ICI-Related Cardiac Injury: Myocarditis, Coronary, Conduction Disease

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The increasing use of immune checkpoint inhibitors (ICIs) in oncology has brought to light a spectrum of immune-related adverse events (irAEs), with cardiac toxicities representing a critical, albeit less common, complication. Clinicians must recognise that ICI-related cardiac injury extends beyond the well-publicised myocarditis, encompassing coronary artery disease and conduction system disorders, necessitating a broad diagnostic approach and multidisciplinary management.

KEY TAKEAWAYS

- The Pivot: ICI-related cardiac injury is not limited to myocarditis but includes coronary and conduction abnormalities.
- The Data: Myocarditis incidence is approximately 0.3-1.0%, but mortality can reach 30-50% in severe cases.
- The Action: Implement comprehensive cardiac monitoring protocols for patients on ICIs, including baseline and serial ECGs, troponin, and BNP.

Immune checkpoint inhibitors (ICIs), including programmed cell death protein 1 (PD-1), programmed death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibitors, have transformed cancer treatment. While effective, these agents can induce immune-related adverse events (irAEs) affecting various organ systems. Cardiac irAEs, though less frequent than dermatologic or gastrointestinal toxicities, are associated with significant morbidity and mortality. The presentation of ICI-related cardiac injury is diverse, ranging from acute myocarditis to chronic coronary artery disease and conduction system abnormalities, often presenting with non-specific symptoms or as incidental findings on routine monitoring.1

Myocarditis is the most recognised and severe form of ICI-related cardiac toxicity, with an estimated incidence ranging from 0.3% to 1.0% across clinical trials and real-world data.2 However, the mortality rate for severe ICI-myocarditis can be as high as 30-50%, underscoring the need for early detection and aggressive management.3 Histopathologically, ICI-myocarditis is characterised by T-cell and macrophage infiltration, distinct from viral myocarditis.4

The underlying mechanisms of ICI-related cardiac injury involve the disruption of immune tolerance, leading to an autoimmune attack on cardiac tissues. This is particularly relevant given the expression of PD-L1 on cardiomyocytes, which normally helps to prevent immune overactivity. When ICIs block these checkpoints, the immune system can become hyperactive, targeting healthy cardiac cells. This shared mechanism suggests a common immunological basis for the diverse cardiac manifestations observed. Understanding these mechanisms is crucial for developing targeted therapies and preventative strategies.

What the study did

The ESC Cardio-Oncology 2026 session highlighted the expanding understanding of ICI-related cardiac injury beyond myocarditis. Presentations focused on the emerging evidence for ICI-associated coronary artery disease and conduction system disorders. While direct randomised controlled trials on these specific toxicities are limited, data from retrospective analyses, case series, and pharmacovigilance databases were synthesised to illustrate the breadth of cardiac involvement.5

Regarding coronary artery disease, several case reports and small series have documented acute coronary syndromes, including myocardial infarction, in patients receiving ICIs, often in the absence of traditional cardiovascular risk factors or with rapid progression of pre-existing disease.6 The proposed mechanism involves immune-mediated vasculitis or accelerated atherosclerosis. The incidence of ICI-associated acute coronary syndrome is not precisely quantified but is considered rare. However, its occurrence necessitates a high index of suspicion in patients presenting with chest pain while on ICI therapy.7

Conduction system abnormalities represent another facet of ICI-related cardiac injury. These can manifest as new-onset atrioventricular blocks, bundle branch blocks, or sinus node dysfunction.8 The pathogenesis is thought to involve immune cell infiltration and inflammation of the cardiac conduction system. While often asymptomatic in early stages, severe cases can lead to syncope, bradycardia, and require permanent pacemaker implantation. The incidence of clinically significant conduction abnormalities is estimated to be lower than that of myocarditis, but routine electrocardiogram (ECG) monitoring is recommended to detect these changes.9

The session also emphasised the importance of a multidisciplinary approach to managing these complex toxicities, involving cardiologists, oncologists, and critical care specialists. Early recognition through serial monitoring of cardiac biomarkers (troponin, BNP) and ECGs is paramount. Management strategies typically involve the discontinuation of

ICI therapy and the initiation of high-dose corticosteroids, with additional immunosuppressive agents like infliximab or mycophenolate mofetil considered for refractory cases.10

Patient populations at higher risk for ICI-related cardiac injury are not yet fully defined, but emerging data suggest that patients with pre-existing autoimmune conditions or those receiving combination ICI therapy may have an elevated risk. Further research is needed to identify specific genetic predispositions or biomarkers that could predict susceptibility to these adverse events, allowing for more personalised risk stratification before initiating ICI treatment. The clinical presentation of these cardiac irAEs can be subtle, often mimicking other common cardiac conditions, which complicates diagnosis and can delay appropriate intervention.

Limitations in the current understanding include the lack of large prospective studies specifically designed to evaluate the incidence and mechanisms of ICI-associated coronary and conduction disease. Most data are derived from observational studies and case reports, which are prone to reporting bias. Furthermore, the heterogeneity in reporting standards across different institutions and studies makes it challenging to accurately determine the true incidence and prevalence of these less common cardiac irAEs. The absence of standardised diagnostic criteria for ICI-related coronary and conduction disease also contributes to under-recognition and inconsistent management. Further research is needed to establish definitive diagnostic criteria, optimal monitoring strategies, and evidence-based treatment algorithms for these less common but potentially severe cardiac irAEs. Future studies should focus on identifying predictive biomarkers and genetic predispositions to better stratify patient risk.

For a comprehensive overview of cardiac conditions, including those discussed, consult the authoritative Oxford Handbook of Cardiology.

CLINICAL IMPLICATIONS

The expanded understanding of ICI-related cardiac injury presented at ESC Cardio-Oncology 2026 demands a recalibration of clinical vigilance. It is no longer sufficient for clinicians to solely screen for myocarditis; the spectrum of potential cardiac harm now clearly includes coronary events and conduction disorders. This necessitates a more comprehensive baseline cardiac assessment and ongoing monitoring for patients initiating ICI therapy. Oncologists, often the primary prescribers, must integrate cardiology expertise earlier in the treatment pathway, moving beyond reactive consultations to proactive risk assessment. The current reliance on troponin and BNP, while useful for myocarditis, may not fully capture the risk of coronary or conduction issues, suggesting a need for more frequent ECGs and a lower threshold for advanced cardiac imaging.

For the pharmaceutical industry, the increasing recognition of diverse irAEs presents both a challenge and an opportunity. Companies developing new ICIs or combination therapies must incorporate robust cardiac safety endpoints into their clinical trial designs, moving beyond general adverse event reporting to specific cardiac assessments. This will generate the precise data needed to inform risk stratification and management guidelines. Furthermore, the development of predictive biomarkers for specific cardiac irAEs would be invaluable, allowing for personalised risk-benefit assessments and potentially guiding prophylactic strategies, thereby improving patient safety and optimising treatment outcomes.

Patients receiving ICIs, and their families, require clear and concise information regarding the potential for cardiac complications. The non-specific nature of many cardiac symptoms means that patients must be

empowered to report subtle changes, such as new-onset chest discomfort, palpitations, or unexplained fatigue, without delay. Educational initiatives should highlight that while rare, these events are serious and require immediate medical attention. The multidisciplinary approach advocated by the ESC Cardio-Oncology session underscores the importance of integrated care, ensuring that patients benefit from the combined expertise of their oncology and cardiology teams, ultimately leading to safer and more effective cancer treatment.

EDITORIAL & AI STANDARDS

AI tools are used to structure and summarise evidence from peer-reviewed primary sources. Articles that carry a signed Editor's take have been read in full by William Lopes. The others are not individually read by an editor, so check the cited source before relying on a figure.

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