International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Hyperfiltration After Partial Versus Radical Nephrectomy for Localized Renal Tumors: A Systematic Review

INPLASY202680011
doi: 10.37766/inplasy2026.8.0011
Received: 2 August 2026
Published: 2 August 2026

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ADMINISTRATIVE INFORMATION

Support - This systematic review received no specific grant or external funding and is conducted using institutional resources.

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

Conflicts of interest - The authors declare no conflicts of interest. All authors will complete ICMJE disclosure forms at registration and update them at manuscript submission. Any industry relationships relevant to robotic surgery, renal volumetry software, or device manufacture will be disclosed.

INPLASY registration number: INPLASY202680011

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 August 2026 and was last updated on 15 August 2026.

INTRODUCTION

Review question / Objective Primary objective: To determine whether volume-normalized filtration burden (GFR/FRV), used as an operational proxy for hyperfiltration, differs after partial versus radical nephrectomy for localized renal tumors in adults with both kidneys present and no significant contralateral renal disease at baseline.
Secondary objectives: to quantify change in contralateral split renal function; to quantify compensatory contralateral volumetric hypertrophy; to determine the relationship between functional parenchymal volume removed or retained and independent functional responses (total GFR change, contralateral single-kidney GFR, renal functional compensation); to describe the association between hyperfiltration indices and downstream markers of glomerular injury (proteinuria/albuminuria, eGFR trajectory, incident CKD stage 3 or worse); and to characterize measurement heterogeneity in how hyperfiltration has been operationalized.
PICOS:
Population — adults aged 18 or older undergoing partial or radical nephrectomy for a localized renal tumor (cT1-T2, or pT1-T2 when cT unavailable), no distant metastasis, both kidneys present preoperatively, no significant contralateral renal disease. Intervention/exposure of interest — partial nephrectomy (the lesser nephron mass reduction). Comparator — radical nephrectomy (the greater nephron mass reduction). Outcome — volume-normalized filtration burden (GFR/FRV) and related compensatory functional and volumetric outcomes at 6-12 months (primary) and later windows (secondary). Study designs — randomized trials;

prospective and retrospective comparative cohorts; single-arm follow-up cohorts or case series if identified. The comparison direction is partial-versus-radical throughout; independently of this labelling, radical nephrectomy entails the greater nephron-mass reduction.

Rationale Partial nephrectomy is preferred for many T1 renal tumors and may be used in selected stage II-III disease when technically feasible; radical nephrectomy remains common for larger or more complex tumors. Treatment selection depends on patient characteristics, tumor anatomy and stage, technical feasibility, and clinical judgment. The physiological premise for tolerating radical nephrectomy is compensatory adaptation: the remaining nephron mass may increase filtration per surviving nephron, partially restoring global glomerular filtration rate. Sustained glomerular hyperfiltration is the mechanism invoked in the Brenner hypothesis for progressive injury after nephron-mass reduction. Published nephrectomy studies report global eGFR, split renal function, and functional volumetry in heterogeneous combinations. Global eGFR does not distinguish loss of filtering mass from adaptation of the remaining tissue. This review therefore uses filtration rate per unit functional renal volume (GFR/FRV) as an operational measure of volume-normalized filtration burden, organizing the evidence around this and related compensatory functional and structural responses rather than global eGFR alone.

Condition being studied Adults with a localized renal tumor (cT1-T2/pT1-T2, non-metastatic) treated by partial or radical nephrectomy, in whom the postoperative renal response of interest is hyperfiltration — an elevated filtration burden per unit remaining functional nephron mass — together with compensatory functional and structural adaptation of the remaining renal tissue. This encompasses volume-normalized filtration burden (GFR/FRV) as a proxy for per-nephron filtration, contralateral compensatory hypertrophy and split-function change, and downstream markers of glomerular injury (proteinuria/albuminuria, eGFR decline, incident chronic kidney disease). The clinical concern is that greater nephron-mass reduction (radical nephrectomy) may impose a higher filtration burden on the remaining nephrons, potentially accelerating chronic kidney disease per the Brenner hyperfiltration hypothesis.

METHODS

Search strategy Electronic databases: PubMed (NLM), Web of Science, Scopus, and Cochrane CENTRAL. Embase will not be searched (unavailable through the authors' institutions); this is reported as a coverage limitation.
Structure: each database strategy combines an intervention block (explicit nephrectomy/renal-resection terminology; high-specificity nephron-sparing terminology; or broader kidney-/renal-preserving or enucleation terminology when renal-tumor vocabulary is present) with one of three outcome pathways: (1) high-specificity hyperfiltration, renal functional compensation, or filtration-per-volume terminology; (2) lower-specificity compensation, split/differential renal-function, structural-compensation, or parenchymal-volume terminology when accompanied by renal-tumor vocabulary or a measurement, paired-kidney, or volumetry anchor; or (3) renal-tumor terminology with a generic renal outcome plus a measurement/contextual anchor, or laterality terminology in the title. The renal-tumor population block is conditional because physiology-framed nephrectomy reports may omit the indication from indexed text.
Term groups span: renal tumor/RCC vocabulary; nephrectomy and nephron-sparing surgery; hyperfiltration and filtration-per-volume; split/differential renal function; compensatory hypertrophy and renal adaptation; nephron mass and parenchymal volume; renal function tests, GFR, CKD, and proteinuria/albuminuria; nuclear renography and functional imaging (DTPA, MAG3, DMSA, measured GFR); volumetry/segmentation; and laterality (contralateral/ipsilateral/remnant/solitary kidney).
Limits and filters: no date, language, adult, or publication-type filter. PubMed excludes animal-only records via the Animals NOT Humans construction. Title-only exclusions for five-sixths nephrectomy and remnant-kidney animal models are applied in all four databases. Strategies were peer-reviewed against PRESS and revised, and will be checked in each native database interface before screening begins. Complete line-by-line strategies for all four databases are provided in the protocol's Appendix A and will be deposited at OSF (PRISMA-S).

Participant or population Adults aged 18 or older undergoing partial or radical nephrectomy for a localized renal tumor (cT1-T2; or pT1-T2 when cT is unavailable; or organ-confined with compatible size when neither T category is reported), with no distant metastatic disease (nodal status recorded but not an eligibility criterion), both kidneys present preoperatively, and no clinically or radiographically significant contralateral renal disease at baseline.

Intervention Partial nephrectomy — the intervention (exposure) of interest, entailing the lesser nephron-mass reduction — performed for a localized renal tumor by any surgical approach (open, laparoscopic, or robot-assisted). Percentage functional parenchymal volume removed or retained will be extracted for independent mass-function analyses where reported.

Comparator Radical nephrectomy — the comparator, entailing the greater nephron-mass reduction — performed for a localized renal tumor by any surgical approach (open, laparoscopic, or robot-assisted). The comparison direction is partial-versus-radical throughout; radical nephrectomy carries the greater nephron-mass reduction independently of this intervention/comparator labelling.

Study designs to be included Randomized trials; prospective and retrospective comparative cohorts (partial vs radical nephrectomy); and, if identified, single-arm follow-up cohorts or case series, requiring at least 5 participants per eligible procedure group. Comparative studies inform the PN-versus-RN association; single-arm studies contribute procedure-specific descriptive evidence only.

Eligibility criteria Additional inclusion: renal mass by any surgical approach; reports at least one eligible hyperfiltration outcome at 6 months or later with a preoperative/baseline reference permitting calculation of change; original research with extractable quantitative data; at least 5 participants per eligible procedure group. Mixed cohorts eligible only when a conforming subgroup is separately extractable.
Exclusion: solitary kidney (anatomic or functional), or bilateral/multifocal tumors requiring bilateral intervention; baseline CKD stage 4 or worse (eGFR below 30), dialysis, or prior transplant; hereditary syndromes with bilateral/multifocal tumors (von Hippel-Lindau, hereditary leiomyomatosis and renal cell cancer, Birt-Hogg-Dube, hereditary papillary renal cell carcinoma); contralateral kidney with significant pathology (atrophy, obstruction, prior nephrectomy/ablation, significant stone burden with hydronephrosis); ablative therapy, enucleation without parenchymal-volume accounting, living donation, or benign/non-oncologic nephrectomy as the sole population; clinical T3-T4 (or pathological T3-T4 when cT unavailable) unless an eligible T1-T2 subgroup is separately extractable; M1 disease, cytoreductive/palliative nephrectomy, or systemic therapy for kidney cancer before the eligible renal-function assessment unless an untreated subgroup or pre-treatment assessment is separately extractable; outcome reported only as global eGFR without a per-mass or split-function denominator; reviews, editorials, case reports, series with fewer than 5 participants, abstracts without extractable data, animal or pediatric studies; follow-up shorter than 6 months.
No language or date restriction. Overlapping reports assessed by center, accrual dates, and authorship; the index report is chosen by largest sample, then most complete outcome data.

Information sources Electronic databases: PubMed, Web of Science, Scopus, and Cochrane CENTRAL (Embase unavailable; reported as a limitation). Supplementary: backward citation chasing (reference lists of included studies and relevant systematic reviews); forward citation chasing (Scopus and Google Scholar cited-by); trial registries (ClinicalTrials.gov, WHO ICTRP, ISRCTN); grey literature (CORE, ProQuest Dissertations & Theses via Web of Science, OpenGrey archive); conference abstract archives (American Urological Association, European Association of Urology, Societe Internationale d'Urologie, Philippine Urological Association, preceding five years); and author contact (corresponding authors of eligible studies with incomplete data, and of abstracts without full publications — two emails at three-week intervals, non-response logged). Hand-searching of tables of contents (preceding ten years) in European Urology, Journal of Urology, BJU International, Urologic Oncology, World Journal of Urology, Urology, Urologia Internationalis, International Journal of Urology, Investigative and Clinical Urology, and Clinical and Experimental Nephrology.

Main outcome(s) Primary outcome: volume-normalized filtration burden (GFR/FRV), expressed as mL/min/1.73 m2 per cm3 (or per mL) of functional renal parenchyma, at 6-12 months postoperatively, treated as a proxy for average filtration burden per unit functional tissue. The denominator is total remaining functional renal parenchymal volume; after radical nephrectomy this is the single preserved kidney, and after partial nephrectomy it comprises both the operated remnant and the contralateral kidney (a ratio on the operated kidney alone after partial nephrectomy does not qualify). Primary estimand: change from preoperative value to 6-12 months within each procedure group, and the within-study partial-versus-radical contrast. Accepted forms: study-reported global GFR / total remaining functional volume; an author-reported hyperfiltration or GFR-

per-volume index with a conforming denominator; or a value derived by the review team from separately reported components under defined non-circularity and same-timepoint conditions (flagged as derived). Mean within-person ratios and ratios of group means are distinct estimands, coded and synthesized separately; derived ratios without a valid standard error are tabulated, not meta-analyzed. Effect measures: within-study change and within-study partial-versus-radical contrasts; standardized mean difference where the same construct is measured on different scales.

Additional outcome(s) Secondary outcomes: (S1) contralateral split renal function change — percentage change in contralateral functional contribution or absolute single-kidney GFR, pre- to postoperative; (S2) contralateral volumetric hypertrophy — percentage change in contralateral parenchymal volume; (S3) renal functional compensation — ratio of observed to predicted postoperative contralateral function; (S4) nephron mass-function relationship — association of functional parenchymal volume removed/retained with independent outcomes (total GFR change, contralateral single-kidney GFR change, or renal functional compensation), avoiding regression of GFR/FRV on the same volume used in its denominator; (S5) proteinuria/albuminuria — new-onset or worsening by dipstick, albumin-creatinine ratio, or protein-creatinine ratio (threshold recorded); (S6) eGFR trajectory — annualized slope beyond 12 months where reported; (S7) incident CKD stage 3 or worse — new eGFR below 60 sustained at least 3 months; (S8) measurement heterogeneity — count and taxonomy of operationalizations across the literature. Extraction windows: 6-12 months (primary), greater than 12 to 36 months, and greater than 36 months. Effect measures: mean or standardized mean difference for continuous outcomes; odds or risk ratio (adjusted preferred) for binary outcomes.

Data management Records exported to Zotero and deduplicated using DOI, title/year, and author/bibliographic fields; the deduplicated library imported into Rayyan for screening. Per-database and post-deduplication counts recorded. Screening conducted in Rayyan blind mode with decisions concealed until both reviewers complete each record. Search dates, database settings, executed strategies, and yields preserved and reported per PRISMA-S. Study flow reported via the PRISMA 2020 flow diagram (records identified per database, duplicates removed, records screened). Screening decisions, extraction data, and analysis files maintained in the project archive; the extraction form is version-controlled with dated, logged revisions. Analysis scripts are version-controlled and deposited at OSF. A designated data manager and reproducibility lead administers Zotero and Rayyan, the PRISMA flow diagram, and OSF deposition.

Quality assessment / Risk of bias analysis Risk of bias assessed independently and in duplicate by two reviewers, with disagreements escalated through a defined adjudication hierarchy. Tools by design: RoB 2 (2019) for randomized trials; ROBINS-I (2016) for comparative non-randomized studies (partial vs radical nephrectomy); the revised JBI critical appraisal tool for single-arm cohorts; and the JBI Case Series checklist for case series. A pre-specified target trial anchors ROBINS-I. Pre-specified confounding domains include tumor size/cT-pT/nephrometry complexity (dominant), nodal status and stage, baseline eGFR/CKD stage, baseline split function and parenchymal volume, age, diabetes, hypertension, baseline proteinuria, surgeon/center volume, and accrual era. Pre-specified co-interventions include ischemia type and duration, surgical approach, lymph-node dissection, renin-angiotensin blockade/nephroprotective medication, systemic-therapy timing, and nephrotoxic exposures. Each of the seven ROBINS-I domains is rated Low/Moderate/Serious/Critical/No information, with the overall equal to the worst domain. In addition, a review-specific Measurement Validity domain (seven signalling questions on volumetry method, functional-parenchyma isolation, GFR ascertainment, imaging timing, blinded assessment, reproducibility, and modality consistency) is applied to all studies and reported separately. Studies rated High concern on functional-parenchyma isolation are excluded from the primary analysis (sensitivity only); Critical ROBINS-I results are excluded from all quantitative and directional syntheses; Serious-risk results may be retained with caution and sensitivity analysis. Figures via robvis, with the Measurement Validity domain as a parallel figure.

Strategy of data synthesis Direct comparative synthesis (comparative partial-vs-radical studies) is the primary pathway; a nephron mass-function pathway and a procedure-specific single-arm pathway are undertaken when eligible data support them. Single-arm evidence is never used to estimate a partial-vs-radical effect. Only within-study comparative evidence estimates the comparative association; non-randomized findings are reported as associations, not causal effects. Effect measures grouped by estimand: (1) mean within-person change or log-ratio in GFR/FRV; (2) ratio of group means at follow-up relative to

baseline, then the between-arm ratio of ratios; (3) study-reported adjusted comparative estimates. Pooling requires compatible estimands and GFR/FRV formulas; standardized mean difference is reserved for the same construct on different scales; reviewer-derived ratios of aggregate means are pooled only with a valid standard error, else tabulated. Model: random-effects meta-analysis when at least 3 clinically and methodologically compatible studies with valid variances are available; fixed-effect as sensitivity; REML for tau-squared; Hartung-Knapp-Sidik-Jonkman intervals when at least 3 studies contribute and heterogeneity is greater than zero; prediction intervals when at least 5 comparable studies and no strong small-study asymmetry. Meta-analysis is technically possible with two studies but the primary policy requires at least 3; two-study evidence is displayed side by side and explored only as a labelled sensitivity analysis. Critical ROBINS-I results, High-concern isolation results, and derived ratios without valid variances are not pooled. Where pooling is inappropriate, prespecified tabulation and effect-direction methods are used and reported per SWiM. Heterogeneity: tau-squared/tau (REML), I-squared with 95% CI (descriptive, not a pooling threshold), and Cochran's Q (interpreted cautiously). Software: R (meta, metafor, robvis, dmetar), with scripts deposited at OSF. Certainty assessed by outcome using GRADE (randomized evidence starts High; comparative non-randomized starts Low), with Summary of Findings tables in GRADEpro where direct comparative evidence exists; single-arm summaries receive no comparative rating. Null and contrary findings are reported.

Subgroup analysis Pre-specified subgroups (all exploratory, interpreted without selective emphasis; Q-between tested only when each subgroup has adequate data, generally at least 5 studies): volumetry method (software 3D vs ellipsoid vs length-width-height); functional-parenchyma isolation (Low vs Moderate concern; High-concern excluded from primary, sensitivity only); GFR ascertainment (measured/validated split GFR vs standardized eGFR-based estimation); follow-up window (6-12 vs greater than 12-36 vs greater than 36 months); baseline renal function (eGFR 90 or above vs 60-89); tumor size (4 cm or less vs greater than 4 cm); ischemia type in the partial-nephrectomy arm (none/selective vs warm vs cold); and risk of bias (Low/Moderate vs Serious ROBINS-I; Critical excluded). Additional subgroup analyses will be identified as post hoc and documented as protocol amendments.

Sensitivity analysis Pre-specified sensitivity analyses: correlation coefficient for paired pre-post data set at 0.5, 0.7, and 0.9 (mandatory; working value 0.7 where correlation is unreported); restricted to studies with at least 20 participants per arm; excluding studies with incompletely reported contralateral baseline status; including studies rated High concern on functional-parenchyma isolation (otherwise excluded from primary) to assess their influence; excluding studies with converted medians or derived standard deviations; excluding Serious ROBINS-I results (Critical excluded from all syntheses); fixed-effect versus random-effects comparison; leave-one-out influence analysis; excluding conference abstracts and non-English studies with low translation confidence; and excluding studies with greater than 30 percent attrition at the analyzed timepoint. The proportion of studies and analytic weight relying on an assumed correlation is reported and considered in the GRADE imprecision judgment.

Language restriction No language restriction. Non-English records will be translated, with methods and results verified by a native speaker; low-confidence translations are flagged for sensitivity analysis.

Country(ies) involved Philippines.

Other relevant information Reporting standards: this protocol follows PRISMA-P 2015; the completed review will follow PRISMA 2020, PRISMA-S (search reporting), and SWiM (synthesis without meta-analysis), with certainty via GRADE and Summary of Findings tables (GRADEpro). PROSPERO was the intended primary registry; this INPLASY registration is used as an equivalent registry. Complete line-by-line database search strategies for PubMed, Web of Science, Scopus, and Cochrane CENTRAL are provided in the protocol's Appendix A and will be deposited at OSF. Embase is not searched (institutional access unavailable), reported as a search-coverage limitation. The search strategies were designed by the corresponding author, Dr Baesa. They were peer-reviewed against the PRESS 2015 framework by Maria Lutgarda M. Dorado, MLS, an information specialist who took no part in the strategy design; Dr Baesa revised the strategies in response to that review and returned them to the reviewer, who accepted the revised strategies. Ms Dorado is acknowledged (not an author), having received no compensation beyond her institutional role. Data availability: the review will release the extraction dataset, derived data, analysis scripts, risk-of-bias assessments, search strategies, and screening/

deduplication decisions at OSF where permitted; proprietary or copyrighted licensed content will not be redistributed. Ethics approval is not required (systematic review of published aggregate data); institutional exemption confirmation is referenced where required. Methodological note: GFR/FRV is a volume-normalized proxy for filtration burden, and nephron mass-function analyses avoid outcomes algebraically defined by the same volume used as the predictor (mathematical coupling). The review anticipates completion within six months of registration.

Keywords nephrectomy; partial nephrectomy; radical nephrectomy; hyperfiltration; glomerular filtration rate; renal functional compensation; kidney neoplasms; compensatory hypertrophy; parenchymal volume.

Dissemination plans Results will be submitted to a peer-reviewed urology journal and presented at relevant national and international scientific meetings. A preprint and a plain-language summary may be posted with the registration record.

Contributions of each author

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