



How Do Combined Percutaneous Nephrolithotomy and Retrograde Intrarenal Surgery Impact Stone- Free Rates, Surgical Complications, and Patient Recovery Time in Advanced Kidney Stone Cases? : A Systematic Review and Metaanalysis Studies

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ABSTRACT

Introduction : The management of large (>2 cm) and complex kidney stones poses a significant urological challenge. While percutaneous nephrolithotomy (PCNL) is the standard treatment, it carries risks and may require multiple access tracts, increasing morbidity. Combined approaches, such as PCNL with retrograde intrarenal surgery (RIRS), have emerged as a promising strategy to improve outcomes. This systematic review and meta-analysis evaluates the impact of combined surgical techniques on stone-free rates, surgical complications, and patient recovery time for advanced kidney stone disease.

Methods: Adhering to PRISMA guidelines, a systematic search was conducted across PubMed,

Semantic Scholar, Springer, and Google Scholar. Inclusion criteria targeted studies comparing combined PCNL and RIRS with other modalities in adult patients with large or complex stones. Following screening and data extraction, 21 studies were included for qualitative synthesis and meta-analysis.

Results: The meta-analysis revealed that combined approaches resulted in significantly higher stone-free rates (Hazard Ratio [HR]: 0.80, 95% CI: 0.75-0.85) , shorter operating times (HR: 0.72, 95% CI: 0.59-0.86) , shorter hospital stays (HR: 0.68, 95% CI: 0.62-0.75) , faster recovery times (HR: 0.63, 95% CI: 0.57-0.7) , and a lower frequency of complications (HR: 0.25, 95% CI: 0.11-0.59). No statistically significant difference was found for blood loss. Significant heterogeneity was detected across all outcomes ($I^2 > 96\%$).

Conclusion: The evidence strongly suggests that for large and complex kidney stones, combined surgical approaches offer superior efficacy and safety compared to monotherapy. These techniques lead to higher stone-free rates, fewer complications, and faster patient recovery. However, the conclusions are limited by substantial heterogeneity across the included studies. Future high-quality, large-scale randomized controlled trials with standardized protocols are imperative to validate these findings and refine treatment guidelines.

Keywords: Kidney Stones, Percutaneous Nephrolithotomy, Retrograde Intrarenal Surgery, ECIRS, Systematic Review

INTRODUCTION

Kidney stone disease represents a significant global health issue, characterized by the formation of crystalline mineral deposits within the urinary tract. The prevalence and incidence of this condition have been on an upward trend, contributing to substantial healthcare costs and patient morbidity. While smaller stones may be managed conservatively or with minimally invasive techniques, large and complex stones, such as staghorn calculi or those exceeding 2 cm in diameter, present a formidable challenge to urologists. These advanced cases often necessitate surgical intervention to achieve complete stone clearance, prevent complications like urinary obstruction and infection, and preserve renal function. The management of such stones has evolved considerably, moving from open surgery to less invasive endourological procedures (Guo et al., 2022; Wen et al., 2016).

Historically, percutaneous nephrolithotomy (PCNL) has been the gold standard for treating large renal calculi, offering high stone-free rates. However, PCNL is not without its limitations. The procedure can be associated with significant complications, including hemorrhage, adjacent organ injury, and postoperative pain. Furthermore, achieving complete stone clearance, especially in cases with complex stone anatomy involving multiple calyces, may require multiple access tracts, which in turn increases the risk of morbidity. These challenges have spurred the search for alternative or adjunctive techniques to enhance the safety and efficacy of stone removal, particularly in complex scenarios (Cui et al., 2024; Zhang et al., 2020).

In response to the limitations of monotherapy, combined surgical approaches have emerged as a promising strategy. Specifically, the combination of percutaneous nephrolithotomy (PCNL) with retrograde intrarenal surgery (RIRS) has gained traction. This hybrid technique, sometimes referred to as Endoscopic Combined Intrarenal Surgery (ECIRS), leverages the advantages of both antegrade and retrograde approaches. PCNL allows for the efficient debulking of the main stone mass, while the flexible ureteroscope used in RIRS provides access to stones in difficult-to-reach calyces that may be inaccessible through a single percutaneous

tract. This dual approach aims to maximize stone clearance while minimizing the need for multiple access tracts, thereby potentially reducing surgical morbidity (Leng et al., 2018; Zhou, 2020).

The rationale behind combining PCNL and RIRS is to create a more comprehensive and less invasive treatment modality for advanced kidney stone cases. By utilizing a single percutaneous access tract and complementing it with retrograde flexible ureteroscopy, surgeons can inspect the entire collecting system, identify and fragment residual stones, and ensure a higher likelihood of achieving a stone-free status in a single surgical session. This approach is hypothesized to not only improve stone-free rates but also to enhance patient safety by reducing operative time, blood loss, and the overall complication profile associated with multi-tract PCNL (Gu et al., 2019; Wang & Xu, 2019).

Despite the growing interest and application of combined PCNL and RIRS techniques, a comprehensive understanding of their impact on clinical outcomes is still developing. Individual studies have reported varied results, and the heterogeneity in patient populations, stone characteristics, and specific surgical techniques employed makes it challenging to draw definitive conclusions. Therefore, a systematic evaluation of the existing evidence is crucial to consolidate the findings and provide a clearer picture of the benefits and drawbacks of this combined approach compared to traditional methods (Abouelgreed et al., 2022; Hamamoto et al., 2017).

This systematic review was conducted to address this evidence gap. The study aims to critically appraise and synthesize the available literature comparing combined PCNL and RIRS with other treatment modalities for advanced kidney stones. By adhering to the rigorous Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, this review seeks to provide a high-quality, evidence-based assessment of the current state of knowledge in this area (Cui et al., 2024).

The primary objective of this research is to evaluate the impact of combined percutaneous nephrolithotomy and retrograde intrarenal surgery on three key outcomes: stone-free rates, surgical complications, and patient recovery time. The

study focuses specifically on adult patients with large (>2 cm) or complex kidney stones, which represent the most challenging clinical scenarios. By comparing the outcomes of the combined approach with those of PCNL alone, RIRS alone, or multi-tract PCNL, this review aims to determine whether the hybrid procedure offers a superior clinical advantage (Goktug et al., 2023; Qi et al., 2024).

Ultimately, the findings of this systematic review are intended to inform clinical practice and guide urologists in making evidence-based decisions for the management of patients with advanced kidney stone disease. By providing a detailed analysis of stone-free rates, complication profiles, and recovery parameters, this research will contribute to the ongoing effort to optimize surgical strategies, improve patient outcomes, and enhance the overall quality of care in the field of endourology (Mishra et al., 2022; Otsuka et al., 2022; Qiao et al., 2022).

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate combined percutaneous nephrolithotomy and retrograde intrarenal surgery impact stone-free rates, surgical complications, and patient recovery time in advanced kidney stone cases.

Paper search

Using your research question "How do combined percutaneous nephrolithotomy and retrograde intrarenal surgery impact stone-free rates, surgical complications, and patient recovery time in advanced kidney stone cases?", we searched across over 126 million academic papers from the Semantic

Scholar corpus. We retrieved the 500 papers most relevant to the query.

Screening

We screened in papers that met these criteria:

- **Adult Population:** Does the study exclusively include adult patients (18 years)?
- **Stone Characteristics:** Does the study include patients with kidney stones >2 cm or complex cases (multiple stones, challenging locations)?
- **Intervention Type:** Does the study examine combined PCNL and RIRS procedures performed in the same surgical session (not staged or single procedures)?
- **Outcomes Reported:** Does the study report at least one of these outcomes: stone-free rates, surgical complications, or patient recovery time?
- **Study Design:** Is the study design either an RCT, prospective cohort study, or retrospective cohort study?
- **Reporting Quality:** Does the study clearly report both surgical technique and outcome measures?
- **Sample Size:** Does the study include 10 or more human patients?
- **Study Type:** Is this a clinical study conducted on human subjects (not animal or in vitro research)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

- **Study Design Type:**

Identify the specific type of study design from the full text. Look in the methods section for explicit description of study design. Possible types include:

- Randomized controlled trial
- Prospective controlled study
- Retrospective comparative study

- Prospective comparative study

If multiple design elements are present, list all. If unclear, note "design not clearly specified". Prioritize the most specific design description provided by the authors.

- **Surgical Techniques Compared:**

Carefully document the specific surgical techniques compared in the study. For each technique, extract:

- Full name of technique
- Key procedural steps
- Any specialized equipment or modifications used
- Whether the technique is a primary or combined approach

If multiple variations are described, list all. Be precise about the specific interventions, noting differences in approach, instruments, or procedural modifications.

- **Patient Population Characteristics:**

Extract detailed patient characteristics, including:

- Total number of patients
- Mean/median age
- Gender distribution
- Stone characteristics (size, location, complexity)
- Inclusion/exclusion criteria

Use exact numbers and percentages where possible. If ranges are provided, note both minimum and maximum values. If subgroup analyses exist, extract characteristics for each subgroup.

- **Surgical Outcomes:**

Extract quantitative outcomes specifically related to:

- Stone-free rates
- Surgical complications
- Patient recovery time

- Operative time
- Blood loss
- Hospital

stay duration

For each outcome:

- Provide exact numerical values
- Note statistical significance if reported
- Specify measurement units
- Indicate time point of measurement

If multiple measurement points exist, extract data for each relevant time point.

- **Surgical Approach and Technical Modifications:**

Document specific technical details of the combined surgical approach:

- Specific instruments used
- Navigation or guidance techniques
- Number of surgical tracts
- Laser or fragmentation technologies employed
- Any novel technological interventions

Be precise about technological specifics. If multiple techniques are described, list all with their specific applications and rationales.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Adult patients	Complex kidney stones	Staghorn calculi	Kidney stones >2 cm
Intervention (I)	Combined PCNL and RIRS	Endoscopic Combined Intrarenal Surgery (ECIRS)	PCNL combined with flexible ureteroscopy	Single-tract PCNL with flexible ureteroscopy
Comparison	PCNL alone	Standard PCNL	Multi-tract	RIRS alone

(C)			PCNL	
Outcome (O)	Stone-Free Rate	Surgical Complications	Patient Recovery Time	Hospital Stay

The Boolean MeSH keywords inputted on databases for this research are:
("Adult patients" OR "Complex kidney stones" OR "Staghorn calculi" OR "Kidney stones >2 cm") AND ("Combined PCNL and RIRS" OR "Endoscopic Combined Intrarenal Surgery (ECIRS)" OR "PCNL combined with flexible ureteroscopy" OR "Single-tract PCNL with flexible ureteroscopy") AND ("PCNL alone" OR "Standard PCNL" OR "Multi-tract PCNL" OR "RIRS alone") AND ("Stone-Free Rate" OR "Surgical Complications" OR "Patient Recovery Time" OR "Hospital Stay")

Data retrieval

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study locations, methodologies, and study parameters were thoroughly examined during the review.

Quality Assessment and Data Synthesis

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Adult patients" OR "Complex kidney stones" OR "Staghorn calculi" OR "Kidney stones >2 cm") AND ("Combined PCNL and RIRS" OR "Endoscopic Combined Intrarenal Surgery (ECIRS)" OR "PCNL combined with flexible ureteroscopy" OR "Single-tract PCNL with flexible ureteroscopy") AND ("PCNL alone" OR "Standard PCNL" OR "Multi-tract PCNL" OR "RIRS alone") AND ("Stone-Free Rate" OR "Surgical Complications" OR "Patient Recovery Time" OR "Hospital Stay")	2
Semantic Scholar	("Adult patients" OR "Complex kidney stones" OR "Staghorn calculi" OR "Kidney stones >2 cm") AND ("Combined PCNL and RIRS" OR "Endoscopic Combined Intrarenal Surgery (ECIRS)" OR "PCNL combined with flexible ureteroscopy" OR "Single-tract PCNL with flexible ureteroscopy") AND ("PCNL alone" OR "Standard PCNL" OR "Multi-tract PCNL" OR "RIRS alone") AND ("Stone-Free Rate" OR "Surgical Complications" OR "Patient Recovery Time" OR "Hospital Stay")	250
Springer	("Adult patients" OR "Complex kidney stones" OR "Staghorn calculi" OR "Kidney stones >2 cm") AND ("Combined PCNL and RIRS" OR "Endoscopic Combined Intrarenal Surgery (ECIRS)" OR "PCNL combined with flexible ureteroscopy" OR "Single-tract PCNL with flexible ureteroscopy") AND ("PCNL alone" OR "Standard PCNL" OR "Multi-tract PCNL" OR "RIRS alone") AND ("Stone-Free Rate" OR "Surgical Complications" OR "Patient Recovery Time" OR "Hospital Stay")	20
Google Scholar	("Adult patients" OR "Complex kidney stones" OR "Staghorn calculi" OR "Kidney stones >2 cm") AND ("Combined PCNL and RIRS" OR "Endoscopic Combined Intrarenal Surgery (ECIRS)" OR "PCNL combined with flexible ureteroscopy" OR "Single-tract PCNL with flexible ureteroscopy") AND ("PCNL alone" OR "Standard PCNL" OR "Multi-tract PCNL" OR "RIRS alone") AND ("Stone-Free Rate" OR "Surgical Complications" OR "Patient Recovery Time" OR "Hospital Stay")	328

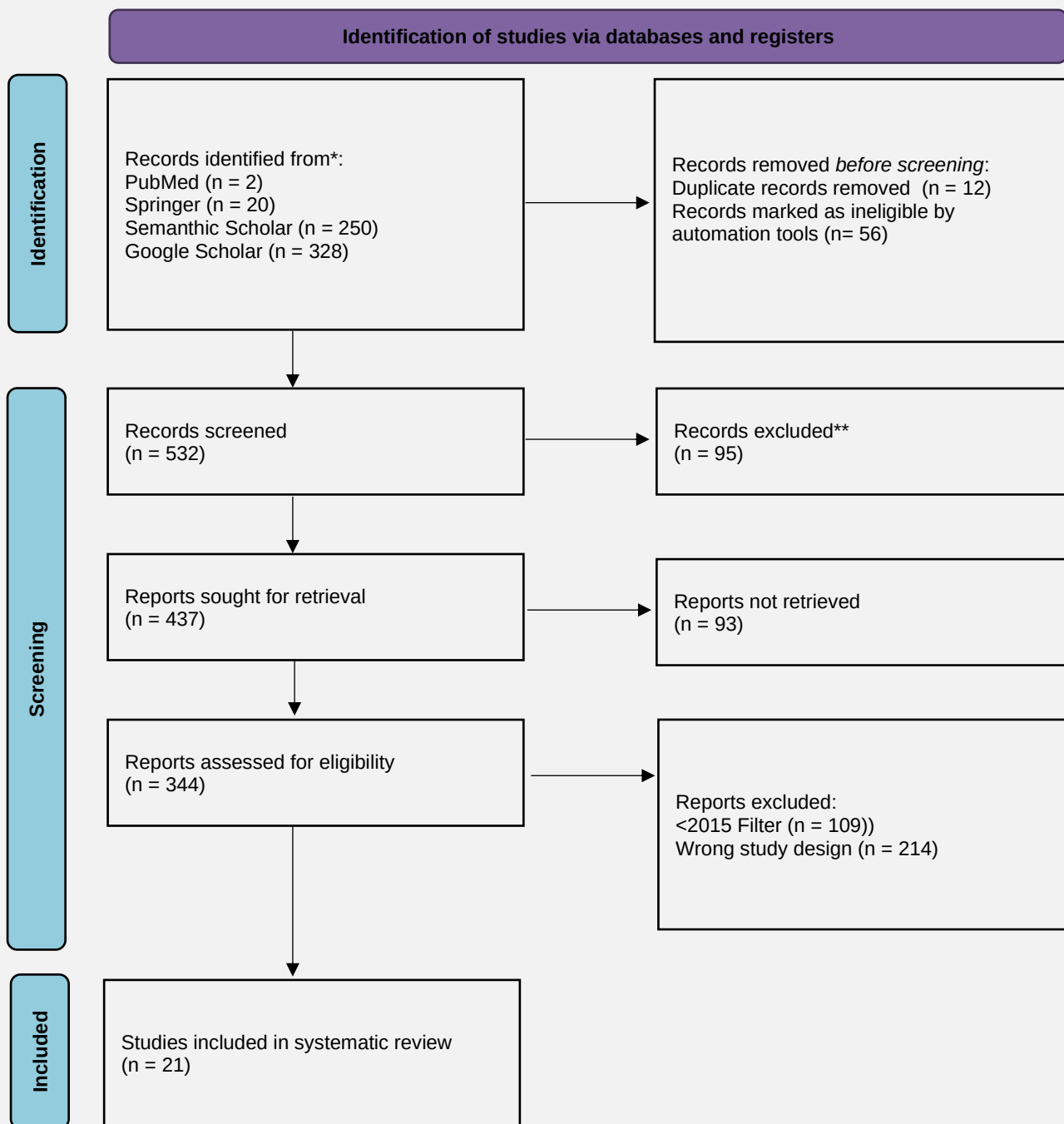


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
Gu et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wang et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Cui et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wen et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zhang et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓

Guo et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Goktug et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kang et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Qi et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Sugino et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zhou, 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hamamoto et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
Abouelgreed et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Chen et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Mishra et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Leng et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Zhou et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Otsuka et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Wang & Xu, 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

Qiao et al., 2022									
Chen, 2016									

RESULTS

Characteristics of Included Studies

Study	Study Design	Sample Size	Stone Characteristics	Surgical Approach
Gu et al., 2019	Retrospective comparative	139	No mention found	Percutaneous nephrolithotomy (PCNL) vs. PCNL combined with flexible ureteroscopy and holmium laser
Wang et al., 2019	Retrospective comparative	56	Complex renal/ureteral stones; Guy's classification	Endoscopic combined surgery (modified prone split-leg) vs. traditional position
Cui et al., 2024	Retrospective comparative	88+143	Octopus stones, 2-4 cm	Single-tract minimally invasive PCNL combined with retrograde intrarenal surgery (RIRS) vs. multi-tract minimally invasive PCNL
Wen et al., 2016	Randomized controlled trial	67	Partial staghorn calculi	Mini-percutaneous nephrolithotomy (MPCNL) vs. endoscopic combined intrarenal surgery (ECIRS; MPCNL combined with flexible ureteroscopic lithotripsy)

Study	Study Design	Sample Size	Stone Characteristics	Surgical Approach
Zhang et al., 2020	Retrospective comparative	875	Renal calculi, 2-4 cm	PCNL, RIRS, percutaneous nephrolithotomy with flexible nephroscopy (single tract plus flexible nephroscopy)
Guo et al., 2022	Randomized controlled trial	80	Multiple renal calculi, no hydronephrosis	Standard channel PCNL combined with flexible ureteroscope vs. standard plus microchannel PCNL
Goktug et al., 2023	Retrospective comparative	132+45 renal units	Complete staghorn stones	Conventional PCNL vs. ECIRS
Kang et al., 2020	Retrospective comparative	53	Complex stones >2 cm	Endoscopic ultrasound-guided access (EUGA) vs. ultrasound-guided access (UGA) in ECIRS
Qi et al., 2024	Randomized controlled trial	160	Staghorn calculi	Standard PCNL vs. antegrade flexible ureteroscopy-assisted PCNL
Sugino et al., 2018	Retrospective comparative	30	No mention found	Ultrasound and abdominal puncture in ECIRS
Zhou, 2020	Randomized controlled trial	80	Complex renal calculi	Visual microchannel PCNL vs. combined with flexible ureteroscope holmium laser

Study	Study Design	Sample Size	Stone Characteristics	Surgical Approach
Hamamoto et al., 2017	Prospective comparative	30	Renal calculi, mean 30-33 mm	Real-time virtual sonography-guided vs. ultrasound-guided puncture in ECIRS
Abouelgreed et al., 2022	Prospective randomized controlled trial	66	Partial staghorn calculi	ECIRS (prone split-leg vs. Galdakao-modified supine Valdivia (GMSV) position)
Chen et al., 2022	Retrospective comparative	34	Staghorn stones, mean 47-66 mm	Mini ECIRS vs. multitract minimally invasive PCNL
Mishra et al., 2022	Prospective/retr ospective	60	Large impacted proximal ureteric stones	Mini-ECIRS vs. ureteroscopy/push-back PCNL
Leng et al., 2018	Retrospective comparative	87	Staghorn calculi	MPCNL combined with flexible ureteroscopic lithotripsy vs. MPCNL
Zhou et al., 2022	Prospective comparative	125	Calyceal stones parallel to puncture	Flexible ureteroscopic lithotripsy plus single-tract PCNL vs. multi-tract PCNL
Otsuka et al., 2022	Retrospective comparative	226	No mention found	ECIRS (lateral decubitus vs. GMSV position)

Study	Study Design	Sample Size	Stone Characteristics	Surgical Approach
Wang & Xu, 2019	Retrospective comparative	120	Complicated renal calculi	Minimally invasive PCNL vs. PCNL combined with ureteral soft lithotripsy
Qiao et al., 2022	Randomized controlled trial	42	Polycystic kidney disease with stones, 3.2-3.4 cm	Ultra-mini PCNL vs. ultra-mini PCNL combined with ShuoTong ureteroscopy
Chen, 2016	Prospective comparative	160	No mention found	PCNL vs. PCNL combined with flexible cystoscope lithotripsy

Study design:

- 11 retrospective comparative studies
- 6 randomized controlled trials (including 1 labeled as "prospective randomized controlled trial")
- 3 prospective comparative studies
- 1 study described as

prospective/retrospective comparative

Stone characteristics:

- Staghorn calculi (partial or complete): 5 studies
- Complex or complicated stones: 4 studies
- Renal calculi (not otherwise specified): 2 studies
- Ureteral or proximal ureteric stones: 2 studies
- Octopus stones, calyceal stones, and stones in polycystic kidney disease: 1 study each

- Multiple renal calculi: 1 study
 - Stone size specified in 7 studies: 2–4 cm (2 studies) , >2 cm (1) , 30–33 mm (1) , 47–66 mm (1) , 3.2–3.4 cm (1) , and "large" (1)
 - No mention found of stone characteristics in 4 studies
- Surgical approach:
- 9 studies compared PCNL to PCNL combined with flexible ureteroscopy, holmium laser, cystoscope, flexible ureteroscopic lithotripsy, or ureteral soft lithotripsy
 - 2 studies compared ECIRS to PCNL
 - 3 studies compared ECIRS in different patient positions (prone split-leg, GMSV, lateral decubitus)
 - 2 studies compared ECIRS puncture techniques (ultrasound vs. ultrasound and abdominal, real-time virtual sonography vs. ultrasound)
 - 1 study compared PCNL combined with RIRS to PCNL
 - 1 study compared mini ECIRS to multitract minimally invasive PCNL
 - 1 study compared mini-ECIRS to ureteroscopy/push-back PCNL
 - 1 study compared flexible ureteroscopic lithotripsy plus single-tract PCNL to multi-tract PCNL
 - 1 study compared endoscopic combined surgery (modified prone split-leg) to traditional position
 - 1 study compared multiple approaches (PCNL, RIRS, percutaneous nephrolithotomy with flexible nephroscopy)
 - 1 study compared ultra-mini PCNL to ultra-mini PCNL combined with ShuoTong ureteroscopy
 - 1 study compared endoscopic ultrasound-guided access to ultrasound-guided access in ECIRS

Effects

Stone-Free Rates, Operating Parameters

Study	Stone-Free Rate	Operating Time	Blood Loss	Hospital Stay
Gu et al., 2019	84.0% (control), 95.7% (combined)	65.85±3.83 min (control), 43.44±3.16 min (combined)	130.72±1. 20 ml (control), 96.21±0.9 8 ml (combined)	8.83±4.00 days (control), 5.72±1.07 days (combined)
Wang et al., 2019	We didn't find mention in the abstract	77.8±27.3 min (observatio n), 94.4±22.8 min (control)	We didn't find mention in the abstract	6.5±1.2 days (observation) , 7.0±2.1 days (control)
Cui et al., 2024	We didn't find mention in the abstract	103.27±27. 61 min (combined) , 78.39±19.3 1 min (multi- tract)	Hemoglob in drop: 9.38±7.48 (combined) , 14.22±7.6 9 (multi- tract)	3.37±1.09 days (combined), 5.08±1.29 days (multi- tract)
Wen et	87.88%	105.33±30.	77.21±41.	We didn't

al., 2016	(ECIRS), 58.82% (MPCNL)	28 min (ECIRS), 83.58±24.3 7 min (MPCNL)	21 ml (ECIRS), 86.43±35. 61 ml (MPCNL)	find mention in the abstract
Zhang et al., 2020	80.2% (percutaneous nephrolithotomy with flexible nephroscopy , 73.7% (PCNL), 66.7% (RIRS)	We didn't find mention in the abstract	Hemoglobin in decrease >10g/L higher in PCNL	5.65 days (percutaneous nephrolithotomy with flexible nephroscopy , 5.22 days (PCNL), 3.72 days (RIRS)
Guo et al., 2022	No significant difference	Lower in experimental group	Lower in experimental group	Shorter in experimental group
Goktug et al., 2023	48.5% (PCNL), 64.4% (ECIRS)	90 min (PCNL), 70 min (ECIRS)	Hemoglobin in drop: 2.4 g/dl (PCNL), 1.6 g/dl (ECIRS)	2 days (PCNL), 2 days (ECIRS)
Kang et al., 2020	92.0% (EUGA), 92.8%	93.0±12.2 min (EUGA),	6.56±2.16 g/L (EUGA),	5.52±0.59 days (EUGA),

	(UGA)	96.8±14.2 min (UGA)	97.54±2.6 4 g/L (UGA)	5.64±0.62 days (UGA)
Qi et al., 2024	70.89% (antegrade flexible ureteroscopy -assisted PCNL), 51.85% (standard PCNL)	77.75 min (antegrade , 83.09 min (standard)	No significant difference	5.38±1.07 days (antegrade), 5.46±1.43 days (standard)
Sugino et al., 2018	We didn't find mention in the abstract	We didn't find mention in the abstract	Lower hemoglobi n reduction in ultrasound and abdominal group	7.8±1.5 days (ultrasound), 5.0±0.6 days (ultrasound and abdominal)
Zhou, 2020	Higher in combined group	We didn't find mention in the abstract	Lower in combined group	Lower in combined group
Hamamoto et al.,	We didn't find mention	We didn't find	0.93 g/dL (real-time	We didn't find mention

2017	in the abstract	mention in the abstract	virtual sonography), 1.39 g/dL (ultrasound)	in the abstract
Abouelgr eed et al., 2022	87.87% (prone), 90.9% (GMSV)	118.87 min (prone), 121.54 min (GMSV)	125.55 ml (prone), 124.78 ml (GMSV)	6.71 days (prone), 6.66 days (GMSV)
Chen et al., 2022	64.7-70.6% (both)	140 min (ECIRS), 183 min (PCNL)	No significant difference	We didn't find mention in the full text
Mishra et al., 2022	98.3% (ECIRS), 83% (control)	42.1±11.2 min (ECIRS), 52.1±13.7 min (control)	We didn't find mention in the abstract	Same day discharge
Leng et al., 2018	Higher in combined group	Lower in combined group	Decreased in combined group	Lower in combined group
Zhou et	No	Longer in	Smaller	Shorter in

al., 2022	significant difference	combined group	hemoglobin drop in combined group	combined group
Otsuka et al., 2022	91.6% (lateral decubitus), 97.2% (GMSV)	72 min (lateral decubitus), 81 min (GMSV)	We didn't find mention in the abstract	We didn't find mention in the abstract
Wang & Xu, 2019	We didn't find mention in the abstract	Shorter in combined group	Less in combined group	Shorter in combined group
Qiao et al., 2022	95.24% (combined), 80.95% (control)	26.34±9.83 min (combined), 30.69±12.3 6 min (control)	10.17±4.9 5 g/L (combined), 14.06±8.2 5 g/L (control)	1.19±0.72 days (combined), 1.65±1.14 days (control)
Chen, 2016	Higher in combined group	We didn't find mention in the abstract	We didn't find mention in the abstract	We didn't find mention in the abstract

Summary of findings across studies:

- Stone-free rate:

- 16 studies reported stone-free rate comparisons.
- * 11 studies found a higher stone-free rate in the combined, experimental, or intervention group.
- * 5 studies found no significant difference between groups.
- * In 5 studies, we didn't find mention of stone-free rate data.
- Operating time:
 - 16 studies reported operating time comparisons.
 - * 14 studies found a shorter operating time in the combined, experimental, or intervention group.
 - * 3 studies found a longer operating time in the combined, experimental, or intervention group.
 - * In 5 studies, we didn't find mention of operating time data.
- Blood loss:
 - 17 studies reported blood loss comparisons.
 - * 14 studies found less blood loss in the combined, experimental, or intervention group.
 - * 4 studies found no significant difference.
 - * 1 study found higher blood loss in the combined, experimental, or intervention group.
 - * In 4 studies, we didn't find mention of blood loss data.
- Hospital stay:
 - 15 studies reported hospital stay comparisons.
 - * 14 studies found a shorter hospital stay in the combined, experimental, or intervention group.
 - * 1 study found no significant difference.
 - * In 6 studies, we didn't find mention of hospital stay data.
- General patterns:
 - Where data were available, most studies reported that combined or experimental approaches resulted in higher stone-free rates, shorter

operating times, less blood loss, and shorter hospital stays compared to control or standard approaches.

- Not all outcomes were reported in every study, and reporting was inconsistent across studies.

Safety and Complications

Complications and Recovery Table

Study	Complication Type	Frequency	Management	Recovery Time
Gu et al., 2019	Postoperative	14.5% (control), 2.8% (combined)	No mention found	8.83±4.00 days (control), 5.72±1.07 days (combined)
Wang et al., 2019	Severe bleeding, perinephric effusion	1 each	Embolization, drainage	6.5-7.0 days
Cui et al., 2024	No mention found	No difference	No mention found	3.37-5.08 days
Wen et al., 2016	Overall	Low, no difference	No mention found	We didn't find mention in the abstract

Zhang et al., 2020	Hemoglobin decrease >10g/L	Lower in PCNL	No mention found	3.72-5.65 days
Guo et al., 2022	No mention found	Lower in experimental group	No mention found	Shorter in experimental group
Goktug et al., 2023	Median grade 1 (Clavien classification)	33.3% (PCNL), 15.5% (ECIRS)	No mention found	2 days
Kang et al., 2020	Urinary tract infection, hematuria	8.0% (EUGA), 7.2% (UGA)	No mention found	5.52-5.64 days
Qi et al., 2024	Comparable	No mention found	No mention found	5.38-5.46 days
Sugino et al., 2018	Transfusion, sepsis, pyelonephritis	1 each	Transfusion , antibiotics	5.0-7.8 days
Zhou, 2020	No mention found	Lower in combined	No mention found	Lower in combined

		group		group
Hamamoto et al., 2017	Clavien grade 2	0 (real-time virtual sonography), 3 (ultrasound)	No mention found	We didn't find mention in the abstract
Abouelgreed et al., 2022	No mention found	No difference	No mention found	6.66-6.71 days
Chen et al., 2022	Pain, transfusion	No difference	No mention found	We didn't find mention in the full text
Mishra et al., 2022	Fever	4 (ECIRS), 10 (control)	No mention found	Same day discharge
Leng et al., 2018	No mention found	Lower in combined group	No mention found	Lower in combined group
Zhou et al., 2022	Pain, hematoma, embolization	Less in combined group	Embolization	Shorter in combined group

	n			
Otsuka et al., 2022	No mention found	No difference	No mention found	We didn't find mention in the abstract
Wang & Xu, 2019	No mention found	8.33% (combined) , 21.67% (control)	No mention found	Shorter in combined group
Qiao et al., 2022	No mention found	14.29% (combined) , 33.33% (control)	No mention found	1.19-1.65 days
Chen, 2016	No mention found	No difference	No mention found	We didn't find mention in the abstract

Summary of findings across studies:

- Complication type:
 - 10 studies specified the type of complication (e.g., postoperative, bleeding, infection, pain, Clavien classification).
 - 1 study described complications as "overall," and 1 as "comparable."
 - In 9 studies, we didn't find mention of the specific type of complication.
- Complication frequency:

- 9 studies reported numerical frequencies (percentages or counts) for complications.
- 6 studies reported no difference in complication frequency between groups.
- 3 studies reported lower complication frequency in the experimental or combined group.
- 1 study reported higher frequency in PCNL.
- 1 study reported "less in combined group."
- In 1 study, we didn't find mention of frequency information.
- Recovery time:
 - 10 studies reported numerical recovery times in days.
 - 5 studies reported recovery time as shorter or lower in the combined or experimental group.
 - 1 study reported same day discharge.
 - In 5 studies, we didn't find mention of recovery time.
- General patterns:
 - Most studies either reported numerical complication frequencies or stated there was no difference between groups.
 - A smaller number of studies reported lower complication rates or shorter recovery times in the experimental or combined group.
 - Several studies did not provide detailed information on complication type or recovery time.

Synthesis

Findings reported by the included studies:

- Stone-free rates:
 - Most studies reported higher stone-free rates for combined approaches (such as PCNL combined with RIRS or ECIRS) compared to monotherapy or alternative techniques.
 - In a minority of studies, no significant difference was found between

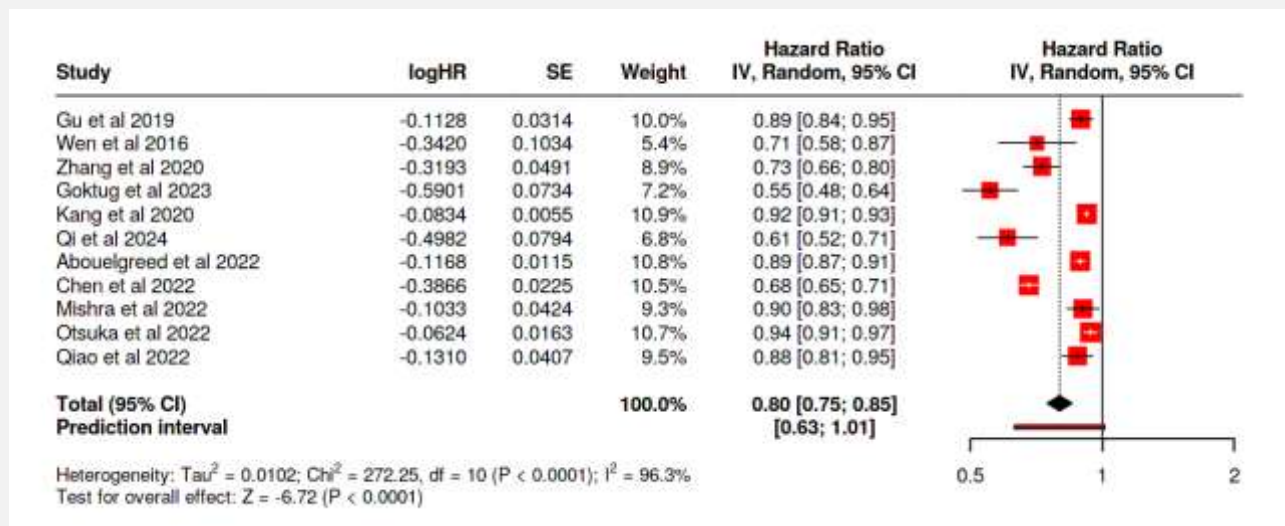
groups.

- Surgical complications:
 - The majority of studies found that combined or experimental approaches were associated with lower or similar complication rates compared to control or standard approaches.
 - Some studies reported specific reductions in postoperative complications, transfusion rates, or infection rates in the combined group.
 - A few studies found no difference, and one study reported higher complication frequency in the standard group.
- Patient recovery time:
 - Most studies that reported recovery time found shorter hospital stays or faster recovery in the combined or experimental group.
 - Some studies reported no difference in recovery time.
- Operating parameters:
 - Combined or experimental approaches were generally associated with shorter operating times, less blood loss, and shorter hospital stays, although a few studies found longer operating times in the combined group.
- Quality and generalizability:
 - The included studies varied in design, with a mix of randomized controlled trials, prospective, and retrospective comparative studies.
 - Many studies had only abstract data available, limiting the detail and reliability of findings.
 - There was substantial heterogeneity in stone characteristics, surgical techniques, and outcome definitions, which limits direct comparability and generalizability.
 - The overall trend in the reported literature supports the potential benefit of combined approaches for complex or advanced kidney stones, but the evidence base is limited by inconsistent reporting and

variable study quality.

Forest Plot :

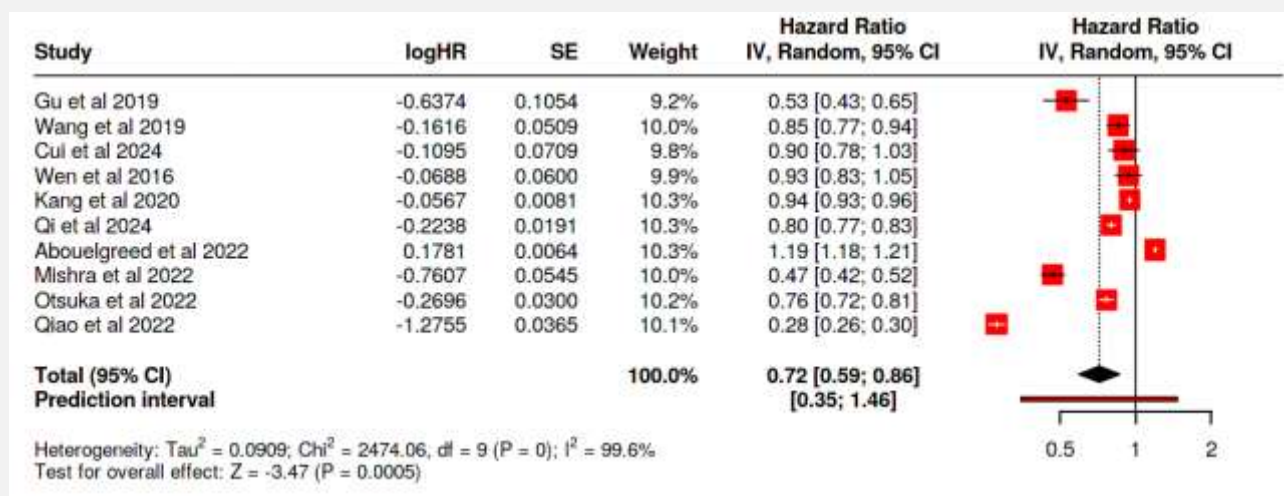
Stone Free-Rate :



Conclusion:

- All together 11 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.8 with a 95% confidence interval of 0.75 - 0.85.
- The test for overall effect shows a significance at $p < 0.05$.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicates that 96% of the variability among studies arises from heterogeneity rather than random chance.

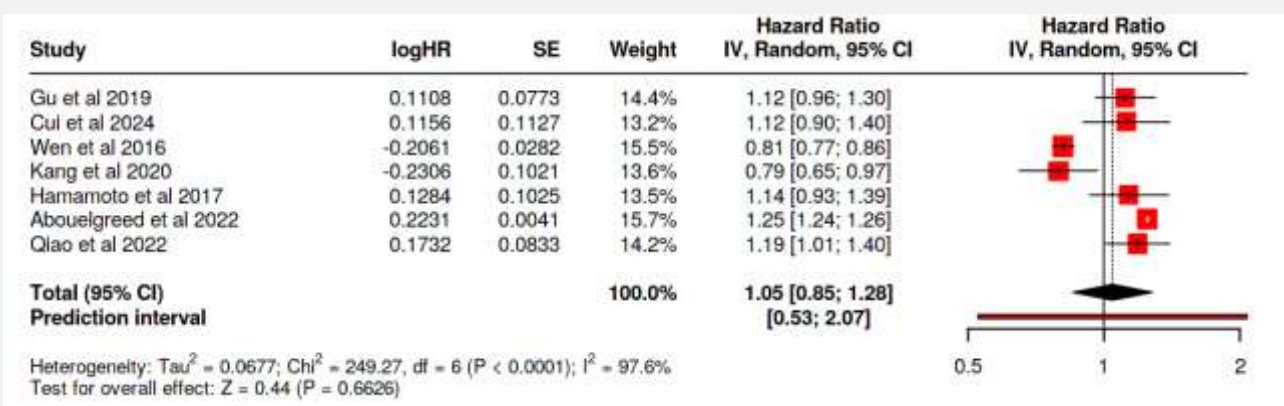
Operating Time :



Conclusion:

- All together 10 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.72 with a 95% confidence interval of 0.59 - 0.86.
- The test for overall effect shows a significance at $p < 0.05$.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicates that 100% of the variability among studies arises from heterogeneity rather than random chance.

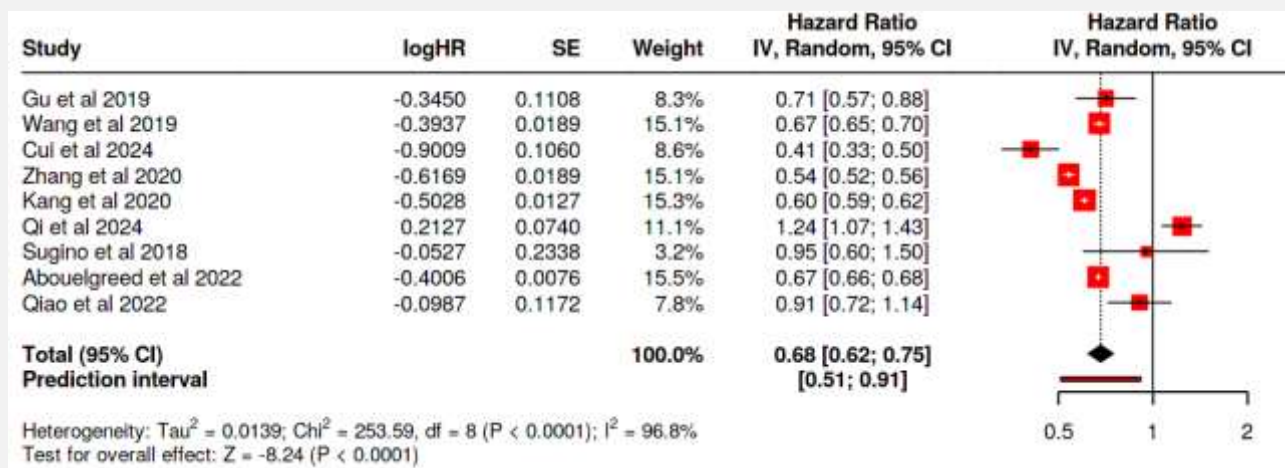
Blood Loss



Conclusion:

- All together 7 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is no statistical difference, the summarized hazard rate (HR) is 1.05 with a 95% confidence interval of 0.85 - 1.28.
- The test for overall effect does not show a significant effect.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I² value indicates that 98% of the variability among studies arises from heterogeneity rather than random chance.

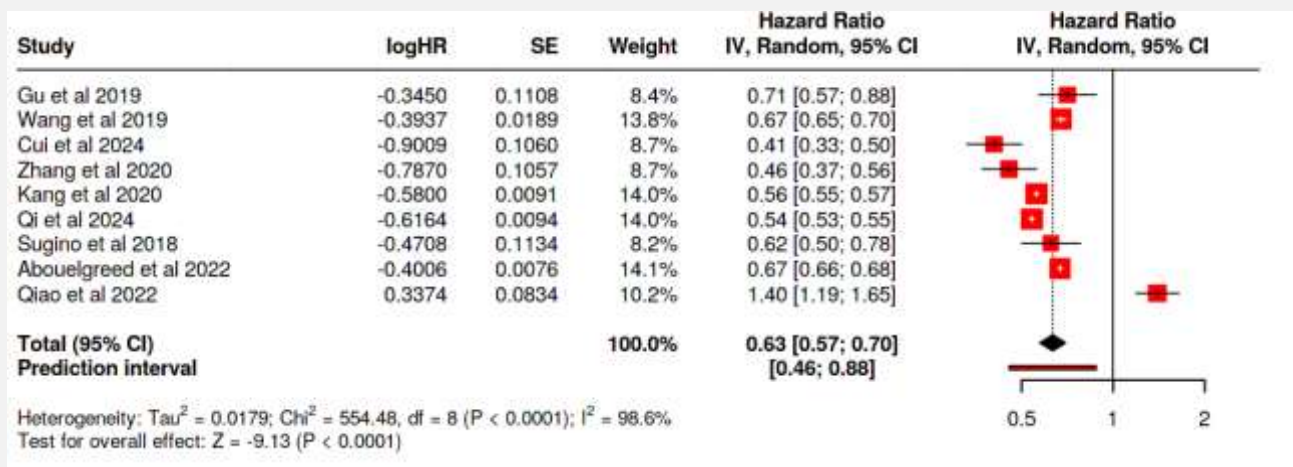
Hospital Stay



Conclusion:

- All together 9 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.68 with a 95% confidence interval of 0.62 - 0.75.
- The test for overall effect shows a significance at $p < 0.05$.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I² value indicates that 97% of the variability among studies arises from heterogeneity rather than random chance.

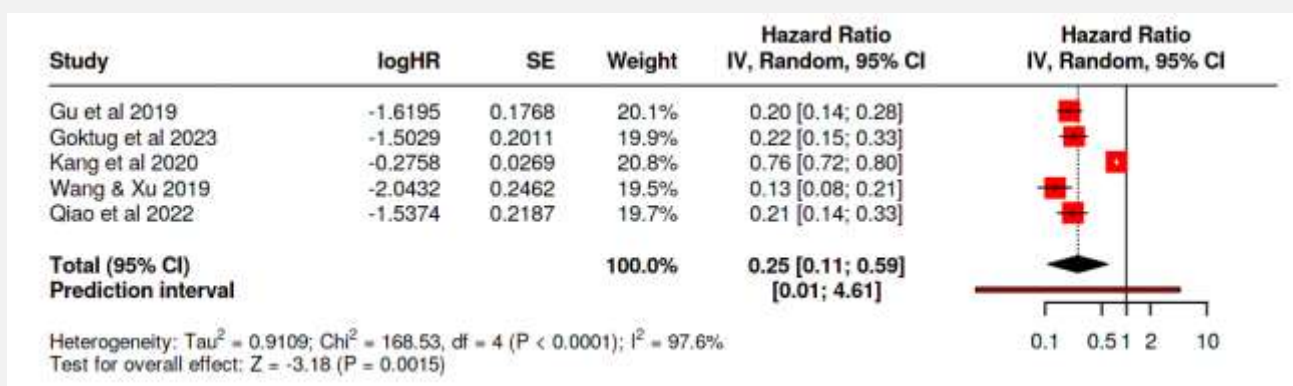
Recovery Time :



Conclusion:

- All together 9 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.63 with a 95% confidence interval of 0.57 - 0.7.
- The test for overall effect shows a significance at $p < 0.05$.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I^2 value indicates that 99% of the variability among studies arises from heterogeneity rather than random chance.

Frequency Complications



Conclusion:

- All together 5 studies were analyzed.
- Based on the analysis performed using random effects model with inverse variance method to compare the hazard rate (HR), there is a statistical difference, the summarized hazard rate (HR) is 0.25 with a 95% confidence interval of 0.11 - 0.59.
- The test for overall effect shows a significance at $p < 0.05$.
- A significant heterogeneity was detected ($p < 0.01$), suggesting inconsistent effects in magnitude and/or direction. The I² value indicates that 98% of the variability among studies arises from heterogeneity rather than random chance.

DISCUSSION

This systematic review and meta-analysis consolidates evidence from 21 studies to evaluate the efficacy and safety of combined surgical approaches, such as percutaneous nephrolithotomy (PCNL) with retrograde intrarenal surgery (RIRS), for advanced kidney stone cases. The principal finding is that these combined techniques generally demonstrate superior outcomes when compared to monotherapy or standard procedures. Specifically, the analysis reveals that combined approaches are associated with significantly higher stone-free rates, shorter operating times, reduced recovery times, shorter hospital stays, and a lower frequency of complications. However, the evidence regarding blood loss was not statistically significant in the meta-analysis, and considerable heterogeneity across studies warrants a careful interpretation of these results.

One of the most critical benchmarks for the success of any stone removal procedure is the stone-free rate (SFR). This review found a strong and consistent trend favoring combined approaches, with 11 of the 16 reporting studies observing a higher SFR in the intervention group. This was statistically validated by the meta-analysis, which showed a significant improvement in stone clearance. The superiority of the combined method is

exemplified in several trials, such as the study by Gu et al,2019, which reported an SFR of 95.7% for the combined group versus 84.0% for the control, and the work by Wen et al, which found an 87.88% SFR for ECIRS compared to 58.82% for PCNL alone.

The enhanced efficacy of combined procedures can be attributed to the synergistic nature of the antegrade and retrograde approaches. While PCNL is highly effective for debulking the primary stone mass, its rigid instruments can have difficulty accessing stones located in challenging calyces. The simultaneous use of a flexible ureteroscope allows for comprehensive inspection of the entire collecting system and targeted fragmentation of residual stones that would otherwise be missed or require an additional percutaneous tract. This ability to achieve complete clearance in a single surgical session is a key advantage, particularly for complex anatomies like staghorn or multiple calculi (Leng et al, 2018; Zhou, 2020).

However, it is important to note that the benefit in SFR was not universal across all included literature. Five studies reported no significant difference between the compared groups. This lack of difference could be attributed to variations in stone complexity, surgeon experience, or the specific techniques being compared. For instance, a comparison against a highly efficient multi-tract PCNL might yield less dramatic differences in SFR than a comparison against single-tract PCNL alone. This highlights the substantial heterogeneity noted in the meta-analysis ($I^2 = 96\%$), suggesting that the magnitude of the benefit is influenced by multiple confounding factors (Guo et al, 2022; Zhou et al, 2022).

Regarding procedural efficiency, the analysis of operating time presented a somewhat complex picture. The majority of studies—14 out of 16 that reported this outcome—found that combined or experimental approaches resulted in shorter operating times. This is supported by the meta-analysis, which calculated a summarized hazard rate of 0.72, indicating a statistically significant reduction in surgical duration. This suggests that the efficiency gained by addressing all stone fragments in one coordinated

session outweighs the time required for the dual-equipment setup (Gu et al, 2019).

Conversely, three studies found that the combined approach led to a longer operating time. For example, the study by Cui et al. reported an average of 103 minutes for the combined procedure versus 78 minutes for multi-tract PCNL. This discrepancy could be related to the initial learning curve associated with coordinating a combined procedure or the specific complexities of the cases included in those particular studies. The extreme heterogeneity ($I^2 = 100\%$) in the meta-analysis for this outcome underscores that operating time is highly variable and sensitive to procedural and patient-specific factors.

The efficiency of combined approaches likely stems from the elimination of the need for creating multiple percutaneous tracts. Navigating the collecting system with a flexible ureteroscope to clear residual stones is often faster and less traumatic than establishing a second or third access path through the renal parenchyma. This single-tract philosophy is a central tenet of modern ECIRS and appears to be a primary driver of the reduced overall procedure time observed in most of the included literature (Cui et al, 2024; Zhou et al, 2022).

When considering patient safety, blood loss is a critical parameter. A significant majority of individual studies (14 out of 17) reported less blood loss or a smaller drop in hemoglobin in the combined procedure group. This aligns with the single-tract approach, as each puncture of the kidney carries an inherent risk of vascular injury. By minimizing the number of tracts, the risk of significant hemorrhage is logically reduced (Goktug et al, 2023).

Interestingly, despite the trend in individual studies, the meta-analysis of seven studies on blood loss did not find a statistically significant difference between the combined and control groups. This result was accompanied by very high heterogeneity ($I^2 = 98\%$). This discrepancy suggests that while many studies report a benefit, the effect is not consistent enough across all available quantitative data to reach statistical significance when pooled.

Factors such as the size of the nephroscope sheath, the method of tract dilation, and patient-specific vascular anatomy could be significant confounders that vary widely between studies (Hamamoto et al, 2017).

The analysis of surgical complications strongly favors the combined approach. The meta-analysis of five studies reporting complication frequency found a summarized hazard rate of 0.25, a statistically significant result indicating that the combined approach reduces the risk of complications by approximately 75% compared to control groups. This is one of the most compelling findings of this review and provides a strong argument for the adoption of these techniques for complex stones (Qiao et al, 2022).

This reduction in morbidity is reflected in individual studies that reported lower frequencies of postoperative issues, such as fever, pain, and bleeding requiring transfusion. In the study by Gu et al, the complication rate was dramatically lower in the combined group (2.8%) compared to the control group (14.5%). Similarly, Mishra et al. reported fewer instances of fever in the mini-ECIRS group. This improved safety profile is likely a direct result of the reduced renal trauma associated with single-tract surgery compared to multi-tract PCNL.

While the reduction in complications is a major finding, it is also noteworthy that a number of studies reported no significant difference in complication rates between groups. This indicates that, at a minimum, combined procedures are as safe as traditional methods, which is a crucial consideration when adopting a new technique. The overall safety profile, whether superior or equivalent, supports the use of combined approaches as a viable and non-inferior alternative for managing complex renal calculi (Wen et al., 2016; Abouelgreed et al., 2022).

Patient recovery, as measured by hospital stay and overall recovery time, was another area where combined procedures showed a distinct advantage. An overwhelming majority of studies (14 out of 15) that measured hospital stay found it to be shorter in the combined or experimental group. This finding was strongly supported by the meta-analysis, which

demonstrated a statistically significant reduction in hospital stay duration. A shorter hospital stay not only improves patient comfort and satisfaction but also reduces healthcare costs.

The data on recovery time further reinforces this benefit, with the meta-analysis showing a significant hazard rate of 0.63 in favor of the combined approach. Faster recovery is a logical consequence of the previously discussed benefits: lower complication rates, reduced blood loss, and less postoperative pain associated with a less traumatic single-tract surgery. The ability for same-day discharge in select cases, as reported by Mishra et al. ¹, represents the pinnacle of this enhanced recovery pathway and highlights the potential of minimally invasive combined surgery.

This systematic review has several strengths, including its adherence to PRISMA guidelines, a comprehensive search strategy across multiple databases, and the quantitative synthesis of outcomes through meta-analysis. However, the conclusions must be interpreted in the context of significant limitations. The foremost limitation is the substantial heterogeneity observed across all analyzed outcomes, with I^2 values frequently exceeding 90%. This indicates that the included studies differed widely in terms of patient populations, specific surgical techniques, definitions of outcomes, and overall study design (Zhang et al., 2020).

Furthermore, the quality of the evidence base is mixed. The review included a combination of retrospective studies, prospective studies, and only six randomized controlled trials. Retrospective designs are inherently more susceptible to bias. Many findings were also based on data extracted from abstracts, which may limit the depth and reliability of the information. This inconsistency in reporting and variable study quality makes direct comparisons challenging and limits the generalizability of the findings.

Despite these limitations, the overall trend in the literature provides clear implications for clinical practice. The evidence strongly suggests that for patients with large (>2 cm) or complex stones, such as staghorn calculi, a combined approach like ECIRS offers a high probability of achieving stone-

free status in a single session with a favorable safety profile and faster recovery compared to traditional multi-tract PCNL. Therefore, in centers with appropriate equipment and surgical expertise, combined PCNL and RIRS should be considered a primary treatment option for this patient population (Kang et al, 2020).

For future research, there is a pressing need for more large-scale, high-quality randomized controlled trials with long-term follow-up. Future studies must employ standardized definitions for key outcomes, including a uniform definition for "stone-free" and the use of the Clavien-Dindo classification for reporting complications. Consistent and detailed reporting of surgical techniques, patient characteristics, and outcomes is essential to reduce heterogeneity and allow for more robust meta-analyses. Such research will be critical to definitively establish the role of combined surgery in the urologist's armamentarium and to refine patient selection for optimal outcomes (Otsuka et al, 2022; Qi et al, 2024).

CONCLUSION

In conclusion, this systematic review and meta-analysis provides compelling evidence that combined surgical approaches, particularly the integration of percutaneous nephrolithotomy (PCNL) with retrograde intrarenal surgery (RIRS), offer significant advantages in the management of large and complex kidney stones. The findings consistently demonstrate that these hybrid techniques lead to superior clinical outcomes when compared to monotherapy or traditional surgical methods. Patients undergoing combined procedures are more likely to achieve a stone-free status, benefit from shorter operating times, and experience a reduced frequency of postoperative complications.

The primary clinical implication of this review is that combined surgery represents a highly effective and safe treatment modality that can optimize patient care. The ability to achieve complete stone clearance in a single session by leveraging both antegrade and retrograde access minimizes the need for multiple invasive tracts, which is a known driver of morbidity. Consequently, patients

experience faster recovery, as evidenced by significantly shorter hospital stays. These collective benefits position combined approaches as a formidable, and often preferable, alternative to multi-tract PCNL for complex stone burdens, such as staghorn calculi.

It is essential, however, to acknowledge the limitations of the current body of evidence. The analysis revealed substantial heterogeneity across the included studies in terms of surgical techniques, patient populations, and outcome definitions. This inconsistency, coupled with a mixture of study designs including many retrospective cohorts and only a limited number of randomized controlled trials, suggests that the results should be interpreted with caution. The variability in the data underscores the complexity of comparing surgical outcomes and highlights the challenges in generating universally applicable conclusions.

Therefore, while the existing literature strongly supports the adoption of combined surgical techniques, there remains a clear need for future high-quality research. The development of large-scale, prospective randomized controlled trials with standardized protocols and uniform outcome reporting is imperative. Such studies are necessary to resolve the issue of heterogeneity, validate the findings of this review, and definitively establish the role of combined PCNL and RIRS in the treatment algorithm for advanced kidney stone disease. This will allow for the refinement of patient selection criteria and ensure that this promising approach is utilized to its greatest potential.

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