CMR and Cardiotoxicity. A Case-based Overview

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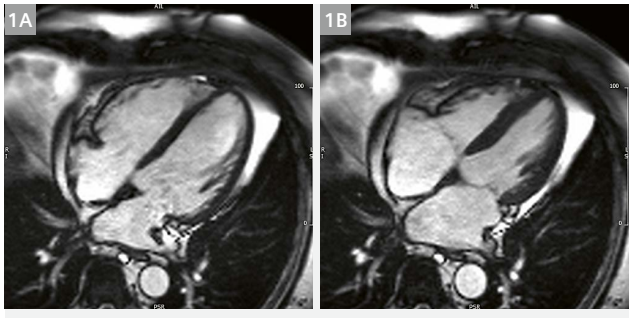
A 55-year-old woman and a 51-year-old man were diagnosed with non-metastatic soft tissue sarcoma of the lower limb, underwent surgical resection, and received an adjuvant course of anthracycline-based chemotherapy. Both patients have a long-standing diagnosis of well-controlled hypertension, but have no other cardiovascular comorbidity. The baseline left ventricular ejection fraction (LVEF) in both individuals was well above 55% before chemotherapy. After following the exact same treatment protocol comprising 450 mg/m^2 doxorubicin over a period of five months both patients are considered cancer free and can hope for a normal life expectancy. However, after completing chemotherapy, the 55-year-old female reported clinical signs of heart failure and showed a drop of LVEF to 45%, while the 51-year-old male maintained a normal LVEF and showed no heart failure symptoms. Representative SSFP cine images at end-systole and end-diastole are shown in Figure 1.

These two patients illustrate a growing issue in cardiology and oncology, namely therapy-associated cardiotoxicity. As the outcomes of most cancer patients have significantly improved over recent decades, the number of cancer survivors has dramatically increased, which has led to the long-term side effects of therapy growing in importance [1]. There are a number of chemotherapeutic agents with known cardiotoxic side effects. The most important of these in terms of patient numbers are anthracyclines and trastuzumab [2].

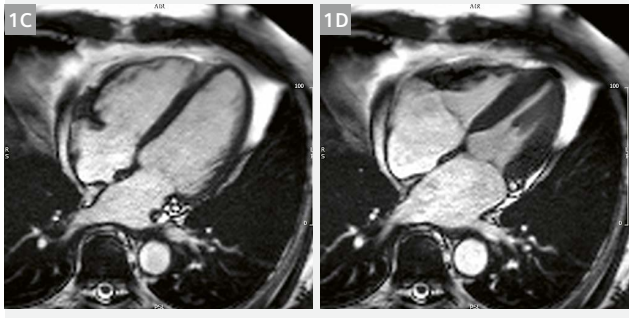
Anthracyclines are the mainstay of treatment for many malignancies. Approximately one third of all breast cancer patients [3], two thirds of lymphoma patients, and almost all soft tissue sarcoma patients receive anthracyclines during the course of their treatment [4].

Heart failure due to anthracyclines has serious prognostic implications as it can lead to mortality rates that are worse than with many malignancies [5].

Multimodality imaging plays an important role in risk assessment for early detection of chemotherapy-related cardiotoxicity, with CMR playing an increasingly important role. In 2016, the European Society of Cardiology (ESC) published a position paper highlighting the importance of CMR in the diagnostic approach to cardiotoxicity [6]. While echocardiography has maintained its role in screening and basic diagnostics, CMR has two unique features with regard to the assessment of early cardiotoxic side effects that increase its importance. First, SSFP cine imaging remains the gold standard for the evaluation of small changes in LVEF and has been shown to be superior to echocardiography in terms of accuracy and reproducibility [7]. Since the early detection of heart failure under anthracycline or trastuzumab therapy is a key factor in successful treatment and reversibility rates, CMR has an advantage over alternative techniques in this regard. Second, as well as a purely functional assessment, CMR also has tissue differentiation capabilities, which help to determine the cause and stage of the underlying cardiac damage.



55-year-old woman after chemotherapy (LVEF 45%)



51-year-old man after chemotherapy (LVEF 65%)

Figure 1:
Representative SSFP cine images of end-diastole and end-systole for two sample patients with and without anthracycline-induced systolic heart failure.

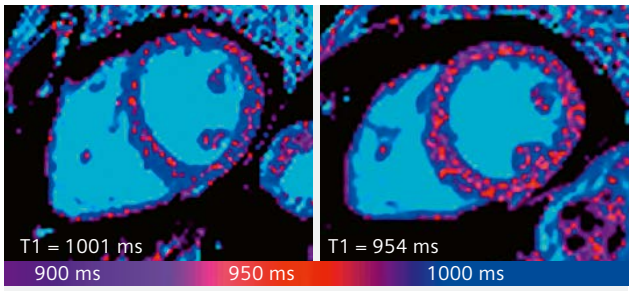


Figure 2:
Short-axis T1 MOLLI maps of the same individual before and 48 hours after administration of the first dose of anthracyclines.

Myocardial T1 and T2 mapping techniques play a pivotal role in detecting myocardial inflammation and edema as signs of acute myocardial damage that may be attributable to chemotherapy-related cardiotoxicity or to acute myocarditis in immunocompromised cancer patients – two pathologic entities with different treatment regimens.

Another increasingly important tool for tissue differentiation in these patients is the evaluation of diffuse fibrosis through extracellular volume (ECV) quantification. Several studies have shown that anthracycline therapy leads to diffuse myocardial fibrosis years after treatment, causing chronic heart failure and severe cardiovascular events in long-term cancer survivors [8, 9].

All the aforementioned capabilities of CMR in the diagnostic approach to cardiotoxicity have a common goal: To detect myocardial injury as early as possible in order to rapidly initiate therapeutic countermeasures. While early detection of cardiotoxicity remains the main strategy, there are newer studies showing the prospective benefit of CMR in the ex ante identification of patients at highest risk for the development of chemotherapy-related heart failure. In a pilot study, our working group reported that an early change of native myocardial T1 time after the first dose of anthracyclines could predict the development of systolic heart failure at the end of treatment [10]. This was also the case in our two patients – while the 55-year-old female with anthracycline-induced cardiomyopathy showed an early drop in native T1 time (see Fig. 2), the 51-year-old male with no development of cardiomyopathy maintained normal myocardial T1 values.

Further studies are underway to assess the predictive role of CMR for other agents such as trastuzumab or VEGF inhibitors. We are confident that CMR will be an increasingly important diagnostic tool in cardio-oncology and has the potential to shift the cardiotoxicity strategy from “early damage detection” to “prospective damage prevention” in the future.

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