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INPLASY

# Minimally Invasive vs Open Hepatectomy and Postoperative Outcomes: Protocol for a Systematic Review and Meta-analysis of Propensity Score–Matched Studies (Retrospective Registration)

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**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:** INPLASY2026110104

**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** Among adults undergoing elective liver resection for benign or malignant indications, how is initiation of minimally invasive hepatectomy, compared with open hepatectomy, associated with postoperative morbidity, transfusion and organ-specific complications in propensity score–matched observational studies? The review will evaluate associations and their robustness to outcome definitions, surgical indication, cohort overlap and analytical assumptions, without claiming causal superiority.

**Rationale** Hepatectomy entails clinically important risks of hemorrhage, major complications and postoperative organ dysfunction. Surgical selection is influenced by hepatic reserve, anatomy, disease burden and expertise. Matching can reduce measured imbalance but cannot eliminate residual confounding. Existing randomized and observational syntheses already compare operative approaches; this review does not claim to be the first. Its proposed contribution is a design-aware assessment of organ-specific outcomes, clinically meaningful PHLF grades and the sensitivity of results to disease indication. A formal search for overlapping reviews and registrations must be completed and documented before submission.

**Condition being studied** Benign and malignant hepatic conditions requiring elective resection, including hepatocellular carcinoma, intrahepatic cholangiocarcinoma, liver metastases and selected benign disease such as hepatolithiasis. Cirrhosis, prior resection and extent of hepatectomy will be recorded as potential modifiers.

## METHODS

**Search strategy** Proposed completion search: MEDLINE via PubMed, Embase, Web of Science Core Collection and Cochrane CENTRAL from inception to the actual search date. Record

platform, exact syntax, date, filters and result counts. Search without outcome terms or language restrictions. A broad search followed by design screening is preferred because matching may not appear in titles or abstracts. Draft PubMed strategy (not yet executed as a complete documented search):

("Hepatectomy"[Mesh] OR hepatectom*[tiab] OR "liver resection"[tiab] OR "liver resections"[tiab] OR "hepatic resection"[tiab] OR "hepatic resections"[tiab]) AND ("Laparoscopy"[Mesh] OR "Robotic Surgical Procedures"[Mesh] OR laparoscop*[tiab] OR robotic*[tiab] OR "minimally invasive"[tiab])

Translate controlled vocabulary and field syntax for the other databases; supplement with backward and forward citation searching and a targeted propensity-score search (propensity score*, propensity match*, matched cohort*). Preserve all exported records and update the search before manuscript submission. Do not report any planned search as already executed.

**Participant or population** Adults aged 18 years or older undergoing elective hepatic resection. Mixed-age cohorts may be included only when adult data are separable or the adult nature of the cohort is established. Record indication, underlying liver disease, extent of resection and primary versus repeat surgery.

**Intervention** Laparoscopic or robotic hepatectomy, including conversions when attributable to the initial minimally invasive strategy. Record pure laparoscopic, robotic, hybrid or hand-assisted techniques separately; hybrid or hand-assisted cases will be analyzed separately if definitions are incompatible. Conversion handling will be extracted and evaluated for bias.

**Comparator** Conventional open hepatectomy in the same propensity score–matched comparison. Studies comparing only robotic versus laparoscopic surgery do not address the primary contrast.

**Study designs to be included** Published comparative observational cohort studies using propensity score matching and reporting postmatching outcomes. Randomized trials may provide contextual evidence but will not be pooled with matched observational studies. Unmatched cohorts, weighting-only analyses, case reports, single-arm series and reviews are excluded from the primary synthesis.

**Eligibility criteria** Include direct adult elective resection comparisons with identifiable matched groups and at least one relevant postoperative outcome. Exclude transplantation, donor hepatectomy, ablation alone, emergency trauma surgery and reports without extractable matched results. Do not exclude studies merely for nonsignificant findings. Reports with missing effect data remain eligible for narrative synthesis when appropriate. Link multiple reports of one cohort and avoid duplicate contributions within an outcome. These operational refinements require author approval and are not claimed to predate preliminary analyses.

**Information sources** Electronic databases in item 11, reference lists, forward citations, relevant reviews, and author contact for missing matched data or uncertain overlap. Search INPLASY and PROSPERO for related registered reviews. Document search access limitations, unsuccessful contacts and any grey-literature sources actually used.

**Main outcome(s)** Major postoperative morbidity (Clavien–Dindo grade III or higher; report exact grading and time window), perioperative blood transfusion (patients receiving transfusion, not units), and all-grade ISGLS posthepatectomy liver failure (PHLF). These outcomes were already examined before registration. Prefer 30-day morbidity where available; analyze in-hospital and other windows separately when incompatible. Record transfusion timing and threshold; do not combine incompatible definitions without a separate sensitivity analysis. Binary effects: OR with 95% CI, with RR as a secondary effect scale.

**Additional outcome(s)** Clinically relevant ISGLS grade B/C PHLF; AKI defined by KDIGO or another explicit criterion; 30- and 90-day mortality separately; blood loss (mL); operative time (minutes); postoperative length of stay (days); readmission and bile leak when available. Do not treat creatinine change, transfusion or PHLF as surrogate proof of renal protection. Analyze alternative PHLF definitions, such as the 50–50 criterion, separately. Secondary outcomes and hierarchy are recorded after preliminary findings were available.

**Data management** Proposed remaining workflow: two human reviewers independently screen titles/abstracts and full texts, extract or independently verify data, and resolve disagreements by consensus or a third reviewer. Confirm reviewers before registration. Assign study and report identifiers; record DOI/PMID, centers and

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recruitment dates, indication, approach, matching ratio, covariates, balance, sample sizes, conversions, outcome definitions/windows, matched event counts or adjusted estimates, precision and source page/table. Keep original values, converted values, decisions and dated changes separately. Resolve duplicate cohorts using center/date/population information and author clarification; choose the most complete relevant report independent of effect direction. Store exports, extraction sheets, code and PRISMA records in a versioned repository. AI has assisted drafting and preliminary calculations; human authors must verify all eligibility, extraction, references, bias judgments and analytical output against sources. No AI output substitutes for reviewer assessment.

**Quality assessment / Risk of bias analysis** Use ROBINS-I (2016 version proposed; confirm version before assessment) for each prioritized outcome, with independent human assessments and documented rationale. Address confounding (age, comorbidity, liver function/cirrhosis, tumor burden/location, resection extent, center, era and expertise), selection, intervention classification, deviations including conversion, missing data, measurement and selective reporting. PSM alone does not imply low risk. Exclude critical-risk results from primary quantitative synthesis; report separately. Use GRADE by outcome, explicitly state the starting-certainty approach and document risk of bias, inconsistency, indirectness, imprecision and publication bias; avoid double-counting confounding. Existing worksheets are preliminary, not completed judgments.

**Strategy of data synthesis** Primary target is the association of initiating minimally invasive versus open surgery among matched patients eligible for either approach. Prefer compatible matched-design or adjusted effect estimates and standard errors; pool log ORs using generic inverse variance only when estimands, definitions and windows are sufficiently comparable. Do not combine conditional and marginal ORs or adjusted and crude measures indiscriminately. Seek discordant pair counts, matched-set estimates or cluster-robust standard errors from authors. For 1:1 matched binary data, discordant pairs permit conditional OR estimation; variable-ratio sets require appropriate matched models. Marginal aggregate counts alone do not recover matched covariance. Existing DerSimonian–Laird (DL) random-effects ORs, with 0.5 added to all cells of a table containing a zero, use independent-arm variances and remain exploratory. For remaining work propose REML random effects with modified Hartung–Knapp intervals (variance multiplier at least 1), alongside the existing DL analysis. Report $tau^2$, Q, $I^2$ and 95% CIs; prediction intervals when sufficiently supported. Double-zero studies do not inform conventional OR pooling; describe them. For continuous outcomes use mean difference in common units, prefer directly reported means/SDs, and separate estimated means/SDs from medians with distributional assumptions; use appropriate methods for IQR/range and retain originals. Do not convert clearly incompatible or severely skewed summaries. Use matched variance if available; otherwise label approximations and examine sensitivity. Report descriptive synthesis when pooling is clinically or statistically unjustified. Do not infer homogeneity from $I^2=0$. Assess funnel asymmetry only with at least 10 reasonably comparable studies and interpret cautiously. Record software, package versions and reproducible code before final analysis.

**Subgroup analysis** If sufficient independent studies are available, investigate malignant versus benign indications, HCC versus other disease, cirrhosis, major versus minor resection (major generally ≥3 Couinaud segments), repeat versus initial resection, and laparoscopic versus robotic approaches. Extract actual definitions and avoid inferring patient-level interactions from study-level subgroups. Use formal interaction tests where defensible; otherwise report descriptive differences. All such analyses are exploratory given retrospective timing and limited evidence.

**Sensitivity analysis** Reproduce already conducted leave-one-out, modified Hartung–Knapp, RR, exclusion of recurrent hepatolithiasis, alternative morbidity definitions, and substitution of potentially overlapping cohorts. For remaining work: compare matched-design versus marginal estimates without pooling incompatible estimands, REML versus DL, direct versus median-derived continuous outcomes, alternative zero-cell handling, exclusion of serious/critical risk of bias, restriction to standardized outcome definitions and windows, and alternative defensible cohort choices. Use covariance sensitivity only when assumptions are explicitly justified; do not invent within-pair correlation. Report all results, not only significant ones. No sensitivity analysis can remove bias from late registration.

**Language restriction** Proposed: no language restriction at search; arrange translation when feasible, and document any reports that cannot be assessed. Protocol submitted in English.

**Country(ies) involved** Taiwan.

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**Other relevant information** Registration is retrospective; no registration number or DOI has been assigned. Preserve prior manuscript and analysis versions and a dated amendment log, indicating which decisions were made after results were available. Report actual registration date and rationale in the final manuscript. No individual participant data were analyzed in the interim work; confirm institutional ethics requirements and any later data access. Report using PRISMA 2020 and MOOSE; use PRISMA-P as a protocol framework. Registration does not constitute peer review or guarantee journal acceptance.

**Keywords** Hepatectomy; minimally invasive surgery; laparoscopy; robotic surgery; propensity score matching; postoperative complications; posthepatectomy liver failure; acute kidney injury; systematic review;.

**Dissemination plans** Submit the completed review to a peer-reviewed journal, with JAMA Network Open as the intended first target. Publish reproducible search strategies, extracted aggregate data and analysis code where permitted; update the registry with amendments, review status and publication link.

**Contributions of each author**

Author 1 - Hung-Jia Pai - Assign screening, extraction verification, statistical analysis, risk-of-bias assessment, drafting and guarantor roles to actual human contributors; obtain approval from all listed authors
Email: baihungjia@gmail.com
Author 2 - Wen-Ke Wang - Assign screening, extraction verification, statistical analysis, risk-of-bias assessment, drafting and guarantor roles to actual human contributors; obtain approval from all listed authors
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