patients without NAFLD (revascularization, n = 13; ACS, n = 3; CV death, n = 2; heart failure, n = 4). Kaplan-Meier analysis showed that patients with NAFLD experienced more CV events than those without NAFLD during follow-up (**Figure 1A**). Stepwise multivariate Cox regression analysis using traditional CV risk factors, NAFLD, HRPs, and >50% stenosis demonstrated that NAFLD (hazard ratio [HR]: 2.302; 95% CI: 1.236 to 4.289; p = 0.009), HRPs (HR: 5.061; 95% CI: 2.092 to 12.244; p < 0.001), and >50% stenosis (HR: 3.689; 95% CI: 1.790 to 7.601; p < 0.001) were independent predictors of CV events.

Figure 1B shows the occurrence of acute coronary events including ACS and CV death in patients with NAFLD according to the presence of HRPs. In patients with NAFLD, the incidence of ACS and CV death was markedly higher in patients with than without HRPs. Cox univariate regression analysis showed that HRPs in patients with NAFLD were significantly associated with ACS and CV death (crude HR: 8.816; 95% CI: 1.058 to 73.440; p = 0.044).

In conclusion, NAFLD was significantly associated with CTA-verified HRPs. CV events were predicted by the presence of NAFLD and HRPs independently. Furthermore, HRPs in patients with NAFLD were a predictor of ACS and CV death. The prognostic significance of these data should be confirmed in larger studies.

Keishi Ichikawa, MD
Toru Miyoshi, MD*
Kazuhiro Osawa, MD
Takashi Miki, MD
Kazufumi Nakamura, MD
Hiroshi Ito, MD

*Department of Cardiovascular Medicine
Okayama University Graduate School of Medicine,
Dentistry and Pharmaceutical Sciences
2-5-1 Shikata-cho, Kita-ku
Okayama 700-8558
Japan
E-mail: miyoshit@cc.okayama-u.ac.jp

https://doi.org/10.1016/j.jcmg.2020.01.022

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

REFERENCES

1. Stepanova M, Younossi ZM. Independent association between nonalcoholic fatty liver disease and cardiovascular disease in the US population. Clin Gastroenterol Hepatol 2012;10:646-50.

2. Puchner SB, Lu MT, Mayrhofer T, et al. High-risk coronary plaque at coronary CT angiography is associated with nonalcoholic fatty liver disease, independent of coronary plaque and stenosis burden: results from the ROMICAT II trial. Radiology 2015;274:693-701.

3. Osawa K, Miyoshi T, Yamauchi K, et al. Nonalcoholic hepatic steatosis is a strong predictor of high-risk coronary-artery plaques as determined by multidetector CT. PLoS ONE 2015;10:e0131138.

T2 Mapping Identifies Early Anthracycline-Induced Cardiotoxicity in Elderly Patients With Cancer

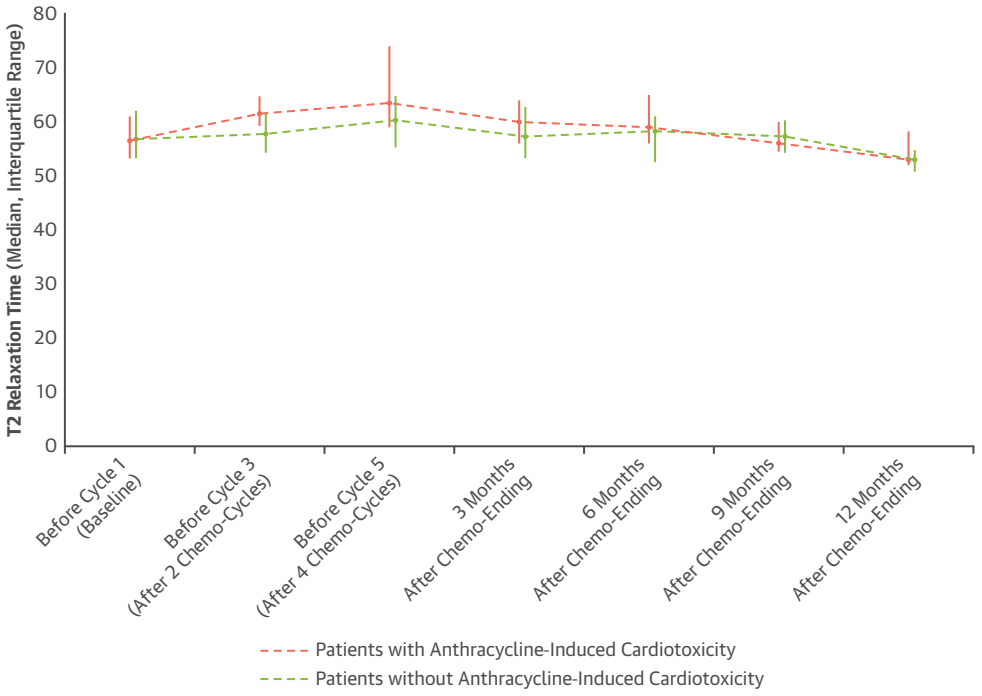
Current measures of anthracycline-induced cardiotoxicity, defined by decreases in left ventricular ejection fraction (LVEF), may become apparent only at a late stage when the myocardium has been significantly damaged, exceeding its ability to compensate (1). Our group has recently shown in a large animal model that T2 relaxation time (T2) cardiac magnetic resonance (CMR) identifies intracardiomyocyte edema as the earliest marker of anthracycline-induced cardiotoxicity. T2 prolongation preceded LVEF decrease and occurred at a reversible stage of cardiotoxicity (2). Here, we present T2 mapping trajectories during treatment in a population of elderly patients with cancer undergoing anthracycline chemotherapy.

CARTIER (Cardiotoxicity in the Elderly; NCT03981588) is a prospective study of elderly patients (≥65 years of age) with cancer undergoing serial CMR before, during, and after chemotherapy. The study protocol was approved by the ethics committee, and participants provided written informed consent. All patients underwent CMR imaging before the first (baseline assessment), third, and fifth cycles of a regular chemotherapy course and 3, 6, 9, and 12 months after the completion of treatment. At all time points, the CMR protocol included LVEF and T2 mapping (3). Cardiotoxicity was defined as any follow-up LVEF <53%, in which case heart failure therapy was initiated (1). Here, we present initial CMR data for CARTIER patients receiving anthracyclines.

Categorical variables are described as percentages and continuous variables as median (interquartile range [IQR]). Nonparametric tests at the ordinal level were used for dependent (Wilcoxon test) or independent (Mann-Whitney *U* test) samples. Area under the receiver-operating characteristic curve (AUC) was used to assess the predictive capacity of T2 mapping.

A total of 110 consecutive patients were enrolled in CARTIER, of whom 34 (31%) received anthracyclines; 20 patients had lymphoma, 8 breast cancer, 2 leukemia, 2 gastric cancer, 1 myxoid chondrosarcoma, and 1 Kaposi sarcoma. One patient with claustrophobia and 5 patients undergoing only baseline CMR (unable to follow the protocol because of poor clinical

FIGURE 1 Time Course of Cardiac Magnetic Resonance Imaging Studies



Time course of T2 relaxation time for patients with and without anthracycline-induced cardiotoxicity.

conditions) were excluded from this analysis. Thus, a final cohort of 28 patients, 169 of the 196 per protocol planned CMR examinations, constituted this study evaluation. The median age was 73 years (IQR: 68 to 79 years), 57% of patients were women, 93% had cardiovascular risk factors, 36% had cardiovascular histories, and 79% had concomitant cardiovascular medications. The majority of patients received 6 cycles of chemotherapy. Compared with 10 sex- and age-matched population-based (NCT03429452) healthy volunteers (median LVEF 69% [IQR: 66% to 73%]; median T2 53 ms [IQR: 48 to 57 ms]), patients in our cohort had similar baseline LVEFs (median 64%; IQR: 59% to 71%; $p = 0.189$) but slightly higher baseline T2 (median 56 ms; IQR: 53 to 62 ms; $p = 0.052$). Cardiotoxicity in our cohort was observed in 8 patients (28.6%): in 5 patients after only 2 cycles of chemotherapy (i.e., on CMR done before the third cycle), in 2 patients after 4 cycles, and in 1 additional patient 3 months after finishing chemotherapy. Baseline characteristics were similar between patients with and those without cardiotoxicity, except for a predominance of men (75% vs. 30%; $p = 0.044$). Baseline T2 was not different between patients with cardiotoxicity and those without (median 56 ms [IQR: 53 to 61 ms] vs. 56 ms [IQR: 53 to 62 ms], respectively; $p = 0.939$). In patients with cardiotoxicity, compared with baseline, T2 was prolonged after 2 (median 61 ms; IQR: 59 to 65 ms; $p = 0.089$) and 4 (median 63 ms; IQR: 59 to 74 ms; $p = 0.027$) cycles of chemotherapy. Conversely, in the group of patients without cardiotoxicity, T2 remained unchanged during chemotherapy (**Figure 1**). T2 (median 53 ms; IQR: 51 to 55 ms) decreased 12 months after chemotherapy for all patients with cancer compared with baseline, to similar measurements to those previously reported among healthy volunteers ($p = 0.921$).

T2 after 2 cycles of chemotherapy was revealed to be a good predictor of cardiotoxicity development, with an AUC of 0.86 (95% confidence interval [CI]: 0.70 to 1.00; $p = 0.012$). A T2 cutoff of 59 ms after 2 cycles had sensitivity of 100% and specificity of 71% for the prediction of cardiotoxicity. Neither baseline T2 (AUC = 0.62; 95% CI: 0.36 to 0.88; $p = 0.386$) nor post-treatment T2 later in time (i.e., before the fifth cycle) (AUC = 0.71; 95% CI: 0.45 to 0.97; $p = 0.149$) was a better predictor of future cardiotoxicity.

These observations are in line with those of a previous clinical study showing changes in T2 following anthracycline initiation in younger patients with breast cancer (4). Our data suggest that if T2 is to be used to best detect early cardiotoxicity, CMR should

be performed soon after anthracycline chemotherapy initiation (2 cycles in our study). The high negative predictive value of a T2 cutoff value of 59 ms after 2 cycles of chemotherapy would make it possible to rule out future cardiotoxicity development and thus limit subsequent CMR examinations.

T2 tended to normalize in the long term in patients who developed cardiotoxicity. We speculate that this is secondary to the initiation of anti-heart failure therapies according to clinical recommendations (1), but it could also be related to the intersection between cancer and cardiovascular disease (5), as it is observed even in patients who do not develop cardiotoxicity. This normalization in T2 after intervention is in line with our experimental data, in which changing the chemotherapeutic protocol after observing T2 prolongation resulted in a normalization of T2 values and precluded overt left ventricular deterioration (2). However, the conclusions of this small-number observational study remain speculative, and further studies are required to confirm our results.

Ana Martin-Garcia, MD, PhD
Elena Diaz-Pelaez, MD
Lucia Lopez-Corral, MD
Clara Sanchez-Pablo, Nr
Guillermo Macias de Plasencia, Nr
Carlos Galan-Arriola, DVM
Javier Sanchez-Gonzalez, PhD
Juan Jesus Cruz, MD, PhD
Borja Ibanez, MD, PhD
Pedro L. Sanchez, MD, PhD*

*Cardiology Department
Hospital Universitario de Salamanca-IBSAL
Paseo de San Vicente 58-187
37007 Salamanca
Spain
E-mail: pedrolsanchez@secardiologia.es

https://doi.org/10.1016/j.jcmg.2020.01.017

Please note: This study was funded by Instituto de Salud Carlos III, Ministerio de Ciencia, Innovación y Universidades, Spain, and the European Union European Regional Development Fund (PIE14/00066 and PI14/00695) as well as by Red de Investigación Cardiovascular and CIBERCV. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

REFERENCES

1. Lopez-Fernandez T, Martin Garcia A, Santaballa Beltran A, et al. Cardio-onco-hematology in clinical practice. Position paper and recommendations. Rev Esp Cardiol (Engl Ed) 2017;70:474–86.

2. Galan-Arriola C, Lobo M, Vilchez-Tschischke JP, et al. Serial magnetic resonance imaging to identify early stages of anthracycline-induced cardiotoxicity. J Am Coll Cardiol 2019;73:779–91.

3. Barreiro-Perez M, Tundidor-Sanz E, Martin-Garcia A, et al. First magnetic resonance managed by a cardiology department in the Spanish public healthcare system. Experience and difficulties of an innovative model. Rev Esp Cardiol (Engl Ed) 2018;71:365–72.

4. Lustberg MB, Reinbolt R, Addison D, et al. Early detection of anthracycline-induced cardiotoxicity in breast cancer survivors with T2 cardiac magnetic resonance. Circ Cardiovasc Imaging 2019;12:e008777.

5. Moslehi JJ. Cardiovascular toxic effects of targeted cancer therapies. N Engl J Med 2016;375:1457–67.

Rapid Cardiovascular Magnetic Resonance for Ischemic Heart Disease Investigation (RAPID-IHD)

Cardiac magnetic resonance (CMR) is widely used for diagnostic and prognostic determination in patients with suspected/known ischemic heart disease (IHD) (1). CMR is advocated in international clinical practice guidelines and recent multicenter trials like CE-MARC-2 (Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease-2) (2) and MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) (3) have shown that CMR as a first-line test is highly effective as a gatekeeper for diagnostic invasive coronary angiography and also to guide coronary revascularization. However, a perceived limitation of CMR is that it is difficult and time consuming to perform. The aim of this feasibility study was to show that using a standard MR scanner, assessment of left ventricular function, ischemia and myocardial viability could be reliably performed in ~20 min while maintaining image quality.

Consecutive stable patients in sinus rhythm, referred for routine comprehensive assessment of suspected/known IHD, were investigated on a 1.5T Philips Ingenia system equipped with a 24-channel digital receiver coil and patient-adaptive radio-frequency shimming. The Rapid-IHD protocol consisted of the following.

1) Free breathing low-resolution survey of the chest and standard cine imaging to define long and short axis (balanced steady-state free precession, single-slice/breath-hold, typical parameters: echotime 1.3 ms, repetition time 2.6 ms, flip angle 40°, field of view 320 to 420 mm, sensitivity encoding (SENSE, undersampling factor 2), slice thickness