Immune Checkpoint Inhibitor Myocarditis: A Rare, High-Mortality Risk

Written by The Life Science Feed Editorial Team · Published 27 August 2026 · Edited by Mara Voss

Immune checkpoint inhibitors (ICIs) have significantly advanced cancer treatment by activating the immune system against tumors. However, this broad immune activation can also lead to immune-related adverse events (irAEs), with cardiovascular toxicities emerging as a critical concern. This review highlights the mechanisms, clinical spectrum, and management strategies for ICI-associated cardiotoxicity, particularly focusing on myocarditis due to its high mortality risk.

KEY TAKEAWAYS

- The Pivot: While ICIs offer significant anti-tumor benefits, their immune activation can paradoxically target cardiac tissue, leading to severe cardiotoxicity.
- The Data: Immune-mediated myocarditis, though rare, carries a disproportionately high mortality risk among ICI-associated cardiovascular toxicities.
- The Action: Clinicians should prioritize early detection through biomarker monitoring and multimodal imaging, alongside exploring targeted immune pathway therapies to mitigate cardiac complications.

Understanding ICI-Induced Cardiotoxicity

Immune checkpoint inhibitors (ICIs) have revolutionized oncology by blocking inhibitory immune pathways like programmed death receptor-1 (PD-1), programmed death ligand-1 (PD-L1), and cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). This action restores the immune system's ability to fight cancer. However, this widespread immune activation can also lead to immune-related adverse events (irAEs), affecting various organ systems. Cardiovascular toxicities are a growing concern within cardio-oncology, encompassing a range of conditions from myocarditis and pericarditis to arrhythmias, heart failure, and vascular complications. Among these, immune-mediated myocarditis is considered the most severe, despite its relatively low incidence, due to its high mortality risk1.

Complex Immunological Mechanisms

The pathophysiology of ICI-induced myocarditis is multifaceted. It is primarily driven by dysregulated immune activation, leading to myocardial inflammation and T-cell-mediated cytotoxicity. Aberrant cytokine release also plays a significant role. A key mechanism involves molecular mimicry, where immune cells mistakenly target cardiac antigens due to their similarity to tumor antigens. Beyond these, additional pathways contribute to myocardial injury and arrhythmogenic susceptibility, including B-cell activation, complement cascade signaling, and engagement of the inflammasome pathway1.

Clinical Spectrum of Cardiovascular irAEs

ICI-associated cardiotoxicity presents across a broad clinical spectrum. While myocarditis is the most critical, other manifestations include pericarditis, which is inflammation of the sac surrounding the heart; various arrhythmias, which are irregular heartbeats; heart failure, characterized by the heart's inability to pump blood effectively; and vascular complications. The severity and presentation can vary widely among patients, making early and accurate diagnosis challenging but crucial for improved outcomes1.

Strategies for Early Detection and Surveillance

Given the severity of ICI-induced myocarditis, strategies for early detection, risk stratification, and clinical surveillance are essential. These strategies include regular biomarker monitoring, such as cardiac troponins, which can indicate myocardial damage. Multimodal imaging techniques, including echocardiography, cardiac magnetic resonance imaging (CMR), and positron emission tomography (PET), are also vital for assessing cardiac function and inflammation. A deeper mechanistic understanding of these toxicities is considered essential for advancing their prevention, diagnosis, and management in oncology practice1.

Emerging Therapeutic Approaches

Current research is exploring emerging therapeutic strategies aimed at mitigating cardiovascular complications without compromising the anticancer efficacy of ICIs. These approaches often target the implicated immune pathways responsible for the cardiotoxicity. The goal is to develop interventions that can specifically dampen the immune response against cardiac tissue while preserving the anti-tumor immune response. Such targeted therapies could significantly improve the safety profile of ICIs and expand their use in cancer treatment1.

Clinical Implications: Why this matters for clinical practice today

The increasing use of immune checkpoint inhibitors in oncology necessitates a heightened awareness among clinicians regarding their potential for severe cardiovascular adverse events, particularly myocarditis. While rare, the high mortality associated with ICI-induced myocarditis means that a missed diagnosis can have devastating consequences. Therefore, oncologists, cardiologists, and primary care providers must maintain a high index of suspicion for cardiac symptoms in patients receiving ICIs. Proactive monitoring with cardiac biomarkers and consideration of advanced imaging like cardiac MRI, even in the absence of overt symptoms, may be warranted in high-risk individuals or those with subtle changes. Establishing clear referral pathways between oncology and cardio-oncology specialists is critical for prompt diagnosis and multidisciplinary management. Furthermore, understanding the underlying immune mechanisms can inform the development of more targeted and safer therapeutic strategies, allowing patients to benefit from life-extending cancer treatments with reduced cardiac risk.

Limitations and Future Directions

This review summarizes current insights into ICI-induced cardiotoxicity. However, the field is rapidly evolving, and a complete understanding of all contributing immune mechanisms is still developing. Further research is needed to precisely delineate the roles of B-cell activation, complement cascade signaling, and inflammasome pathway engagement in myocardial injury. Future studies should focus on refining risk stratification tools to identify patients most susceptible to these adverse events. Additionally, clinical trials are necessary to evaluate the efficacy and safety of emerging targeted therapeutic strategies to mitigate cardiovascular complications while preserving anti-cancer benefits. Continued research into these areas will be crucial for optimizing patient care and improving outcomes for individuals treated with ICIs1.

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REFERENCES

1. 1. Chen NK, Hok KD, Chokshi N, et al. Immune checkpoint inhibitor-induced cardiotoxicity: from immune mechanisms to clinical surveillance and targeted therapies. Front Cardiovasc Med. 2026;13:1872588. doi:10.3389/fcvm.2026.1872588

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