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Advanced imaging modalities to detect cardiotoxicity

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ABSTRACT

Recent advances in cancer treatments have significantly improved survival rates, reemphasizing the focus on reducing the potential complications associated with some therapies. Cardiovascular disease associated with chemotherapies is a major cause of morbidity and mortality in cancer survivors. Early detection of cardiotoxicity improves cardiac outcomes among cancer patients. The review will focus on imaging modalities used to assess cardiotoxicity - the cardiovascular consequences of chemotherapies. The review will discuss the benefits and limitations associated with each technique, as well as the guidelines available to help identify at risk patients. We will discuss novel techniques that may help detect earlier signs of cardiotoxicity, directing management that may improve clinical outcomes.

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Introduction

Due to the improvement in cancer survival, an increasing number of patients may develop treatment-associated cardiac disease, broadly termed as cardiotoxicity. Standard current

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methods for detection of cardiotoxicity primarily involve serial measurement of the left ventricular ejection fraction (LVEF), a parameter that when reduced is a late manifestation in the cardiotoxic paradigm and when the possibility for reversibility declines. Early detection of cardiotoxicity may be important as clinical outcomes can be improved with the early initiation of cardioprotective medications. The past decade has seen rapid advances in imaging modalities such as cardiac magnetic resonance (CMR) and echocardiography. Advances in both echo and CMR allow the early detection of myocardial mechanical changes such as global longitudinal strain that occur prior to the onset of left ventricular (LV) dysfunction, while the main strengths of CMR are improved spatial resolution and complementary tissue characterization.

This comprehensive review will discuss the current as well as emerging advanced imaging modalities available to detect cardiotoxicity and how these may shape the future guidelines for its early detection.

Definitions

Cardiotoxicity related to cancer therapy is a broad term and includes any functional or structural heart injury related to cancer treatment.[1–4] Cardiotoxicity may occur secondary to the cancer, chemotherapy, or radiotherapy.[5] The injury to the heart most commonly involves the myocardium leading to heart failure but can also involve the pericardium, valves, or coronary arteries progressing to pericardial disease, valvular disease, and coronary artery disease.[6,7] The current standard definition for cardiotoxicity is defined by the Cardiac Review and Evaluation Committee (CREC) on trastuzumab-associated cardiotoxicity and the ESMO Clinical Practice Guidelines.[8]

Specifically, cardiotoxicity after chemotherapy is defined as a decrease in LVEF of $\geq$5% to $<$55% in the presence of symptoms of Heart Failure (HF) or an asymptomatic decrease in LVEF by $\geq$10% to less than 55%. There are multiple factors involved in the development of cardiotoxicity and the definition of cardiotoxicity beyond the general and Cardiac Review and Evaluation Committee definition above varies widely; as a result, the estimated incidence varies significantly from $<$1% to nearly 50% when comparing over 40 different studies.[9]

Cardiotoxic chemotherapies

There are several cancer treatments that have been associated with the potential for cardiotoxicity. Some examples include anthracyclines, 5-fluorouracil, cyclophosphamide, tyrosine kinase inhibitors, vascular endothelial growth factor, immune checkpoint inhibitors, HER-2 antagonists and radiation therapy.[2,6,8,10-15] Most of the data that exists relates to the cardiotoxicity that occurs with anthracyclines and trastuzumab (Herceptin, a HER-2 antagonist), and these will be the primary focus for the remainder of this article.

Importance of early detection of cardiotoxicity

Over the last decade, it has become clear that the early detection of cardiac dysfunction, cardiotoxicity or cardiac injury, and the institution of appropriate cardiovascular care can improve outcomes.[6] Cardinale et al. studied the clinical response to heart failure in a group of 200 patients with anthracycline-induced cardiotoxicity and a resultant reduction in LVEF $\leq$ 45%.[6] LVEF was assessed at regular intervals by echocardiography following the initiation of optimal heart failure medication including enalapril and carvedilol. Depending on the level of recovery of the LVEF, the patients were designated as complete recovery (LVEF recovery to $\geq$50%), partial recovery (increase by $\geq$10% to LVEF $<$ 50%), or nonresponders (increase by $<$10% to LVEF $<$ 50%). Complete response was noted in 40% of patients, partial response in nearly 15% and nonresponse in 45%. The most critical determinant of LVEF response was the length of time from diagnosis

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