International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY2026110106

doi: 10.37766/inplasy2026.11.0106

Received: 26 November 2026

Published: 26 November 2026

Corresponding author:
Wen-Ke Wang

2jdiogxl@gmail.com

Author Affiliation:
Taipei Medical University Hospital.

Dialysis-Dependent Versus Non-Dialysis Chronic Kidney Disease and Outcomes After Hepatectomy for Hepatocellular Carcinoma: A Focused Evidence Review and Exploratory Meta-analysis

Pai, HJ; Wang, WK.

ADMINISTRATIVE INFORMATION

Support - No support.

Review stage at the time of initial registration - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2026110106

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 November 2026 and was last updated on 26 November 2026.

INTRODUCTION

Review question / Objective Does preoperative dialysis-dependent end-stage renal disease (ESRD) versus non-dialysis chronic kidney disease (CKD) differentially impact perioperative morbidity, short-term mortality, and long-term oncologic survival compared with preserved renal function in adult patients undergoing curative-intent hepatectomy for hepatocellular carcinoma (HCC)?

Rationale Hepatectomy is a primary curative-intent treatment for selected patients with hepatocellular carcinoma (HCC). However, underlying renal dysfunction complicates perioperative management through impaired fluid homeostasis, uremic platelet dysfunction, infection susceptibility, and cardiovascular risk. Previous syntheses frequently merged dialysis-dependent ESRD and non-dialysis CKD into a single binary exposure, obscuring phenotype-specific risks. This focused evidence review and exploratory meta-analysis aims to evaluate methodological rigor, perioperative morbidity, short-term mortality, and long-term survival after HCC resection across distinct renal phenotypes (dialysis-dependent ESRD vs. non-dialysis CKD vs. preserved renal function).

Condition being studied Hepatocellular carcinoma (HCC); curative-intent hepatic resection (hepatectomy); end-stage renal disease (ESRD) on maintenance dialysis; non-dialysis chronic kidney disease (CKD).

METHODS

Search strategy Targeted literature searches were conducted in PubMed / MEDLINE up to 2026 to identify comparative cohort studies evaluating adult HCC hepatectomy outcomes stratified by renal dysfunction or dialysis dependency. Search terms combined Medical Subject Headings (MeSH) and free-text keywords related to hepatocellular carcinoma ("hepatocellular carcinoma", "HCC",

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"liver neoplasm"), hepatic resection ("hepatectomy", "liver resection", "hepatic resection"), and renal impairment ("end-stage renal disease", "ESRD", "hemodialysis", "peritoneal dialysis", "dialysis", "chronic kidney disease", "CKD", "renal dysfunction", "renal insufficiency"). Reference lists of relevant reviews and cohorts were also screened for full-text eligibility.

Participant or population Inclusion criteria: Adult patients (aged ≥18 years) diagnosed with hepatocellular carcinoma (HCC) undergoing surgical liver resection (open, laparoscopic, or robotic hepatectomy) with documented preoperative renal function or dialysis status.

Exclusion criteria: Studies evaluating mixed hepatic malignancies without an extractable HCC-only subgroup; cohorts lacking an internal non-renal-dysfunction comparator group; non-comparative case series, reviews, or overlapping institutional cohorts without distinct extractable quantitative endpoints.

Intervention Preoperative renal impairment stratified into distinct clinical phenotypes: (1) dialysis-dependent end-stage renal disease (ESRD) receiving maintenance hemodialysis or continuous ambulatory peritoneal dialysis (CAPD), and (2) non-dialysis chronic kidney disease (CKD; e.g., eGFR 2.0 mg/dL without maintenance dialysis).

Comparator Adult HCC patients undergoing hepatectomy without maintenance dialysis or with preserved baseline renal function (non-ESRD / non-dialysis reference group or eGFR ≥45 mL/min/1.73 m^2).

Study designs to be included Comparative observational cohort studies (retrospective or prospective comparative surgical cohorts) reporting quantitative perioperative morbidity, short-term mortality, or long-term survival outcomes.

Eligibility criteria Study selection follows PRISMA 2020 guidelines. Two reviewers independently screened titles, abstracts, and full-text articles against predefined eligibility criteria. Studies were included if they enrolled adults undergoing HCC hepatectomy, compared preoperative dialysis or renal impairment against an internal non-exposed control group, and provided extractable quantitative endpoint data. Discrepancies were resolved by consensus.

Information sources Primary electronic database: PubMed / MEDLINE (searched through 2026 for comparative cohort studies evaluating adult hepatocellular carcinoma [HCC] hepatectomy stratified by renal dysfunction or dialysis dependency).

Additional sources: Manual screening of reference lists and citation trails from identified cohort studies and prior systematic reviews/clinical guidelines on HCC resection and chronic kidney disease (CKD) to ensure full-text eligibility verification.

Main outcome(s) Any postoperative complication: Patient-level incidence of overall postoperative morbidity within the index hospitalization or 30-day postoperative window.

Perioperative / operative-related mortality: Short-term procedural or in-hospital mortality (including Clavien–Dindo Grade V mortality).

Additional outcome(s) Major postoperative complications: Clavien–Dindo Grade >II or Grade III–IV complications (e.g., severe infection, cardiac events, massive ascites, pleural effusion, bile leak, post-hepatectomy liver failure).

90-day postoperative mortality (evaluated narratively/descriptively where reported).

Long-term oncologic survival: 1-, 3-, 5-, and 10-year overall survival (OS) and disease-free or recurrence-free survival (DFS/RFS), plus multivariable-adjusted Cox hazard ratios (HRs) where available.

Data management Two investigators independently extracted publication year, country/institution, study period, renal dysfunction and dialysis definitions, sample sizes, baseline demographics, viral hepatitis etiology (HBV/HCV), liver functional reserve (Child–Pugh class, MELD score, ALBI grade, ICG R15), surgical approach (open vs. minimally invasive) and resection extent, perioperative transfusion/blood loss, postoperative complications, short-term mortality, and long-term survival rates.

Quality assessment / Risk of bias analysis Methodological quality and risk of bias of included cohort studies were evaluated using the Newcastle–Ottawa Scale (NOS) across three domains: Selection (maximum 4 stars), Comparability (maximum 2 stars, accounting for hepatic reserve/cirrhosis and demographic/surgical covariates), and Outcome (maximum 3 stars), with

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total scores of 7–9 stars indicating high methodological quality / low risk of bias.

Strategy of data synthesis Primary quantitative meta-analysis was restricted to strictly harmonized dialysis/ESRD versus control contrasts. Unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from 2 × 2 contingency tables, applying a 0.5 continuity correction to all cells when zero-event cells occurred. Pooled log-ORs were estimated using inverse-variance DerSimonian–Laird random-effects models alongside inverse-variance fixed-effects sensitivity models. Statistical heterogeneity was quantified via Cochran's Q test, τ^2, and the I^2 statistic. Exploratory 4-study leave-one-out sensitivity analyses across broader renal dysfunction definitions were conducted to verify robustness. Long-term survival metrics (OS and DFS/RFS) and non-harmonizable major morbidity endpoints were synthesized descriptively and visually via paired slope plots without mathematical reconstruction of unverified Kaplan–Meier risk tables.

Subgroup analysis Outcomes were stratified by renal phenotype: (1) strictly defined maintenance dialysis-dependent ESRD versus controls (primary quantitative synthesis), (2) non-dialysis CKD (e.g., eGFR <45 mL/min/1.73 m²) versus preserved renal function, and (3) broader renal dysfunction definitions (4-study leave-one-out sensitivity synthesis).

Sensitivity analysis To assess the robustness of the primary exploratory meta-analyses under sparse-event conditions and heterogeneous renal impairment definitions, the following sensitivity analyses were performed:Statistical model comparison: Inverse-variance fixed-effects models were evaluated alongside primary DerSimonian–Laird random-effects models for both any postoperative complication and operative-related mortality.Broader renal dysfunction exposure & leave-one-out analysis: Exploratory 4-study leave-one-out sensitivity analyses across all included East Asian cohorts (Cheng et al., 2001; Toshima et al., 2012; Yeh et al., 2013; Watanabe et al., 2026) were conducted by expanding beyond strictly harmonized dialysis/ESRD contrasts to broader renal dysfunction definitions, sequentially omitting one study at a time to verify that pooled odds ratios (ORs), 95% confidence intervals (CIs), and heterogeneity (I^2) were not driven by any single study.

Language restriction English.

Country(ies) involved Taiwan.

Other relevant information Retrospective registration & submission status: This protocol registration was completed retrospectively after manuscript drafting and journal submission (PLOS ONE) to provide transparent documentation of the review scope, phenotype stratification, and analytical methods.

Methodological scope & non-pooled outcomes: Because included retrospective cohorts used heterogeneous renal impairment definitions (maintenance dialysis/ESRD, eGFR 2.0 mg/dL) and lacked uniform multivariable-adjusted hazard ratios for long-term survival, primary quantitative pooling was restricted to strictly harmonized dialysis/ESRD contrasts, while non-dialysis CKD morbidity and 5-year overall/recurrence-free survival were synthesized descriptively and visually via paired slope plots.

Cohort overlap & reporting standards: Potential patient overlap between Taiwanese single-center and nationwide administrative cohorts was noted transparently. Reporting aligns with PRISMA 2020 principles.

Keywords hepatocellular carcinoma; hepatectomy; end-stage renal disease; hemodialysis; chronic kidney disease; meta-analysis.

Dissemination plans The completed systematic review and exploratory meta-analysis has been submitted for peer-reviewed publication in an open-access international medical journal (PLOS ONE). Upon publication, the findings, PRISMA 2020 flow diagram, and extracted aggregate datasets will be made publicly accessible without subscription barriers to inform hepatobiliary surgeons, nephrologists, and perioperative care teams. Additionally, key results may be presented at relevant national or international surgical and hepatology conferences.

Contributions of each author

Author 1 - Hung-Jia Pai - Hung-Jia Pai contributed to study conceptualization, literature screening and data curation, methodological and statistical analysis, drafting the original manuscript, and critical review and editing of the final manuscript.
Email: baihungjia@gmail.com

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Author 2 - Wen-Ke Wang - Wen-Ke Wang contributed to study conceptualization, data curation, formal and statistical analysis, methodology verification, drafting the original manuscript, and reviewing and editing the final manuscript.
Email: 2jdiogxl@gmail.com

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