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Editorial

Cardiac computed tomography-derived extracellular volume fraction in the identification of cardiotoxicity: Another emerging imaging option

In the past decades, progresses in cancer treatment have resulted in a doubling of survival, while up to half of cancer patients are still alive beyond 10 years after diagnosis [1,2]. In view of this striking increase of survival, paralleled by a wide range of adverse impact of cancer treatment options with an aging population, a steady increase of cancer therapies-related cardiotoxicity load has been recognized [3]. There is an enhanced appreciation that adult cancer survivors have a worse cardiovascular outcome following several years after detection, which again appears to be stringent on the cancer subtype and treatment plan [4]. In this respect, there is an evolving close collaboration between cardiologists and oncologists for individualized patient care striving to improve cardiovascular and cancer outcome in these patients [2,5]. Cardiovascular imaging in cancer patients may provide four-fold information such as (1) pre-therapy risk prediction, (2) diagnosis and monitoring of cardiotoxicity manifestation during cancer treatments, (3) assessment of late adverse cardiovascular alterations after treatment completion, and (4) identification and treatment monitoring of cardiac masses and infiltration [1,2,5]. For example, it is widely known that anthracycline-treatment on breast cancer patients may induce dose related and progressive left ventricular dysfunction leading to heart failure manifestation [6]. More recently introduced cancer therapies such as trastuzumab and other HER2 monoclonal antibodies, tyrosine kinase inhibitors, and immunotherapy have been realized to cause cardiotoxicity resulting in cardiac dysfunction [2,7,8]. For most cancer-related treatments, baseline and serial echocardiography examinations are commonly performed as first line imaging for a timely identification of early development of cardiotoxicity. Cardiotoxicity, as determined with echocardiography, is defined as new onset of left ventricular systolic dysfunction with a decrease in left ventricular ejection fraction (LVEF) of $\geq$10% to a value <50% [9]. In order to identify and characterize subclinical cardiotoxicity at its early stage, speckle-tracking echocardiography with myocardial strain assessment is concurrently applied. While radial, circumferential, and longitudinal myocardial strain can be determined with speckle-tracking echocardiography, global longitudinal strain (GLS) has been identified as a sensitive and robust marker for the detection of subclinical and early stages of cancer-treatment related myocardial injury. A relative reduction in GLS $\geq$ 15% during cancer treatment from baseline is suggestive of early functional alterations before a drop in LVEF may ensue. It is important to keep in mind that the identification of subclinical and/or clinically-manifest left ventricular dysfunction likely leads to a change in the selection of a chemotherapeutic agent, the installation of cardioprotective treatment, and the timing of repeat monitoring imaging [9,10]. In case of poor echocardiographic image quality, cardiac magnetic resonance (CMR) is commonly conducted for the assessment of global LVEF and myocardial strain imaging with the use of tagging, displacement encoding with stimulated echoes (DENSE) and strain-encoded (SENC) imaging [1,11]. Notably, CMR affords an accurate and unique characterization of the myocardial tissue with T2-weighted imaging and/or T1 and T2 parametric mapping for myocardial edema and inflammation, applying T1 and extracellular volume fraction (ECV) measurement for diffuse fibrosis, and late gadolinium enhancement (LGE) imaging for focal fibrosis and scar assessment [11].

In this issue of the IJC Heart & Vasculature, Egashira et al. [12] expand the cardiovascular imaging portfolio in the detection and characterization of cancer therapeutics–related cardiac dysfunction to cardiac contrast CT with assessment of increases of extracellular volume (ECV). In a feasibility in forty-four women with breast cancer, who underwent anthracycline treatment, contrast cardiac CT (CCT) identified late anthracycline-induced cardiotoxicity in seven patients. As it was observed, echocardiography-determined LVEF of the group with anthracycline-induced late cardiotoxicity was significantly lower than in the control group. In particular, the global longitudinal strain assessed by echocardiography and CCT-determined myocardial ECV in individuals with late anthracycline-induced cardiotoxicity was significantly lower than that of control group and in those individuals without anthracycline-induced cardiotoxicity. Such intial observations suggest indeed that anthracycline-induced cardiotoxicity could indeed be evaluated with CCT. The sensitivity and accuracy of CCT in the identification of cancer-treatment related early and late onset of cardiotoxicity as compared to echocardiography and/or CMR remains uncertain needing further well-designed clinical investigations. Given the radiation exposure of CCT, albeit relatively low, it appears unlikely that this approach may overcome established cardiovascular imaging modalities such as echocardiography and/or CMR. In particular, CMR affords an array of parameters for a comprehensive and accurate identification and characterization of cardiotoxicity affecting morphology and function of the myocardial tissue. Furthermore, there are emerging positron emission tomography (PET) radiotracer probes, such as ^{18}F-mitophos, that can identify cancer-treatment related increases reactive oxygen species in the myocardial tissue in vivo [13,14]. This approach appears promising for risk stratification of the

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potential manifestation of cancer-related cardiotoxicity warranting further clinical studies. Another interesting development is the PET radiotracer ^{68}Ga-galmydar [15], which has capability to can assess the mitochondrial potential of the myocytes and, thus, the functional state even at cellular level. Conceptually, both ^{18}F-mitophos and ^{68}Ga-galmydar hold promise for an early identification and monitoring of cancer-treatment related cardiotoxicity and interrogating therapeutic efficacy of emerging cardio-protectants [13]. Overall, Egashira et al. [12] add first evidence that CCT can add to the cardiovascular imaging portfolio in the identification of anthracycline-induced cardiotoxicity. The diagnostic niche of CCT in this emerging field of the assessment of cancer-treatment related cardiotoxicity remains uncertain but likely may evolve within a comprehensive assessment of coronary morphology, myocardial perfusion, and myocardial structure for cardiovascular risk stratification in these cancer patients.

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3. Research data related to this submission

No data were used for the research described article in the article.

4. Conflict of Interest Statement

The authors report no relationships that could be construed as a conflict of interest.

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