CTRCD Incidence Varies by Cancer Therapy in KP CHEMO Study

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> Cancer therapy-related cardiac dysfunction (CTRCD) contributes to incident heart failure (HF) in cancer survivors, yet population-based estimates of its incidence have been limited.2 The Kaiser Permanente Cardiovascular Health Enhancement and Monitoring for Oncology (KP CHEMO) study provides real-world data on CTRCD incidence, timing, and treatment-specific variation, offering a clearer understanding of this complication.1

KEY TAKEAWAYS

- The Pivot: Real-world data now quantifies CTRCD incidence and its variation across specific cancer therapies in a large, diverse cohort.
- The Data: The KP CHEMO study determined the incidence, timing, and treatment-specific variation in CTRCD.1
- The Action: Clinicians should consider specific cardiotoxic cancer therapies when monitoring for CTRCD, utilising multimodality imaging as per consensus statements.

Contemporary oncologic treatments, while effective against cancer, carry a known risk of cardiac complications, particularly cancer therapy-related cardiac dysfunction (CTRCD). This dysfunction is a significant contributor to the development of heart failure (HF) among cancer survivors.1,2 Despite the recognition of certain cardiotoxic cancer therapies, comprehensive population-based estimates of CTRCD incidence in large, diverse, and contemporary patient cohorts have been scarce.1,2

The KP CHEMO Study and Multimodality Imaging Consensus

The Kaiser Permanente Cardiovascular Health Enhancement and Monitoring for Oncology (KP CHEMO) study aimed to address this data gap by determining the incidence, timing, and treatment-specific variation of CTRCD within an integrated US health system.1 This study provides essential real-world data on how frequently CTRCD occurs and when it typically manifests in relation to different cancer treatments. The findings from KP CHEMO contribute to a more precise understanding of the burden of CTRCD, moving beyond theoretical risks to observed outcomes in a broad patient population.1

Complementing these incidence data, a clinical consensus statement from the ESC Council of Cardio-Oncology and the European Association of Cardiovascular Imaging (EACVI) of the ESC addresses the role of multimodality imaging in detecting and managing cardiovascular complications.2 This statement specifically focuses on coronary and peripheral arterial disease in patients receiving cardiotoxic antineoplastic treatments.2 The consensus highlights the importance

of various imaging techniques to identify and monitor cardiovascular issues that may arise from cancer therapies. This includes, but is not limited to, the detection of CTRCD, which is a primary concern in cardio-oncology.2 The statement underscores that a comprehensive imaging approach is necessary for effective management, allowing for early detection and intervention to mitigate the long-term cardiac sequelae of cancer treatment.2

Both the KP CHEMO study and the ESC/EACVI consensus statement reinforce the necessity of vigilant cardiovascular monitoring in patients undergoing cancer therapy. The KP CHEMO data provides the epidemiological context, detailing the real-world occurrence of CTRCD.1 The consensus statement, in turn, offers practical guidance on how to implement effective surveillance using advanced imaging modalities.2 Together, these publications provide a more complete picture for clinicians, from understanding the prevalence of CTRCD to establishing best practices for its detection and management in patients with cancer and cancer survivors.1,2

Clinical Context and Patient Populations

The increasing survival rates for many cancers have brought the long-term side effects of cancer therapy into sharper focus. Cardiotoxicity, particularly CTRCD, represents a significant challenge in this context. Anthracyclines, such as doxorubicin, and human epidermal growth factor receptor 2 (HER2)-targeted therapies, like trastuzumab, are well-established causes of CTRCD. However, other agents, including certain tyrosine kinase inhibitors and immune checkpoint inhibitors, also carry cardiotoxic potential, necessitating a broader understanding of risk across the spectrum of modern oncology. The clinical presentation of CTRCD can range from asymptomatic left ventricular ejection fraction (LVEF) decline to overt heart failure, emphasizing the need for proactive screening and monitoring. Early detection of LVEF decline, even in the absence of symptoms, allows for the initiation of cardioprotective strategies, potentially preventing irreversible cardiac damage and improving long-term outcomes for cancer survivors.

Methodological Approach of KP CHEMO

The KP CHEMO study leveraged the extensive electronic health records of the Kaiser Permanente integrated health system, which encompasses a diverse patient population across multiple regions in the United States. This integrated system facilitates comprehensive data collection, including detailed information on cancer diagnoses, specific chemotherapy regimens, cardiac imaging results (such as echocardiograms), and subsequent cardiovascular outcomes. The study defined CTRCD based on established criteria, typically involving a significant decline in LVEF from baseline, often below a specific threshold (e.g., 10% absolute decline from baseline). The researchers employed robust statistical methods to analyze the incidence of CTRCD across different cancer types and treatment protocols, accounting for potential confounding factors such as pre-existing cardiovascular disease, age, and other comorbidities. This rigorous methodology enhances the generalizability and reliability of the study's findings, providing valuable insights into the real-world epidemiology of CTRCD. The study's ability to track patients longitudinally within a single health system also allowed for a detailed examination of the timing of CTRCD onset relative to the initiation and duration of specific cancer therapies.

Limitations and Future Directions

While the KP CHEMO study offers significant contributions, it also has inherent limitations. As an observational study, it cannot establish causality definitively, although strong associations are evident. The reliance on electronic health records means that the accuracy of CTRCD diagnosis is dependent on the completeness and quality of clinical documentation

and imaging reports. Furthermore, the study population, while diverse, is drawn from an integrated health system, which may not perfectly represent all demographic or socioeconomic groups within the broader US population. Future research should aim to validate these findings in other large cohorts and explore the genetic and molecular mechanisms underlying individual susceptibility to CTRCD. Further investigation into the efficacy of various cardioprotective strategies in real-world settings is also warranted. The ESC/EACVI consensus statement, while providing crucial guidance on imaging, highlights the ongoing need for standardized protocols and training to ensure consistent application of multimodality imaging techniques across different clinical centers. Continued collaboration between cardiologists and oncologists remains paramount to optimize cardiovascular care for patients undergoing cancer treatment.
For a comprehensive overview of cardiovascular management and related interdisciplinary challenges discussed here, readers may consult the definitive Oxford Handbook of Cardiology.

CLINICAL IMPLICATIONS

The KP CHEMO study's quantification of CTRCD incidence by specific cancer therapy is a welcome dose of reality. For too long, discussions around cardiotoxicity have been broad, often lumping disparate agents together. This new data allows clinicians to move beyond general awareness to a more nuanced risk assessment, particularly when selecting or monitoring patients on known cardiotoxic agents. It should prompt a re-evaluation of current monitoring protocols, ensuring that surveillance is tailored to the specific treatment regimen rather than a one-size-fits-all approach. The days of simply 'being aware' of cardiotoxicity are over; now, we have a clearer picture of when and with what agents to be most vigilant.
The ESC/EACVI consensus on multimodality imaging further solidifies the need for proactive cardiovascular assessment. It is no longer sufficient to wait for symptomatic heart failure. Early detection of subclinical changes via advanced imaging, as outlined in the consensus, is paramount. This places a greater onus on cardiologists and oncologists to collaborate, integrating imaging protocols into the patient's cancer treatment pathway. Investment in appropriate imaging infrastructure and training for specialists will be critical. Without it, the insights from KP CHEMO on incidence will remain academic, failing to translate into improved patient outcomes.
From an industry perspective, these findings highlight the ongoing need for novel cancer therapies with improved cardiovascular safety profiles. The data from KP CHEMO provides a baseline against which new agents can be compared. Furthermore, the emphasis on multimodality imaging may drive innovation in diagnostic technologies, particularly those offering non-invasive, high-resolution assessment of cardiac function. Pharmaceutical companies developing cardiotoxic agents should consider robust cardio-oncology programmes as standard, not an afterthought, ensuring that the benefits of cancer treatment are not undermined by preventable cardiac morbidity.

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