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Corresponding author:

Marco Ladino

mladino@med.miami.edu

Author Affiliation:

Katz Family Division of Nephrology,
University of Miami / Miami Veterans
Affairs Healthcare System, Miami,
FL, USA.

Kidney transplantation in systemic sclerosis: post-transplant outcomes and allograft recurrence of scleroderma renal crisis. Protocol for a systematic review and meta-analysis

Carpintero, MF; Ladino, MA.

ADMINISTRATIVE INFORMATION**Support** - No support.**Review Stage at time of this submission** - Formal screening of search results against eligibility criteria.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100040**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 October 2026 and was last updated on 9 October 2026.**INTRODUCTION**

Review question / Objective Review question: In patients with systemic sclerosis (SSc) and kidney failure who undergo kidney transplantation, what are patient survival, graft survival, and the frequency, timing and consequences of recurrence of scleroderma renal crisis (SRC) in the allograft, and how does access to waitlisting and transplantation compare with that of patients with other causes of kidney failure?

PICOS. Population: patients with SSc (limited or diffuse cutaneous disease, SSc overlap syndromes, or kidney failure attributed to scleroderma or SRC in registry coding) with kidney failure. Intervention: kidney transplantation from deceased or living donors. Comparator: kidney transplant recipients without SSc or with other specified primary kidney diseases, and patients with SSc remaining on dialysis or on the waiting list; no comparator is required for single-group outcomes. Outcomes: primary, SRC recurrence in

the allograft (frequency, timing, graft outcome), patient survival and graft survival; secondary, access to waitlisting and transplantation, time on dialysis before transplantation, recovery of native kidney function on dialysis, early graft outcomes, causes of graft loss and death, immunosuppression, extrarenal disease course and de novo SRC after transplantation. Study designs: registry analyses, cohort studies, case series, case reports, conference abstracts and preprints with extractable data.

Rationale Scleroderma renal crisis (SRC) remains a principal route to kidney failure in systemic sclerosis (SSc); despite angiotensin-converting enzyme inhibitors, a substantial proportion of patients require permanent dialysis, and survival on dialysis is poor. Registry studies indicate that patients with SSc are less likely than other patients with kidney failure to be waitlisted and transplanted. Transplant candidacy and timing are shaped by concern about recurrence of SRC in the allograft, progression of extrarenal (particularly cardiopulmonary) disease, exposure to

glucocorticoids and ciclosporin, both implicated as precipitants of SRC, and the possibility of late recovery of native kidney function on dialysis. The evidence is dispersed across overlapping national registry analyses, small single-centre series, case reports, conference abstracts and preprints. Existing narrative reviews have not applied systematic search methods, have not accounted for overlap between registries, and have not distinguished recurrence recorded as a cause of graft loss from recurrence ascertained clinically or histologically. Recent registry analyses released as conference abstracts and a preprint have not been incorporated into any synthesis. A systematic review with explicit handling of registry overlap and recurrence ascertainment is needed to inform candidacy, timing, immunosuppression and post-transplant surveillance.

Condition being studied Systemic sclerosis is a chronic autoimmune connective tissue disease characterized by vasculopathy, immune dysregulation and fibrosis of the skin and internal organs. Scleroderma renal crisis is its most severe kidney manifestation: abrupt, usually accelerated hypertension with acute kidney injury, frequently accompanied by thrombotic microangiopathy, occurring predominantly in early, rapidly progressive diffuse cutaneous disease. A proportion of affected patients progress to permanent kidney replacement therapy. The condition of interest in this review is kidney failure attributed to SSc or SRC in patients who receive a kidney transplant, together with the post-transplant course of the underlying disease, including recurrence of SRC in the allograft and de novo SRC after transplantation.

METHODS

Search strategy All sources were searched on 7 October 2026 from inception, without date, language or publication-type filters.

MEDLINE (PubMed; records retrieved with NCBI E-utilities):

#1 ("Scleroderma, Systemic"[MeSH] OR "systemic sclerosis"[tiab] OR scleroderma*[tiab] OR "renal crisis"[tiab] OR "CREST syndrome"[tiab] OR "progressive systemic sclerosis"[tiab]) [37,946]

#2 ("Kidney Transplantation"[MeSH] OR "renal transplant*[tiab] OR "kidney transplant*[tiab] OR "kidney allograft*[tiab] OR "renal allograft*[tiab] OR "kidney graft*[tiab] OR "renal graft*[tiab] OR "transplant recipient*[tiab]) [176,407]

#3 ((transplant*[tiab] OR "Transplantation"[MeSH] OR "Waiting Lists"[MeSH] OR "waiting list*[tiab] OR waitlist*[tiab]) AND (kidney*[tiab] OR renal[tiab]

OR "Renal Insufficiency"[MeSH] OR "Renal Replacement Therapy"[MeSH] OR dialysis[tiab] OR "end-stage"[tiab] OR ESRD[tiab] OR ESKD[tiab])) [193,345]

#4 #1 AND #2 [143]

#5 #1 AND (#2 OR #3) [302; final set]

Scopus: TITLE-ABS-KEY("systemic sclerosis" OR scleroderma* OR "renal crisis" OR "CREST syndrome") AND TITLE-ABS-KEY("kidney transplant*" OR "renal transplant*" OR "kidney allograft*" OR "renal allograft*" OR "kidney graft*" OR "renal graft*" OR "transplant recipient*") [422]

Web of Science Core Collection: TS=("systemic sclerosis" OR scleroderma* OR "renal crisis" OR "CREST syndrome") AND TS=("kidney transplant*" OR "renal transplant*" OR "kidney allograft*" OR "renal allograft*" OR "kidney graft*" OR "renal graft*" OR "transplant recipient*") [188]

Europe PMC: (TITLE_ABS:("systemic sclerosis" OR scleroderma OR "scleroderma renal crisis" OR "CREST syndrome")) AND (TITLE_ABS:("kidney transplantation" OR "kidney transplant" OR "kidney transplants" OR "renal transplantation" OR "renal transplant" OR "renal transplants" OR "kidney allograft" OR "renal allograft" OR "kidney graft" OR "renal graft" OR "transplant recipient" OR "transplant recipients" OR "kidney recipient" OR "kidney recipients")) [118]

Embase (Embase.com) and Cochrane CENTRAL (Cochrane Library): the same two concept blocks (systemic sclerosis, scleroderma, renal crisis, CREST syndrome; kidney or renal transplantation, allograft, graft, transplant recipient) translated into each platform's syntax [Embase 461; CENTRAL 33].

ClinicalTrials.gov: systemic sclerosis or scleroderma combined with kidney transplantation [4].

Other methods: backward and forward citation searching of 12 included reports through the Europe PMC references and citations services [172 additional records]; ACR Convergence abstract archive for companion abstracts [2]. Google Scholar (first 200-300 records by relevance) will be searched by the authors.

Participant or population Patients of any age with systemic sclerosis (limited or diffuse cutaneous SSc, SSc sine scleroderma or SSc overlap syndromes, under any classification criteria) or with kidney failure attributed to scleroderma or scleroderma renal crisis in registry coding, who

received a kidney transplant, or whose access to waitlisting or transplantation was compared with that of a reference group.

Intervention Kidney transplantation (first or repeat; deceased or living donor), with any induction and maintenance immunosuppression.

Comparator Where reported: kidney transplant recipients without SSc (all other causes, or specified primary kidney diseases such as diabetes, IgA nephropathy or systemic lupus erythematosus), and patients with SSc remaining on dialysis or on the waiting list. Single-group studies without a comparator are eligible for absolute outcomes (recurrence, patient and graft survival).

Study designs to be included Registry analyses, prospective or retrospective cohort studies, case-control studies, case series and case reports with original data on kidney transplantation in SSc, including conference abstracts and preprints with extractable data. Randomized trials were sought. Reviews, editorials and commentaries without original transplant data are excluded.

Eligibility criteria Inclusion: original data on outcomes after kidney transplantation in patients with SSc (recurrence of SRC, patient or graft survival, complications, disease course), or comparative data on access to waitlisting or transplantation in SSc-related kidney failure; any publication date, language or setting. Exclusion: reviews without original transplant data; haematopoietic stem cell or non-kidney solid organ transplantation only; populations without SSc (graft-versus-host disease, nephrogenic systemic fibrosis, localized scleroderma); SSc without kidney transplantation or transplant-access data; reports in which SSc-specific outcomes cannot be separated from those of other diagnoses. Companion reports (conference abstracts, preliminary or later publications of the same cohort) are linked to the parent study and counted once. Overlap between registry analyses is recorded by data source and period.

Information sources Electronic databases: MEDLINE (PubMed), Embase (Embase.com), Scopus, Web of Science Core Collection, Europe PMC and the Cochrane Central Register of Controlled Trials (Cochrane Library), accessed through the University of Miami library subscription or public interfaces. Trial register: ClinicalTrials.gov. Grey literature: conference abstracts indexed in Embase and Web of Science, the ACR Convergence abstract archive, and preprints.

Citation searching: reference lists of included reports and reports citing them (Europe PMC references and citations services). Google Scholar (first 200-300 results). All database searches were run on 7 October 2026 from inception. Authors of included studies may be contacted to clarify inconsistent or missing data.

Main outcome(s) 1. Recurrence of SRC in the allograft: proportion of grafts or recipients with recurrence (clinical or histological diagnosis as defined by each study), with recurrence recorded only as a reported cause of graft loss in registries analysed separately; time from transplantation to recurrence; graft outcome after recurrence. 2. Patient survival after transplantation at 1, 3, 5 and 10 years, and hazard ratios versus comparators. 3. Graft survival (overall and death-censored) at the same time points, and hazard ratios versus comparators. Effect measures: proportions with exact (Clopper-Pearson) 95% confidence intervals; survival estimates as reported (Kaplan-Meier or cumulative incidence); hazard ratios with 95% confidence intervals from the most adjusted model reported.

Additional outcome(s) Access to waitlisting and transplantation (hazard ratios, cumulative incidence); time on dialysis before transplantation; pre-emptive transplantation; recovery of native kidney function on dialysis and time to recovery; primary non-function, delayed graft function and acute rejection; causes of graft loss and death; induction and maintenance immunosuppression; extrarenal disease course after transplantation (skin, lung, heart, gastrointestinal tract); de novo SRC after transplantation.

Data management Records from each source are retrieved from the platform's results interface, deduplicated sequentially by PubMed identifier, DOI, normalized title plus publication year, and Embase record identifiers shared with Scopus, and screened in two stages (title/abstract, then full text). Screening decisions, retrieval status and reasons for full-text exclusion are logged in a spreadsheet. Data are extracted into a structured form that records, for every value, the type of source text (full text, author accepted manuscript, abstract, conference abstract, preprint or secondary report). First-pass screening and extraction were performed by one reviewer with large language model assistance under author supervision; independent duplicate screening and extraction by two authors, with disagreements resolved by consensus, will be completed before submission. Search strategies, the full-text

assessment log, extracted data and analysis code will be provided as supplementary material.

Quality assessment / Risk of bias analysis

Comparative registry and cohort analyses: Newcastle-Ottawa Scale (7-9 stars high quality, 5-6 moderate, 4 or fewer low). Non-comparative cohorts and case series: JBI critical appraisal checklist for case series. Case reports: the tool of Murad et al. (selection, ascertainment, causality, reporting). Reports available only as abstracts are rated provisionally and marked as not fully appraisable. Certainty of evidence for each outcome is rated with GRADE, using the GRADE approach to prognosis for event rates (starting at high certainty) and starting observational comparative evidence at low certainty.

Strategy of data synthesis Recurrence proportions are pooled only from non-overlapping centre-based cohorts that report recurrence among all of their transplanted patients. Logit-transformed proportions are pooled with a DerSimonian-Laird random-effects model, with a Hartung-Knapp-Sidik-Jonkman adjustment as a sensitivity analysis and a continuity correction of 0.5 for zero-event studies; the Freeman-Tukey double arcsine transformation is not used. Study-level confidence intervals are exact (Clopper-Pearson). Heterogeneity is described with tau-squared, I-squared and Cochran's Q, and a 95% prediction interval is reported. Registry estimates of recurrence are displayed but not pooled, because the United States registry analyses (USRDS, UNOS, SRTTR) overlap in time and patients and capture recurrence mainly as a reported cause of graft loss. Patient survival, graft survival, hazard ratios and access outcomes are synthesized narratively following the SWiM guideline, grouped by outcome and design, with the direction and range of reported estimates tabulated, because registries overlap, outcome definitions and time points differ, and variances are not consistently extractable. Analyses are run in Python 3 (NumPy, SciPy, Matplotlib).

Subgroup analysis Formal subgroup analyses and meta-regression are not planned, because too few studies are expected to contribute to any pooled outcome. Results are presented descriptively by data source (registry versus centre-based cohort), method of recurrence ascertainment (reported cause of graft loss versus clinical or histological diagnosis), transplant era and donor type where reported.

Sensitivity analysis For the pooled recurrence proportion: (1) patients rather than grafts as the

denominator; (2) addition of a centre series reported within a registry publication; (3) exclusion of a series with internally inconsistent reporting; (4) restriction to studies with full-text data; (5) Hartung-Knapp-Sidik-Jonkman versus DerSimonian-Laird confidence intervals.

Language restriction None. Reports in any language are eligible and are translated when necessary.

Country(ies) involved United States.

Other relevant information Retrospective registration. All searches listed in items 11 and 17 were completed on 7 October 2026. First-pass title/abstract and full-text screening, data extraction, provisional risk-of-bias assessment and the analyses described in items 22-24 have been performed, and a manuscript has been drafted. Eligibility criteria, outcomes and the synthesis plan were specified before the searches were run. Outstanding before submission: independent duplicate screening, extraction and risk-of-bias assessment by the authors; the Google Scholar search; and retrieval of full texts not yet obtained. Any deviation from this record will be reported in the publication.

A large language model (Claude, Anthropic) was used under author supervision to run database searches through institutional access, assist with screening and data extraction, perform the analyses and draft the manuscript. The authors verify all sources and take responsibility for the content.

Keywords systemic sclerosis; scleroderma renal crisis; kidney transplantation; recurrence; graft survival; patient survival; end-stage kidney disease.

Dissemination plans Publication in a peer-reviewed journal and presentation at nephrology, transplantation or rheumatology meetings. Search strategies, the full-text assessment log, extracted data and analysis code will be provided as supplementary material.

Contributions of each author

Author 1 - Maria Carpintero.
Email: mladino@med.miami.edu
Author 2 - Marco Ladino.