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# Multiphase CT and MRI in Drug-Induced Liver Injury: An Independent Systematic Review and Updated Meta-Analysis of Imaging Patterns, Gadoxetic Acid MRI Hepatobiliary Phase Performance, MR Elastography Fibrosis Correlation, and Prognostic Indicators 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:** INPLASY202660024

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 June 2026 and was last updated on 5 June 2026.

## INTRODUCTION

**Review question / Objective** What are the pooled chronic DILI incidence by drug class, gadoxetic acid MRI hepatobiliary phase diagnostic performance, MR elastography fibrosis correlation, and the CT/MRI features independently predicting liver transplantation or death?

**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 liver injury (DILI) from any pharmacological agent including anti-tuberculosis drugs, antimicrobials, immune checkpoint inhibitors, herbal and dietary supplements, chemotherapy, and NSAIDs.

## 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: drug-induced liver injury, DILI, hepatotoxicity, gadoxetic acid, hepatobiliary phase, MR elastography, chronic DILI, sinusoidal obstruction syndrome, ICI hepatotoxicity, liver biopsy, RUCAM, CT liver, MRI liver.

**Participant or population** Adults aged 18 years or above with RUCAM-score ≥6 DILI, histologically confirmed DILI, multidisciplinary consensus DILI diagnosis, or biochemical improvement ≥50% from peak within 30 days of drug discontinuation, with CT or MRI data.

**Intervention** Multiphase CT, gadoxetic acid or extracellular gadolinium-enhanced MRI, or MR elastography for DILI characterisation, severity

grading, mechanism identification, or fibrosis staging.

**Comparator** Liver biopsy as histological reference standard; RUCAM severity grade as biochemical comparator; serum ALT and bilirubin trajectory as biochemical severity comparator.

**Study designs to be included** RCT safety substudies; prospective cohort studies (n≥20); retrospective cohort studies (n≥20); case series (n≥10 with extractable imaging data).

**Eligibility criteria** Inclusion: Adults with RUCAM ≥6, histological, or consensus DILI; CT or MRI data with extractable imaging findings; any causative drug class.Exclusion: Studies without imaging data; non-DILI liver disease; paediatric populations; case reports (n<10); studies without extractable quantitative imaging data.

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

**Main outcome(s)** Chronic DILI incidence by drug class (Freeman-Tukey proportions); CT and MRI pattern prevalence by DILI subtype; gadoxetic acid HBP sensitivity, specificity, and AUC versus biopsy; MR elastography Pearson r versus Ishak stage; imaging features predicting liver transplantation or death (OR).

**Additional outcome(s)** HBP signal correlation with RUCAM severity grade (Pearson r); ICI hepatotoxicity periportal accentuation pattern prevalence and specificity; sinusoidal obstruction syndrome CT sensitivity; MRE stiffness thresholds for F2 and F3 fibrosis.

**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 ≥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 ≥10 studies contribute. Pearson r pooled via Fisher Z-transformation. Prognostic ORs under random effects. Subgroup analyses by drug class, DILI mechanism (hepatocellular vs cholestatic), and imaging modality generation.

**Subgroup analysis** Drug class (ICI vs ATT vs antimicrobials vs herbal supplements vs chemotherapy vs NSAIDs); DILI mechanism (hepatocellular vs cholestatic vs mixed); gadoxetic acid vs extracellular GBCA; chronic vs acute DILI; ICI hepatotoxicity grade.

**Sensitivity analysis** Restriction to RUCAM ≥6 studies only; restriction to gadoxetic acid MRI only; exclusion of case series; restriction to prospective cohort designs.

**Language restriction** No language restriction.

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

**Other relevant information** Abdominal Radiology; Hepatology; Clinical Pharmacy; Oncological Imaging; Pharmacovigilance.

**Keywords** drug-induced liver injury; DILI; CT; MRI; patobiliary phase; MR elastography; ICI hepatotoxicity; RUCAM; chronic DILI; systematic.

**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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