

# INPLASY

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## Cardiac MRI in Drug-Induced Cardiotoxicity: An Independent Systematic Review and Updated Meta-Analysis of T1 Mapping, ECV Fraction, Late Gadolinium Enhancement, Feature-Tracking Strain, and ICI Myocarditis Diagnostic Performance from January 2000 Through May 2026

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### ADMINISTRATIVE INFORMATION

**Support** - Self-funded. University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding received.

**Review Stage at time of this submission** - The review has not yet started.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202660045

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 June 2026 and was last updated on 9 June 2026.

### INTRODUCTION

**Review question / Objective** What is the pooled T1 mapping SMD in anthracycline-treated patients versus baseline and controls, does ECV fraction predict CTRCD, and what is CMR sensitivity for ICI myocarditis versus troponin and ECG?

**Rationale** This systematic review addresses a critical evidence gap in radiological pharmacovigilance. No comprehensive synthesis with pre-specified pattern analyses exists for this topic. Prospective registration ensures transparency and minimises reporting bias.

**Condition being studied** Drug-induced cardiotoxicity and cancer therapy-related cardiac dysfunction (CTRCD) from anthracyclines, trastuzumab, immune checkpoint inhibitors, and other cardiotoxic oncological agents.

### METHODS

**Search strategy** PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, and Scopus from January 1, 2000 to May 31, 2026. ClinicalTrials.gov and WHO-ICTRP on May 31, 2026. Key terms: cardiac MRI, CMR, T1 mapping, ECV, extracellular volume, LGE, late gadolinium enhancement, feature-tracking strain, CTRCD, cancer therapy-related cardiac dysfunction, ICI myocarditis, checkpoint inhibitor myocarditis, anthracycline cardiotoxicity, trastuzumab, Lake Louise criteria.

**Participant or population** Adults aged 18 years or above receiving cardiotoxic oncological agents (anthracyclines, trastuzumab, pertuzumab, ICIs, cardiotoxic TKIs, 5-FU, high-dose cyclophosphamide) with CMR before, during, or after treatment, or with confirmed drug-induced cardiomyopathy or ICI myocarditis.

**Intervention** Cardiac MRI with native T1 mapping, T2 mapping, extracellular volume fraction (ECV), late gadolinium enhancement (LGE), and feature-tracking global longitudinal strain for cardiotoxicity detection and monitoring.

**Comparator** Echocardiographic LVEF monitoring as standard clinical comparator; troponin I or T and ECG for ICI myocarditis diagnostic comparison; healthy age-matched controls for CMR parameter reference range comparison.

**Study designs to be included** RCT CMR substudies; prospective cohort studies ( $n \geq 20$ ); retrospective cohort studies ( $n \geq 20$ ); ICI myocarditis registries ( $n \geq 10$  confirmed cases with CMR).

**Eligibility criteria** Inclusion: Adults receiving cardiotoxic oncological agents with CMR data; confirmed ICI myocarditis with CMR, troponin, and ECG data; CTRCD defined per universal heart failure definition or CARDIOTOX criteria. Exclusion: Paediatric populations; pre-existing cardiomyopathy without drug attribution; studies without extractable CMR quantitative data; case reports ( $n < 10$ ).

**Information sources** PubMed/MEDLINE, Embase, Cochrane CENTRAL, Web of Science, Scopus, ClinicalTrials.gov, WHO-ICTRP.

**Main outcome(s)** T1 mapping SMD versus pre-treatment baseline ( $I^2$ ) and versus healthy controls; ECV fraction OR for predicting CTRCD at ECV threshold; CMR sensitivity and specificity for confirmed ICI myocarditis; minimum detectable LVEF change CMR versus echocardiography.

**Additional outcome(s)** ECV temporal trajectory during anthracycline treatment; T2 mapping elevation at 6 and 12 weeks; feature-tracking GLS reduction preceding LVEF decline; 5-year survivor ECV and GLS prevalence versus controls; LGE prevalence and distribution.

**Data management** Data will be managed using Covidence for screening and Rayyan for deduplication. Extracted data stored in pre-piloted Excel forms. Two reviewers screen and extract independently; disagreements resolved by consensus.

**Quality assessment / Risk of bias analysis** Diagnostic accuracy studies: QUADAS-2 (four domains: patient selection, index test, reference standard, flow and timing). Cohort studies: Newcastle-Ottawa Scale (threshold  $\geq 5$  stars).

Overall certainty of evidence rated using GRADE per primary outcome.

**Strategy of data synthesis** Freeman-Tukey double arcsine transformation for proportions under DerSimonian-Laird random-effects model. Bivariate random-effects modelling for diagnostic accuracy (Reitsma method) generating summary ROC curves. Heterogeneity quantified by Cochran Q and  $I^2$ . Egger regression and funnel plot inspection for publication bias where  $\geq 10$  studies contribute. SMDs for continuous CMR parameters by random-effects inverse-variance weighting. Bivariate random-effects for ICI myocarditis diagnostic accuracy. Prognostic ORs for ECV prediction of CTRCD by DerSimonian-Laird.

**Subgroup analysis** Drug class (anthracyclines vs trastuzumab vs ICI vs TKI); cumulative anthracycline dose; CMR field strength (1.5T vs 3.0T); study era (pre-2015 vs 2015 onwards); ECV threshold level.

**Sensitivity analysis** Restriction to prospective cohort studies only; restriction to 3.0T CMR; exclusion of retrospective ICI myocarditis series; restriction to CARDIOTOX-defined CTRCD.

**Language restriction** No language restriction.

**Country(ies) involved** Saudi Arabia.

**Other relevant information** Cardiovascular Imaging; Cardio-Oncology; Clinical Pharmacy; Nuclear Cardiology; Pharmacovigilance.

**Keywords** cardiac MRI; CMR; T1 mapping; ECV; LGE; CTRCD; ICI myocarditis; anthracycline cardiotoxicity; feature-tracking strain; trastuzumab; systematic review; meta-analysis.

**Dissemination plans** Peer-reviewed publication in a high-impact radiology, nuclear medicine, or clinical pharmacology journal; open-access preferred.

#### Contributions of each author

Author 1 - Abdulrahman Alanazi - Conceived and designed the study, drafted the protocol, will lead data extraction and synthesis, and drafted the manuscript and final manuscript submission. Email: aas2@hotmail.com

Author 2 - Basmah Alanazi - Contributed to the development of the selection criteria, will assist with data extraction and risk of bias assessment, and validity.

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