

LETTERS

RESEARCH LETTER

Cardiac Surveillance for Anthracycline Cardiotoxicity: Clinical Yield in Low-to-Intermediate Risk Patients



MATRIX Study

Andrea Moreno-Arciniegas, MD,^{a,b} Sandra Gómez-Talavera, MD,^{a,c,d} Alvaro Navarro-Guzman, BSc,^e Carlos Galán-Arriola, DVM, PhD,^{a,d} Sergio Ramos-Cillán, MD,^c Daniel Morillo, MD,^c Laura Pardo, MD,^c María A. Pérez-Sáenz, MD,^c Raul Córdoba, MD, PhD,^c Virginia Mass, BS,^a Noemi Escalera, BPT,^a Valentín Fuster, MD, PhD,^{a,f} Teresa López-Fernández, MD,^{g,h} Javier Sánchez-González, PhD,^e Borja Ibáñez, MD, PhD^{a,c,d}

Anthracycline-based regimens remain central in lymphoma therapy but may cause cancer therapy-related cardiac dysfunction (CTRCD). Most surveillance recommendations are derived from expert consensus and are often applied to patients at low to intermediate baseline risk, in whom the balance among early detection, clinical benefit, and resource use is uncertain.^{1,2} We assessed the clinical yield of intensive serial cardiac surveillance in Heart Failure Association (HFA)-International Cardio-Oncology Society (ICOS)³ low- to intermediate-risk patients receiving anthracyclines, with particular attention to how biomarker thresholds influence European Society of Cardiology (ESC)-defined CTRCD classification.

MATRIX is a prospective, single-center cohort study that enrolled cancer treatment-naïve adults with newly diagnosed lymphoma scheduled to receive anthracycline-based chemotherapy between June 2020 and May 2025. The protocol was approved by the local Institutional Review Board/Ethics Committee (FJD Research Ethics Committee), and written informed consent was obtained from all participants. During the study period, 55 eligible patients were approached; 5 declined participation (not willing to

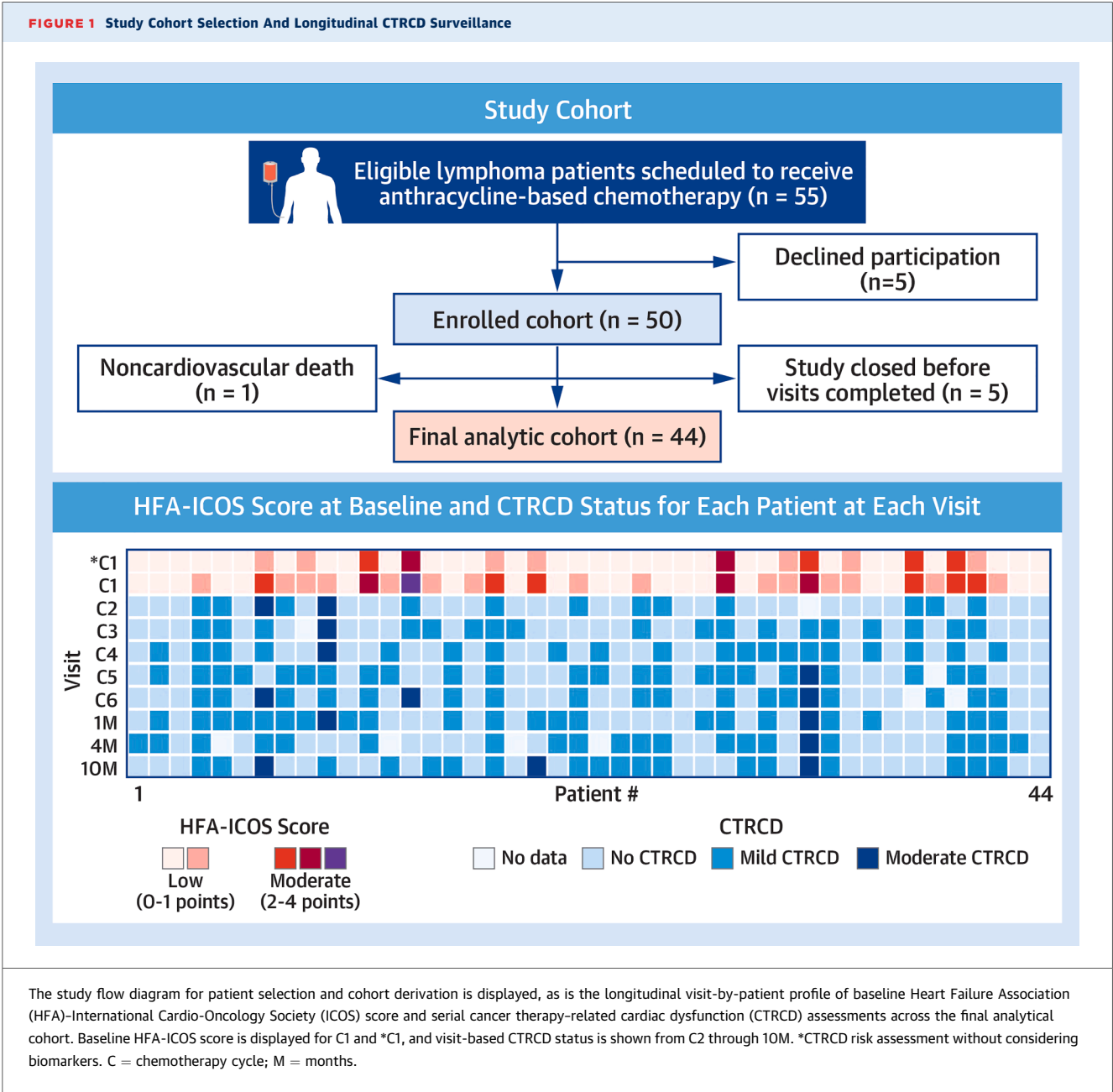
undergo cardiac magnetic resonance [CMR] imaging or study visits). Among the 50 patients who consented, 1 died of a noncardiovascular cause before completing follow-up, and 5 had incomplete protocol-specified follow-up because the study closed before they completed the scheduled visits, yielding a final analytical cohort of 44 participants (Figure 1).

The median age was 55 years (Q1-Q3: 48-59 years), 61.4% were women, and the median cumulative anthracycline dose was 298 mg/m² (Q1-Q3: 290-302 mg/m²). Baseline cardiovascular risk was determined per HFA-ICOS³ as either low risk with a score of 0 or 1 (n = 34 [77.3%]) or intermediate risk with a score of 2 to 4 (n = 10 [22.7%]). Participants underwent clinical assessments, CMR imaging, transthoracic echocardiography with assessment of global longitudinal strain, and biomarker measurement (B-type natriuretic peptide [BNP] or N-terminal pro-B-type natriuretic peptide [NT-proBNP] and troponin I) at baseline, during treatment, and at 1, 4, and 10 months after treatment completion.⁴ Follow-up by modality and time point is summarized in Figure 1. Among the 44 patients, some scheduled assessments were not completed at specific time points because of

From ^aCentro Nacional de Investigaciones Cardiovasculares Carlos III, Madrid, Spain; ^bHospital La Luz, Madrid, Spain; ^cCardiology Department, Instituto de Investigación Sanitaria Fundación Jiménez Díaz, Madrid, Spain; ^dCentro de Investigación Biomédica en Red en Enfermedades Cardiovasculares, Madrid, Spain; ^ePhilips, Madrid, Spain; ^fMount Sinai Fuster Heart Hospital, New York, New York, USA; ^gCardio-Oncology Unit, Cardiology Department, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain; and the ^hCardiology Department, Quironsalud Madrid University Hospital, Madrid, Spain.

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 [Author Center](#).

Manuscript received January 15, 2026; revised manuscript received April 23, 2026, accepted April 24, 2026.



clinical circumstances related to the underlying oncologic process; these intermittent missing visits are shown as white spaces in **Figure 1**. CTRCD was classified according to the 2022 ESC cardio-oncology guidelines,¹ incorporating ventricular function parameters derived from CMR together with transthoracic echocardiography-derived GLS and biomarker thresholds, as applicable. To explore the influence of biomarkers on event classification in this cohort, we also recategorized ESC-defined CTRCD after excluding biomarker criteria.

No participant developed symptomatic heart failure, cardiovascular death, or other major

cardiovascular events during the 10-month follow-up period. At the end of follow-up, ESC-defined CTRCD was identified in 48% of patients (41% mild and 7% moderate), whereas excluding biomarker criteria reduced CTRCD classification to 30% (25% mild and 5% moderate) (**Figure 1**). Across visits, surveillance findings were dominated by mild abnormalities and were often intermittent rather than sustained or progressive, underscoring the uncertain short-term clinical significance of these findings in this low- to intermediate-risk cohort (**Figure 1**).

Using the cutoff values recommended in the 2022 ESC cardio-oncology guidelines (BNP $\geq$ 35 pg/mL and

NT-proBNP ≥ 125 pg/mL) and the local laboratory reference for troponin I (>0.1 ng/mL), 43% of patients met the criteria for biomarker elevation at baseline, driven entirely by elevated natriuretic peptides. Specifically, 27% had elevated BNP levels at baseline, all of whom also had elevated NT-proBNP. By the end of follow-up (10 months after the completion of chemotherapy), 18% of patients had elevated BNP and 20% had elevated NT-proBNP. Most patients with elevated BNP and/or NT-proBNP at baseline showed an early trend toward normalization after the initial chemotherapy cycles, which was significant for NT-proBNP ($P = 0.014$). Troponin I remained below the upper reference limit in all participants across all measured time points. Overall, natriuretic peptide levels decreased over time, suggesting that elevations in this cohort may have reflected factors other than progressive cardiotoxicity, including underlying disease burden or systemic stress. Incorporating biomarker thresholds increased ESC-defined CTRCD classification from 30% to 48% at the end of follow-up.

In this small cohort, with no major cardiovascular events during 10 months of follow-up, biomarker abnormalities appeared to contribute more to CTRCD classification than to the identification of patients with clear, clinically meaningful deterioration in ventricular function. Taken together, these data suggest that in HFA-ICOS low- to intermediate-risk patients with lymphoma treated with anthracyclines, intensive serial surveillance over 10 months predominantly identified mild CTRCD, often intermittent; the clinical significance remains uncertain. In this cohort, multimodality surveillance frequently detected subclinical abnormalities without evidence of major cardiovascular events during short-term follow-up. Biomarker incorporation increased ESC-based CTRCD classification, but whether this translates into improved identification of clinically meaningful cardiotoxicity in lower risk patients remains uncertain. These findings support a risk-stratified surveillance approach and highlight the need for larger studies with longer follow-up to

better define the clinical utility of imaging and biomarker-based surveillance across treatment settings.

Limitations include the single-center design, modest sample size ($n = 44$), and restriction to lymphoma patients, which may limit generalizability. The relatively short follow-up duration (10 months) limits conclusions regarding longer term cardiotoxicity and clinical cardiovascular outcomes. Follow-up completeness was high overall, with only a small proportion of incomplete scheduled assessments. Intermittent missed visits were related primarily to clinical circumstances associated with the underlying oncologic processes. Although these sources of incompleteness may have influenced classification at isolated time points, they are unlikely to have materially altered the overall findings. Because no participant experienced symptomatic heart failure or cardiovascular death, the clinical implications of mild biomarker- or imaging-based abnormalities cannot be fully determined. Thus, observations regarding the contribution of biomarkers should be interpreted cautiously and considered hypothesis generating. Nonetheless, these prospective findings may help inform future refinements in surveillance strategies by supporting a more risk-stratified approach, rather than broad, systematic screening in lower risk populations.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

MATRIX is a prospective, single-center cohort study funded by the European Commission (GA-819775). Drs Navarro-Guzman and Sánchez-González are affiliated with Philips. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Borja Ibáñez, Translational Laboratory for Cardiovascular Imaging and Therapy, Centro Nacional de Investigaciones Cardiovasculares Carlos III and IIS-Fundación Jiménez Díaz, UAM, c/Melchor Fernández Almagro, 3, 28029 Madrid, Spain. E-mail: bibanez@cnic.es.

REFERENCES

1. Lyon AR, Lopez-Fernandez T, Couch LS, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J*. 2022;43:4229-4361.
2. Lopez-Sendon J, Alvarez-Ortega C, Zamora Aunon P, et al. Classification, prevalence, and outcomes of anticancer therapy-induced cardiotoxicity: the CARDIOTOX registry. *Eur Heart J*. 2020;41:1720-1729.
3. Rivero-Santana B, Saldana-Garcia J, Caro-Codon J, et al. Anthracycline-induced cardiovascular toxicity: validation of the Heart Failure Association and International Cardio-Oncology Society risk score. *Eur Heart J*. 2025;46:273-284.
4. Negishi T, Thavendiranathan P, Penicka M, et al. Cardioprotection using strain-guided management of potentially cardiotoxic cancer therapy: 3-year results of the SUCCOUR trial. *JACC Cardiovasc Imaging*. 2023;16:269-278.

KEY WORDS anthracycline, cardiac magnetic resonance, risk prediction