifestations of platinum-induced cardiotoxicity are heterogeneous and may range from subclinical or asymptomatic alterations detectable only through imaging or biomarkers to severe, life-threatening cardiovascular events [2,3]. Acute toxicity can occur during or shortly after drug administration and may present as arrhythmias (such as atrial fibrillation or ventricular ectopy), transient ischemic changes, coronary vasospasm, or even acute myocardial infarction in rare cases. Patients may also experience chest pain, palpitations, or syncope in the acute setting.

Chronic toxicity, on the other hand, often develops insidiously and may manifest months or even years after completion of chemotherapy [8]. Long-term complications

include persistent hypertension, accelerated atherosclerosis, coronary artery disease, and chronic heart failure. The delayed nature of these effects highlights the importance of long-term surveillance, as patients may remain asymptomatic until significant cardiovascular damage has already occurred. Subclinical changes, such as reduced left ventricular function or increased arterial stiffness, may precede overt clinical disease.

Risk Factors

Several risk factors have been identified that increase the likelihood of developing platinum-induced cardiotoxicity [9,10]. Advanced age is a well-recognized factor, as older patients often have reduced physiological reserve and a higher prevalence of underlying cardiovascular conditions. Pre-existing cardiovascular disease—including hypertension, coronary artery disease, and heart failure—significantly amplifies susceptibility to treatment-related cardiac complications.

Treatment-related factors also play an important role. High cumulative doses of platinum agents, prolonged treatment duration, and the use of combination chemotherapy regimens can increase cardiotoxic risk. In particular, patients receiving concurrent cardiotoxic therapies—such as anthracyclines, targeted agents, or thoracic radiotherapy—are at especially high risk due to potential synergistic effects on cardiac tissue.

Other contributing factors may include renal dysfunction, which can exacerbate electrolyte imbalances, as well as lifestyle-related factors such as smoking, obesity, and physical inactivity. Genetic predisposition and individual variability in drug metabolism may also influence susceptibility, although these aspects are still under investigation.

Identification and careful assessment of these risk factors are crucial for the implementation of preventive strategies, risk stratification, and individualized patient management, ultimately aiming to reduce the incidence and severity of cardiovascular complications associated with platinum-based chemotherapy.

Prevention and Monitoring

Preventive strategies play a crucial role in minimizing the risk of platinum-induced cardiotoxicity and should begin prior to the initiation of chemotherapy. A comprehensive baseline cardiovascular assessment is recommended, including detailed medical history, physical examination, electrocardiography (ECG), and echocardiography to evaluate cardiac structure and function [9]. In selected patients—particularly those with pre-existing cardiovascular disease or multiple risk factors—additional investigations such as cardiac biomarkers (e.g., troponins, natriuretic peptides) and advanced imaging techniques may be considered to improve risk stratification.

Table 1: Risk Factors for Platinum-Induced Cardiotoxicity

<i>Risk factor</i>	<i>Mechanism</i>	<i>Clinical impact</i>
Age >60	Reduced cardiac reserve	Higher risk of HF
CVD	Baseline dysfunction	Increased complications
High dose	Cumulative toxicity	Myocardial damage
Electrolyte imbalance	Arrhythmogenic effect	Arrhythmias
Combination therapy	Synergistic toxicity	Severe cardiotoxicity

Electrolyte monitoring is especially important, given the high incidence of hypomagnesemia and hypokalemia associated with platinum agents. Baseline and periodic assessment of serum electrolytes, renal function, and metabolic parameters should be routinely performed to prevent arrhythmogenic complications.

During treatment, regular cardiovascular monitoring is essential to detect early signs of toxicity. This may include serial ECGs, repeat echocardiography, and biomarker evaluation in high-risk patients. Early identification of subclinical changes allows timely intervention and may prevent progression to overt cardiovascular disease.

In addition to medical monitoring, lifestyle interventions such as smoking cessation, dietary optimization, weight control, and regular physical activity should be encouraged, as they can significantly reduce overall cardiovascular risk. Pharmacological strategies—such as the use of antihypertensive agents, statins, or cardioprotective medications—may be considered in selected high-risk individuals. Close collaboration between oncologists and cardiologists is fundamental to ensure a balanced approach between effective cancer treatment and cardiovascular safety.

Management

Management of platinum-induced cardiotoxicity depends on the type and severity of cardiovascular involvement and requires an individualized approach [3,11]. Initial measures often include correction of reversible factors, particularly electrolyte imbalances such as hypomagnesemia and hypokalemia, which are critical in the prevention and treatment of arrhythmias.

Pharmacological treatment should be guided by the specific clinical manifestation. For example, antihypertensive therapy is indicated in patients with treatment-induced hypertension, while standard heart failure therapies—including ACE inhibitors, beta-blockers, and diuretics—are used in cases of ventricular dysfunction. Antiarrhythmic agents may be required for rhythm disturbances, and anticoagulation should be considered in patients with thromboembolic complications.

In some cases, modification of the chemotherapy regimen may be necessary. This can include dose reduction,

treatment delay, or substitution with less cardiotoxic alternatives, depending on the balance between oncological efficacy and cardiovascular risk. Decisions regarding treatment modification should be made collaboratively within a multidisciplinary team.

A dedicated cardio-oncology approach is strongly recommended to optimize patient outcomes. Such collaboration facilitates early detection, coordinated management, and long-term follow-up of patients at risk for or experiencing cardiotoxicity.

Conclusion

Platinum-based chemotherapy remains a cornerstone in the treatment of a wide range of malignancies; however, its association with cardiovascular toxicity represents a significant clinical challenge [1,12]. As cancer survival rates continue to improve, the long-term cardiovascular health of patients has become an increasingly important aspect of comprehensive oncological care.

Early detection through appropriate screening and monitoring, implementation of preventive strategies, and timely, individualized management are essential to reduce the burden of cardiotoxicity and improve both quality of life and survival outcomes.

Further research is needed to better elucidate the underlying mechanisms of toxicity, identify reliable predictive biomarkers, and develop targeted cardioprotective strategies. Advances in the field of cardio-oncology will play a key role in achieving a more personalized and safer approach to cancer treatment.

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