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REVIEW

Cardiac Imaging in Oncology Patients in Europe: a Model for Advancement of CV Safety and Development of Comprehensive CV Care

Teresa López-Fernández[1]

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Abstract

Cancer therapy-related cardiovascular events are widely recognized as a global problem, and cardio-oncology has been proposed as a new approach to coordinate preventive strategies in oncologic patients. Cardiac imaging plays a critical role in this process. This article summarizes current practices and future needs in cardiac imaging to improve the cardiovascular surveillance of cancer patients.

Keywords Cardio-oncology · Cancer · Cardiac imaging · Echocardiography

Cancer therapy-related cardiovascular (CV) events are widely recognized as a global problem, and cardio-oncology has been proposed as a new approach to coordinate preventive strategies that improve the CV health of oncologic patients [1, 2]. Cancer and CV diseases are connected by complex pathophysiological mechanisms (inflammation, oxidative stress, neuro-hormonal activation, immune system), and both entities shared modifiable and non-modifiable risk factors that may increase the risk of CV complications beyond anticancer therapies (Fig. 1) [3–7]. For that reason, a comprehensive CV evaluation and monitoring, throughout the cancer process, is needed [8].

While in recent years, much of the focus has been in the early detection and prevention of myocardial damage, and new targeted therapies are associated with a broad range of arrhythmic and vascular toxicities that may also trigger heart failure (HF) if poorly controlled. Therefore, a new strategy based on precision cardio-oncology is required.

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✉ Teresa López-Fernández
teresa.lopez@salud.madrid.org

[1] Cardiology Department, Cardiac Imaging and Cardio-Oncology Unit, IdiPAZ, CIBER CV, La Paz University Hospital, Madrid, Spain

What Is the Role of Cardiac Imaging in Cardio-Oncology?

Cardiac imaging plays a critical role in clinical decision-making during the cancer process, particularly in patients at risk of HF [9, 10]. New imaging techniques may help us to stratify cardiotoxicity (CTox) risk, to optimize CV therapy, to prevent and manage CTox, and to guide long-term survivors' follow-up (Fig. 1).

The prevention of CTox starts before cancer therapy with the cardiologist and the oncologist working together to stratify how robust or frail a patient is. At this stage, cardiac imaging allows us to quantify myocardial function and to rule out unknown structural heart diseases that may require stricter monitoring protocols [1, 2, 11, 12]. During treatment, the main goal is to minimize cancer therapy interruptions, and cardio-oncology teams should be focused on promoting preventive strategies to minimize CV complications [11, 12], particularly in patients with pre-existing heart diseases [13, 14]. The surveillance and diagnosis of cancer-induced myocardial damage are currently performed by echo-derived left ventricular ejection fraction (LVEF), and the most common definition is a symptomatic or asymptomatic decrease of LVEF > 10% to an LVEF < 50% [2]. However, this definition is not universally accepted to guide clinical and research strategies and does not give us information regarding preclinical myocardial dysfunction. To guide the diagnosis and

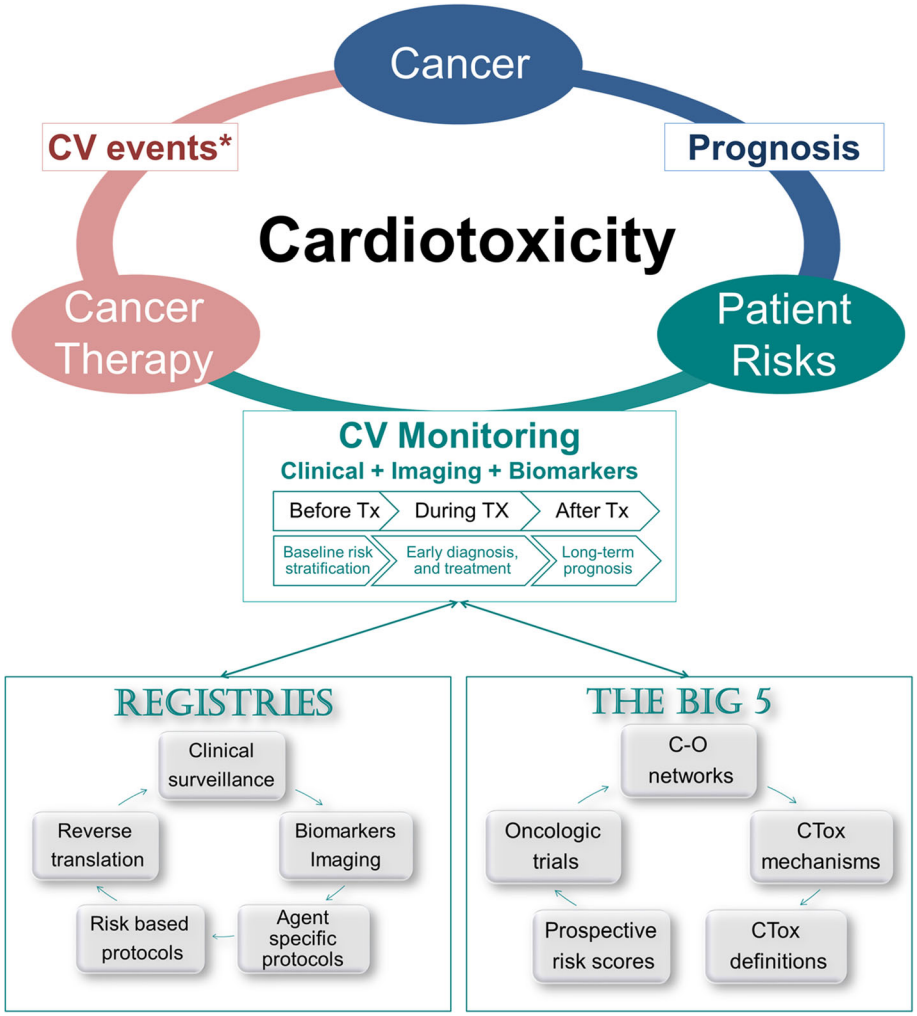

Fig. 1 Cancer and cardiotoxicity (central illustration). The development of cardiotoxicity depends mainly on three factors: the type of cancer, the risk of cancer therapy, and the baseline CV patient's profile. The first two factors determine the potentially expected toxicity*, and the second defines CV prevention and monitoring strategies during and after cancer treatment to minimize late CV events. To expand cardio-oncology culture, we need to improve our knowledge in the field, and for that purpose, robust collaborative networks, clinical trials, and registries are critical. Nowadays, registries have an increasing role in clinical practice, post-market surveillance, and research. They contribute to build robust prospective risk scores and to define standards for CV monitoring to prevent late diagnosis of irreversible myocardial damage. The big 5 initiatives to improve cardio-oncology are also summarize in this figure (see main text). *CV events; heart failure, cardiac arrhythmias, ischemic heart diseases, hypertension, vascular diseases, pericardium diseases, valvular heart diseases, and pulmonary hypertension

management of early reversible stages of myocardial damage, echo-based myocardial strain and cardiac magnetic resonance (CMR) myocardial tissue characterization are the preferred techniques [9, 15, 16].Regarding non-myocardial toxicities (arrhythmic, metabolic, vascular, and thromboembolic events), cardiac imaging testing may help to stratify baseline risk and to optimize CV treatment [9]; however, during cancer treatment, monitoring is generally based on biomarkers, ECG, and clinical findings [2, 3].

How Cardiac Imaging Is Implemented in Daily Practice?

Although cardio-oncology has emerged as a new subspecialty in Europe over the last decades, the lack of widely available dedicated cardio-oncology structures is a major challenge (https://www.escardio.org/Councils/council-of-cardio-oncology/cardio-oncology-in-your-country). In fact, in Europe, 65.7% of cancer patients are reviewed in general cardiology clinics [17], and the use of 3D echo, strain, or CMR is restricted to selected cases [18, 19] and academic centers with cardio-oncology clinics [20]. Additionally, imaging prescription practices of oncologist and cardiologists are disparate in the field of CV toxicity and inconsistent with the expected CTox cumulative incidence. A recently published survey, submitted to French oncologists, has shown that only 35% of them manage CV toxicity according to oncology guidelines and none was aware of the recommendations settled by cardiology societies. Imaging prescription was particularly inconsistent in patients treated with angiogenic inhibitors and other targeted therapies, and the post-therapy evaluation was prescribed significantly less often than pre-therapy assessment [21]. Unfortunately, this is not an isolated finding. In a Canadian population-based retrospective cohort study of breast cancer women, the proportion of patients who underwent pre-treatment imaging was driven by chemotherapy regimen rather than by the risk of major adverse cardiac events [22].

These findings underline the complexity of managing a large number of patients, not all with the same CTox profile

or expected risks, as well as the lack of formal guidelines to standardize a CTox definition and the use of advanced cardiac imaging, based on the risk of clinical CV events [23].

Recently, our group has published a new classification of cancer therapy-induced myocardial damage, based on the risk of clinical events [24]. As in other HF scenarios, the prognosis impact of different clinical, echo, and biomarkers changes should be graded to facilitate clinical decisions. We prospectively studied 865 cancer patients (mean age 54.7 ± 13.9; 16.3% men) treated with moderate-/high-risk cardiotoxic schemes. CTox was defined as new or worsening myocardial damage from baseline during follow-up. Four degrees of progressive myocardial damage were considered according to current HF guidelines (Table 1) [25, 26]. After a median follow-up of 24 months, 37.5% of the patients present objective data of myocardial dysfunction, and their overall prognosis was directly related with their CTox class. In the severe CTox group, mortality rate was 22.9 deaths per 100 patients-year vs 2.3 deaths per 100 patients-year in the rest of groups (HR 10.2; 95% CI 5.5 to 19.2; $p < 0.001$) [24]. Any grade of cancer therapy-induced myocardial dysfunction should be taken into consideration in order to initiate cardioprotection and minimize adverse remodeling. Whether it means that oncological treatment should be stopped remains unclear. In fact, in our study, a decrease in LVEF > 10% with a final LVEF < 50% but over 40% was an insensitive marker to predict mortality at 2 years follow-up, and cancer treatment interruptions certainly increase cancer mortality. This leads to raising the question of whether LVEF should be used as the gold standard to guide cardioprotection or cancer treatment interruptions in clinical and research practices.

Future Needs

If we really want to increase the cardio-oncology workforce, we need to develop sustainable long-term models of provision of CV care for cancer patients. This is particularly important nowadays, due to the rapidly changing environment created by COVID-19 pandemia [27, 28], (https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance). Continuation of CV care for cancer patients is considered critical, but we need to reorganize ourselves in this new normality. To anticipate future health crises, we must focus on prioritizing e-consultations for remote triage, organizing physical protection plans for patients and professionals, and minimizing unnecessary cancer treatment interruptions in stable patients.

Figure 1 summarizes the strategies that we need to expand in this new cardio-oncology culture [29, 30]. From the imaging point of view, the next step is to build robust prospective risk scores to identify vulnerable patients and to reduce current mismatch between CTox risks and imaging prescription,

Table 1 Cardiotoxicity classification proposed by the CardioTox registry

CTox degree	No CTox	Mild CTox	Moderate CTox	Severe CTox
Number of patients in each category	$N = 541$ (62%)	$N = 273$ (31.6%)	$N = 24$ (2.8%)	$N = 27$ (3.1%)
Mortality rate at 24 months F/U	2.3 deaths per 100 patients-year	22.9 deaths per 100 patients-year	Mortality rate at 24 months F/U	2.3 deaths per 100 patients-year
Diagnostic criteria	Normal hs-cTnT and NT-proBNP and normal left ventricular function	LVEF ≥ 50% with abnormal biomarkers and/or at least 1 abnormal echo parameter*	LVEF 40–49% and abnormal biomarkers or echo parameters*	LVEF ≤ 40% or symptomatic heart failure
Clinical status	Asymptomatic No cardiotoxicity criteria	Asymptomatic Mild myocardial damage	Asymptomatic Moderate myocardial damage	HF signs and symptoms Any symptomatic degree of HF
CV management		Consider cardioprotection	HF therapy according to clinical guidelines	CV management
Oncologic management	No change	No change	Multidisciplinary team discussion to review risk-benefit and alternative therapies	Interrupt cancer therapy Multidisciplinary team discussion to resume therapy

CTox cardiotoxicity defined as new or worsening cancer therapy induced myocardial damage/dysfunction, *LVEF* left ventricular ejection fraction, *HF* heart failure

Stages of new or worsening cancer therapy-induced myocardial damage/dysfunction

*Increased left ventricular end systolic volume, left atrial area > 30 cm^2, 10% decrease of LVEF to a LVEF <53% with LVEF>50%, average E/E' > 14, GLS > − 18% or 15% relative reduction of GLS from baseline

during cardiotoxicity surveillance. For that purpose, we need to promote the use of more reproducible and automatic imaging parameters (strain, 3D echo, CMR) for the longitudinal follow-up of cancer patients to avoid unnecessary study repetitions. Our main task is to improve the identification of high risk patients and those with mild to moderate forms of CTox, to agree on cardioprotection strategies. Focused exams (on myocardial function, on right ventricle, on vascular effects) may be more relevant than ever in the time of rapidly changing environment to optimize medical resources. For example, in patients at risk of HF after a comprehensive baseline echo, follow-up studies in asymptomatic patients should be limited to advanced myocardial function parameters. Recent technological improvements in artificial intelligence (AI) may also help in the identification of the vulnerable cardio-oncology patient, but once more, we need structured image, clinical, and biomarker data to feed AI algorithms [31].

Figure 1 is original figure from the author.

Compliance with Ethical Standards

Conflict of Interest The author declares that she has no conflict of interest.

Research Involving Human Participants and/or Animals None.

Informed consent None.

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