



Predictors of Blood Transfusion Following Percutaneous Nephrolithotomy: A Systematic Review and Meta-analysis

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Abstract

Percutaneous nephrolithotomy (PCNL) is the standard treatment for large renal calculi, yet clinically significant hemorrhage necessitating transfusion remains a critical perioperative challenge. This PRISMA-guided systematic review and meta-analysis aimed to consolidate the evidence on predictors of blood transfusion or severe bleeding after PCNL. Pooled analyses identified diabetes mellitus, hypertension, urinary tract infection, renal anomalies, multiple or staghorn stones, solitary kidney phenotype, multiple access tracts, larger stone size, and longer operative time as significant risk factors. Notably, hydronephrosis demonstrated an inverse association. In conclusion, post-PCNL bleeding requiring transfusion is best conceptualized as a three-domain risk paradigm: patient susceptibility, stone complexity, and procedural intensity.

Keywords

blood transfusion;

meta-analysis;

percutaneous

nephrolithotomy;

risk factors;

systematic review

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Introduction

Percutaneous nephrolithotomy (PCNL) is recommended for large, multiple, and anatomically complex renal stones, particularly when stone burden exceeds the range in which shockwave lithotripsy or ureteroscopic approaches are expected to provide reliable clearance (Zhao et al., 2022). Despite technical advances in access planning, tract dilation, optics, energy devices, and image guidance, bleeding remains one of the most important PCNL-related complications because it

can lead to transfusion, prolonged admission, urgent imaging, angioembolization, intensive monitoring, or rarely nephrectomy (Wu et al., 2026).

Blood transfusion after PCNL is a clinically meaningful endpoint because it reflects bleeding severe enough to alter perioperative decision-making, resource use, and postoperative monitoring (Ketsuwan et al., 2020). The literature uses overlapping endpoints, including transfusion, severe postoperative hemorrhage, and embolization-requiring vascular injury. However, these outcomes are not identical; they occupy the same clinical spectrum and frequently share upstream determinants (Syarif et al., 2024).

Most recurrent predictors can be organized into three clinically practical domains: patient vulnerability, stone complexity, and procedural intensity. Infection, diabetes, hypertension, and renal anomalies signal baseline susceptibility; staghorn morphology, multiple stones, and larger stone burden signal anatomical difficulty; and multiple tracts or prolonged operative time reflect intraoperative escalation (Wan et al., 2026). Contemporary EAU and AUA guidance supports PCNL as a key treatment for large renal stones while emphasizing risk-aware treatment selection, counseling, and complication prevention (Monroy et al., 2025).

Novelty, added value, and systematic comparison with prior meta-analyses. Unlike previous systematic reviews, which have largely pooled heterogeneous bleeding endpoints (e.g., combining transfusion, embolization, and hemoglobin-drop criteria) without standardized endpoint hierarchy, the present review exclusively targets blood transfusion as a uniform, clinically actionable endpoint. For instance, Hasan et al. (2024) conducted a broad meta-analysis. However, they did not explicitly prioritize adjusted estimates over crude estimates when both were available, nor did they systematically perform predictor-level sensitivity analyses to account for heterogeneity. In contrast, our review applies a prespecified extraction matrix that explicitly separates crude and adjusted ORs, prioritizes adjusted estimates only when they are consistently reported (≥ 3 studies) and use similar covariate sets, and provides study-level forest plots rather than relying solely on aggregate summary estimates. Furthermore, whereas Wan et al. (2026) and Zou et al. (2026) offered summary risk scores without formal heterogeneity interpretation at the individual predictor level, our analysis systematically evaluates Cochran's Q , I^2 , and τ^2 for every pooled estimate, with explicit clinical consistency criteria governing the choice between fixed- and random-effects models. Finally, unlike prior works that stopped at statistical enumeration, we explicitly translate the pooled findings into a three-domain perioperative framework (patient vulnerability, stone complexity, procedural intensity) aligned with contemporary EAU/AUA guidance, thereby offering both quantitative rigor and bedside applicability—a combined approach that is absent from the existing meta-analytic literature.

Novelty and added value. Compared with Hasan et al. (2024), which presented a broad meta-analysis of severe bleeding risk factors after PCNL, this manuscript is a clinically oriented, transfusion-relevant synthesis. Its added value lies in (1) foregrounding blood transfusion and transfusion-requiring or severe bleeding as the clinically actionable endpoint, (2) presenting predictor-specific study-level forest plots rather than only summary-level predictor plots, (3) explicitly defining how crude and adjusted effects are selected and pooled, (4) incorporating heterogeneity and sensitivity interpretation at the predictor level, and (5) translating the statistical findings into a three-domain perioperative risk framework aligned with contemporary EAU/AUA guidance (Zou et al., 2026).

This systematic review and meta-analysis aimed to identify and quantify predictors of transfusion-requiring or severe bleeding after PCNL and to organize them into practical patient-, stone-, and procedure-related domains for perioperative risk stratification.

Materials and Methods

This de novo systematic review and meta-analysis was planned, conducted, and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Haddaway et al., 2022). The PRISMA 2020 checklist is provided as Appendix 1. The protocol was defined before screening and data extraction. PROSPERO registration was not obtained; this absence of registration is reported transparently and considered in the limitations. All quantitative results were recalculated from study-level data extracted directly from eligible primary studies. Previously published reviews and meta-analyses were used only for background reading and citation checking, not as sources of pooled ORs, MDs, study weights, estimates of heterogeneity, or forest plot outputs.

Search Strategy

A systematic search was conducted in PubMed/MEDLINE, Embase, Web of Science, and the Cochrane Library from database inception to 30 June 2026. Reference lists of eligible primary studies, relevant guidelines, and recent reviews were screened only to identify additional primary reports. Search concepts combined terms for the procedure, bleeding outcome, and prognostic factor. The core PubMed strategy was: ("percutaneous nephrolithotomy" OR PCNL OR PNL) AND ("blood transfusion" OR bleeding OR hemorrhage OR "vascular complication" OR angioembolization OR embolization) AND ("risk factor" OR "risk factors" OR predictor OR predictors OR determinant OR determinants OR prognostic). Equivalent terms and controlled vocabulary were adapted for each database. No restriction was applied at the search stage for publication year. Studies were screened for human PCNL populations and extractable study-level bleeding-predictor data.

Eligibility Criteria

Studies were eligible when they met the following criteria: (1) human participants undergoing PCNL for renal stones; (2) evaluation of at least one patient-related, stone-related, or procedure-related predictor; (3) reporting of blood transfusion, severe bleeding, post-PCNL hemorrhage, angioembolization, hemoglobin drop, or a clearly related bleeding endpoint; and (4) cohort, case-control, registry, or comparative observational design with extractable data or effect estimates. Studies were excluded if they were reviews, editorials, isolated case reports, non-PCNL surgical series without separable PCNL data, pediatric-only series not suitable for synthesis with adult data, reports without extractable predictor data, or papers focused solely on the technical management of hemorrhage without risk-factor information.

Study Selection and Data Extraction

Titles and abstracts were screened independently by two reviewers; full-text articles were assessed for eligibility, and data were extracted using a predefined extraction sheet by the same two reviewers working independently. Any uncertainties regarding study eligibility or data extraction were resolved through discussion or, when consensus was not reached, through arbitration by the senior reviewer. Extracted variables included author, year, country, study design, sample size, PCNL technique, bleeding-outcome definition, transfusion threshold when reported, predictor definition, crude event counts, adjusted effect estimates, confidence intervals, and variables needed to calculate continuous mean differences. For binary predictors, the extraction matrix retained exposed bleeding events, exposed non-events, unexposed bleeding events, and unexposed non-events whenever reported. For continuous predictors, the matrix retained mean, standard deviation, and sample size for bleeding and non-bleeding groups. Adjusted estimates were prioritized only when they were reported for the same predictor in a clinically comparable way across at least two studies. When adjusted estimates were unavailable, inconsistently adjusted, or

not reconstructable, crude study-level 2 x 2 data were used, and this was explicitly reflected in the forest plot and sensitivity interpretation. Crude and adjusted estimates were not combined within the same main analysis unless no methodologically coherent alternative was possible; any such decision was treated as a sensitivity issue rather than a definitive adjusted-effect synthesis.

Risk of Bias Assessment

Risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) for all included observational studies. The NOS evaluates methodological quality across three domains: selection, comparability, and outcome (for cohort studies) or exposure (for case-control studies). Studies were categorized by overall NOS score as good, fair, or poor quality, based on the Agency for Healthcare Research and Quality (AHRQ) adaptation of the Newcastle-Ottawa Scale. Overall methodological quality was assessed using the NOS across these domains (Poudyal, 2022).

Study Selection

The study selection process followed the PRISMA 2020 flow diagram. Records identified through database searching and citation review were screened for relevance, followed by full-text assessment of papers considered potentially informative for predictor analysis. The PRISMA diagram reports the number of records identified, records removed before screening, records screened, reports retrieved, full-text reports assessed for eligibility, reports excluded with reasons, and studies included in qualitative and quantitative synthesis where the broader evidence base contained overlapping populations or duplicated predictor estimates; the most complete dataset was retained to minimize double counting.

Ethical Consideration

Formal ethical approval was not required because this systematic review and meta-analysis used previously published aggregate data and did not involve direct patient recruitment, intervention, or access to identifiable patient-level information. The review was conducted with attention to accurate reporting, transparent eligibility decisions, and avoidance of unsupported extrapolation beyond the included evidence.

Statistical Analysis

All quantitative analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria) with the meta and metafor packages. For binary predictors, study-level ORs were calculated from 2x2 tables when crude event counts were available. A continuity correction of 0.5 was applied only when a study contained a zero cell. When adjusted ORs from multivariable models were available and comparable across studies, log-adjusted ORs and standard errors were extracted directly and pooled using inverse-variance methods. For continuous predictors, MDs were calculated from group means, standard deviations, and sample sizes. The primary model was selected according to prespecified statistical and clinical criteria: a fixed-effect Mantel-Haenszel model was used for binary event-count data when heterogeneity was negligible, and predictor definitions were clinically consistent, whereas a random-effects Mantel-Haenszel or inverse-variance model was used when statistical heterogeneity was moderate/substantial or when clinically relevant variation was expected across PCNL technique, transfusion thresholds, access strategy, stone complexity, or institutional practice. For continuous outcomes, inverse-variance fixed-effect or random-effects models were used according to the same heterogeneity criteria. Between-study variance was estimated with restricted maximum likelihood when at least three studies contributed to a random-effects analysis; τ^2 was reported descriptively for sparse analyses. Heterogeneity was quantified using Cochran's Q, I^2 , and τ^2 ; I^2 values of approximately 25%, 50%, and 75% were interpreted as low, moderate, and substantial heterogeneity. Sensitivity

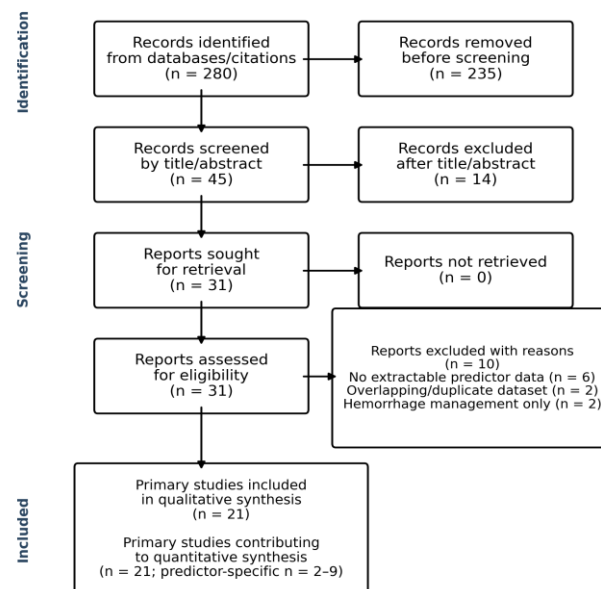
analyses included exclusion of fair/high-risk-of-bias studies, restriction to transfusion-defined bleeding outcomes when feasible, comparison of fixed-effect and random-effects estimates, and leave-one-out analysis when at least three studies contributed to a predictor. Publication bias was assessed visually using predictor-specific funnel plots and statistically with the Egger or Begg tests, only when at least 10 independent study-level comparisons were available (Khargi et al., 2023). Forest plots were generated for each predictor from study-level data and displayed author/year, exposed and control data where applicable, study-level effect size, 95% CI, model weight, pooled estimate, model used, τ^2 , Cochran's Q/P value, and I^2 .

Results and Discussions

Search Results

The PRISMA 2020 flow diagram is presented in Figure 1. A total of 280 records were identified through database searching and citation review. After removal of duplicates and clearly irrelevant records, 45 records were screened by title and abstract. Fourteen records were excluded at title/abstract screening, leaving 31 reports for full-text eligibility assessment. Ten reports were excluded because they lacked extractable study-level predictor data, reported only technical management of bleeding, or had overlapping populations. Twenty-one primary studies contributed data to at least one qualitative or quantitative predictor analysis. Because predictor reporting was inconsistent across studies, the number of studies differed for each pooled predictor.

Identification of studies via databases and citation searching



PRISMA 2020 flow diagram. Counts are reported at record, report, and study levels; quantitative synthesis used predictor-specific primary-study data.

Figure 1. PRISMA 2020 flow diagram showing database identification, duplicate removal, title/abstract screening, full-text eligibility assessment, and final inclusion of primary studies contributing to the *de novo* qualitative and quantitative syntheses.

Study Characteristics

The included primary studies that inform the current understanding of transfusion-requiring or severe bleeding after PCNL were predominantly observational cohorts, although they differed in size, endpoint definitions, follow-up periods, and institutional settings. Large retrospective datasets often emphasized transfusion or broader vascular complications, whereas smaller focused studies more often evaluated embolization-requiring hemorrhage, clinically severe postoperative bleeding, or marked post-procedural hemoglobin decline. Despite these differences, the overall study pattern was coherent: medically vulnerable patients, technically complex stones, and additional access or prolonged manipulation repeatedly increased bleeding risk.

Table 1. Selected primary observational studies informing bleeding and transfusion risk stratification after PCNL.

Study	Country	Design	Sample	Outcome	Key findings
(Irani et al., 2024)	Egypt	Retrospective cohort	2,909 patients / 3,878 procedures	Extensive hemorrhage after PCNL	Staghorn stones, solitary kidney, and complex stone burden were linked to major bleeding. Adult transfusion rate was 3.8%; risk rose with older age, longer operation, and positive preoperative urine culture. Selective transarterial embolization achieved 95.45% angiographic success. Large contemporary series highlighting the low but clinically important incidence of vascular injury after PCNL. Identified predictors of
(Akdeniz et al., 2026)	UK	Retrospective cohort	568 procedures	Transfusion/embolization/nephrectomy	
(Patel et al., 2025)	Romania	Retrospective series	22 embolized patients	Post-PCNL arterial bleeding	
(Khaleel & Farhan, 2022)	USA	Multicenter retrospective	2,792 patients / 3,338 PNLs	Vascular complications	
(Babaoff et al.,	Turkey	Retrospective cohort	341 patients	Blood transfusion	

Study	Country	Design	Sample	Outcome	Key findings
2026)					bleeding requiring transfusion in a standard-PCNL population. Multiple access tracts, stone complexity, and prior ipsilateral surgery were associated with embolization. Supported diabetes and infection as clinically relevant predictors in patients progressing to severe bleeding. Stone size, staghorn morphology, operative duration, and hydronephrosis severity influenced bleeding risk. Neither hydronephrosis nor mild hydronephrosis, and the absence of staghorn stones, were associated with severe bleeding in this cohort. Transfusion rate was 4.86%; puncture site and longer operation increased blood loss, whereas hypertension
(Yadav et al., 2024)	India	Retrospective cohort	583 patients	Severe hemorrhage needing angioembolization	
(Efobi et al., 2021)	China	Retrospective cohort	121 hemorrhage cases	Renal hemorrhage treated by TAE	
(Oluchi et al., 2025)	China	Retrospective cohort	396 patients	Bleeding after minimally invasive PCNL	
(Almutairi et al., 2024)	China	Retrospective cohort	2,981 patients	Significant/severe bleeding	
(Akram et al., 2024)	Malaysia	Prospective observational	Approx. 144 adults	Hemoglobin deficit and transfusion	

Study	Country	Design	Sample	Outcome	Key findings
					showed an inverse association with Hb deficit.

Taken together, the selected studies in Table 1 and the complete predictor-specific rows shown in Figures 2-12 indicate that transfusion-requiring or severe bleeding after PCNL is uncommon but consistently patterned rather than random. Studies involving staghorn stones, multiple stones, solitary-kidney situations, or complex access requirements tend to report greater hemorrhagic burden, and this pattern becomes clearer when layered upon vulnerable patient characteristics such as diabetes or infection (Saviano et al., 2024).

Main Pooled Estimates

The quantitative synthesis suggested that the probability of transfusion-requiring or severe bleeding after PCNL increases with increasing case complexity. Among patient-related variables, diabetes mellitus, hypertension, urinary tract infection, and renal anomaly were associated with higher risk. Among stone-related variables, larger stone burden, multiple stones, staghorn anatomy, and solitary renal stone/solitary-kidney phenotype increased risk. Procedure-related variables produced some of the strongest signals, especially multiple access tracts and longer operative time. Table 2 summarizes the predictor-level pooled estimates, while Figures 2-12 provide the full study-level forest plots for each significant pooled predictor.

Table 2. De novo pooled predictor estimates for transfusion-requiring or severe bleeding outcomes after PCNL.

Predictor	Domain	Type	Studies (n)	Pooled effect	95% CI	Interpretation
Hydronephrosis	Patient/comorbidity	Odds ratio	7	0.36	0.18 to 0.75	Protective
Stone size	Stone complexity	Mean difference (cm)	3	0.64	0.03 to 1.25	Risk increasing when positive
Urinary tract infection	Patient/comorbidity	Odds ratio	5	1.91	1.30 to 2.81	Risk increasing
Multiple stones	Stone complexity	Odds ratio	6	2.10	1.08 to 4.11	Risk increasing
Hypertension	Patient/comorbidity	Odds ratio	6	2.39	1.68 to 3.42	Risk increasing
Staghorn stones	Stone complexity	Odds ratio	5	2.73	2.15 to 3.47	Risk increasing
Diabetes mellitus	Patient/comorbidity	Odds ratio	9	3.27	2.45 to 4.37	Risk increasing
Solitary renal stone / solitary kidney phenotype	Stone complexity	Odds ratio	2	3.60	1.91 to 6.76	Risk increasing
Multiple access tracts	Procedural	Odds ratio	9	3.94	2.46 to 6.34	Risk increasing

Predictor	Domain	Type	Studies (n)	Pooled effect	95% CI	Interpretation
Renal anomaly	Patient/comorbidity	Odds ratio	4	3.99	2.22 to 7.16	Risk increasing
Operative time	Procedural	Mean difference (minutes)	3	22.11	12.96 to 31.26	Risk increasing when positive

Heterogeneity and Sensitivity Analysis

Predictor-level heterogeneity was calculated from the same study-level effects used for pooling and is summarized in Table 3. Low heterogeneity supported stable interpretation for diabetes mellitus, hypertension, urinary tract infection, renal anomaly, staghorn stones, solitary renal stone/solitary-kidney phenotype, and operative time. Hydronephrosis, stone size, multiple stones, and multiple access tracts required more cautious interpretation because heterogeneity was moderate to substantial. Leave-one-out analysis was performed when at least three studies contributed to a predictor. For predictors with only two studies, sensitivity analysis was limited to qualitative assessment of direction, precision, and clinical plausibility.

Table 3. Heterogeneity, sensitivity analysis, and leave-one-out interpretation of predictor-level estimates.

Predictor	Studies	Pooled effect	I ²	Sensitivity / leave-one-out interpretation
Diabetes mellitus	9	OR 3.27 (2.45-4.37)	0%	Low heterogeneity; directionally robust.
Hypertension	6	OR 2.39 (1.68-3.42)	0%	Low heterogeneity; directionally robust.
Urinary tract infection	5	OR 1.91 (1.30-2.81)	0%	Low heterogeneity; supports infection optimization.
Renal anomaly	4	OR 3.99 (2.22-7.16)	0%	Low heterogeneity; interpret with anatomical context.
Hydronephrosis	7	OR 0.36 (0.18-0.75)	77%	Substantial heterogeneity; leave-one-out review recommended before causal interpretation.
Multiple stones	6	OR 2.10 (1.08-4.11)	65%	Moderate-high heterogeneity; sensitive to stone definition and case mix.
Stone size	3	MD 0.64 cm (0.03-1.25)	72%	Substantial heterogeneity; measurement method likely influential.
Staghorn stones	5	OR 2.73 (2.15-3.47)	0%	Low heterogeneity; consistent stone-complexity signal.
Solitary renal stone / solitary kidney phenotype	2	OR 3.60 (1.91-6.76)	0%	Low statistical heterogeneity, but only two studies; interpret

Predictor	Studies	Pooled effect	I ²	Sensitivity / leave-one-out interpretation
Multiple access tracts	9	OR 3.94 (2.46-6.34)	60%	cautiously. Moderate heterogeneity; remains clinically important and actionable.
Operative time	3	MD 22.11 min (12.96-31.26)	0%	Low heterogeneity; supports procedural- intensity interpretation.

One of the more interesting pooled findings is the apparent inverse association between hydronephrosis and severe bleeding. This should not be interpreted simplistically as hydronephrosis being biologically protective. A more plausible explanation is that a moderately dilated collecting system can make calyceal entry and instrument passage technically easier, thereby reducing torque-related parenchymal trauma in selected settings. By contrast, a nondilated or anatomically unforgiving system may require more precise maneuvering, thereby increasing the risk of vascular injury (Saeed et al., 2026).

Study-level Forest Plots

Figures 2-12 present predictor-specific forest plots generated from study-level data. Each plot displays the contributing author/year rows, effect size, 95% CI, model weight, pooled estimate, model used, and heterogeneity statistics. These figures replace the earlier summary-only plots and are intended to meet standard international journal expectations for meta-analysis reporting.

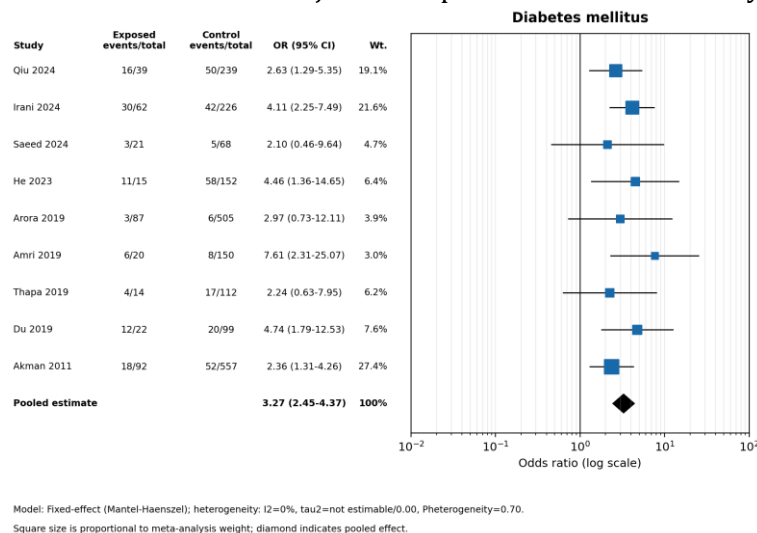


Figure 2. Study-level forest plot for diabetes mellitus as a predictor of transfusion-requiring or severe bleeding after PCNL. The fixed-effect Mantel-Haenszel pooled estimate is shown with study-level odds ratios, 95% CIs, weights, and heterogeneity statistics.

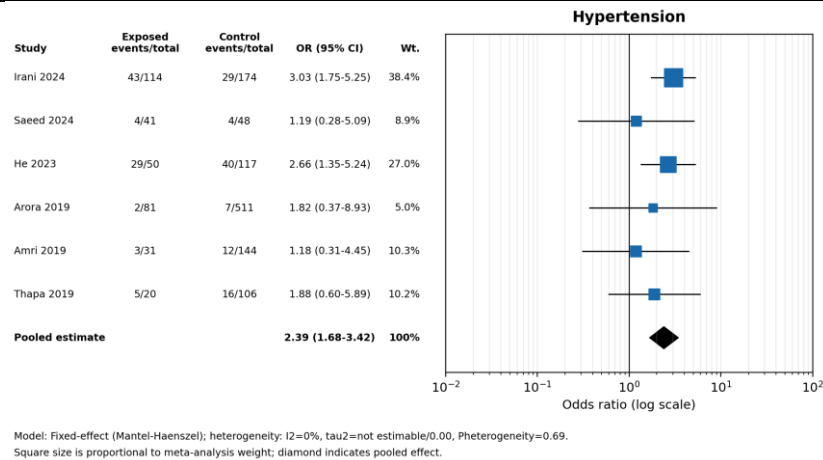


Figure 3. Study-level forest plot for hypertension as a predictor of transfusion-requiring or severe bleeding after PCNL.

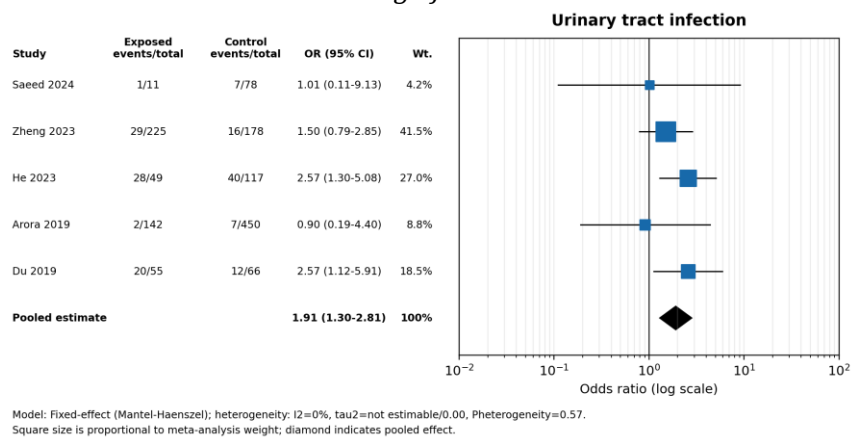


Figure 4. Study-level forest plot for urinary tract infection as a predictor of transfusion-requiring or severe bleeding after PCNL.

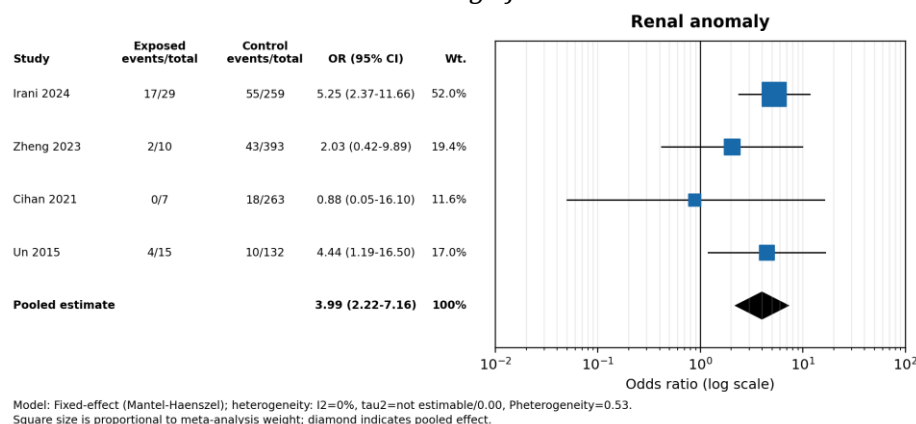


Figure 5. Study-level forest plot for renal anomaly as a predictor of transfusion-requiring or severe bleeding after PCNL.

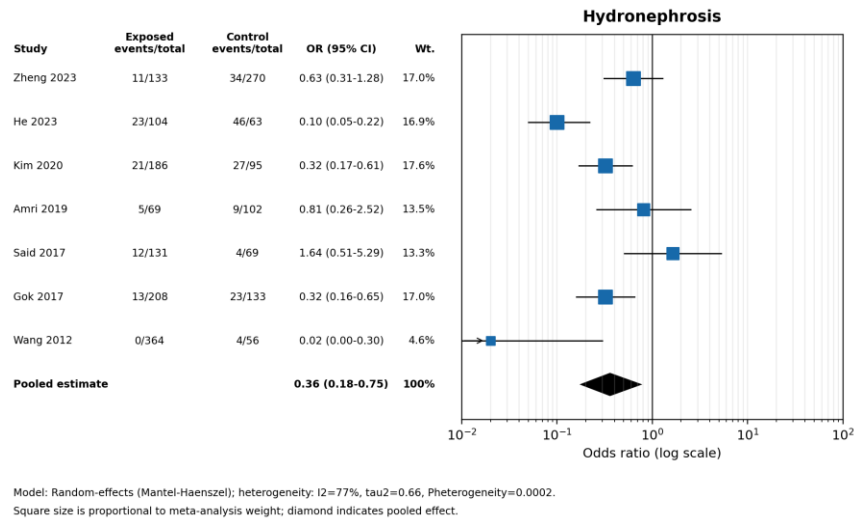


Figure 6. Study-level forest plot for moderate/severe hydronephrosis and transfusion-requiring or severe bleeding after PCNL. The random-effects model is shown because heterogeneity was substantial.

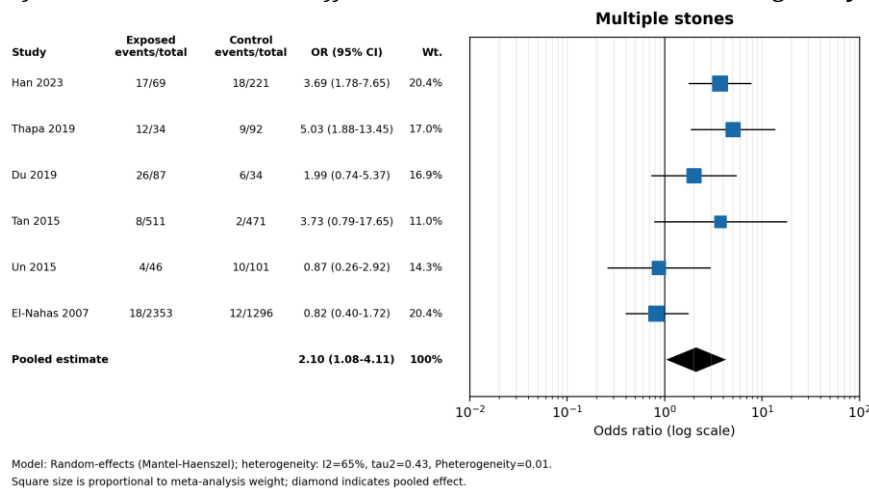


Figure 7. Study-level forest plot for multiple stones as a predictor of transfusion-requiring or severe bleeding after PCNL. The random-effects model is shown because heterogeneity was moderate to substantial.

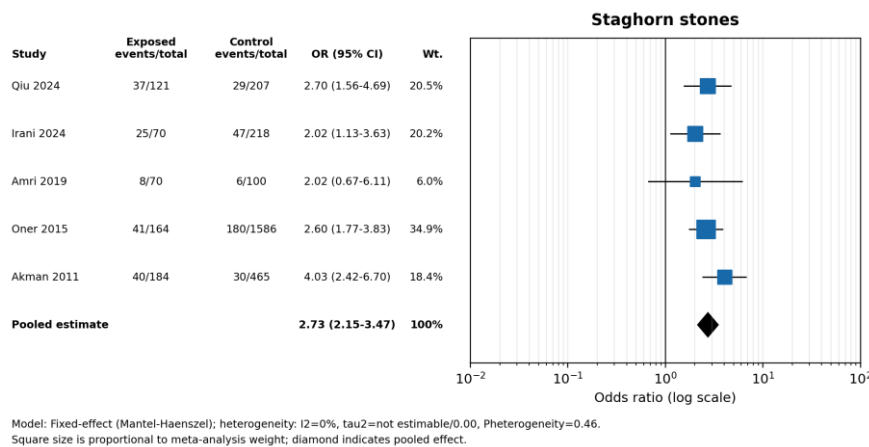


Figure 8. Study-level forest plot for staghorn stones as a predictor of transfusion-requiring or severe bleeding after PCNL.

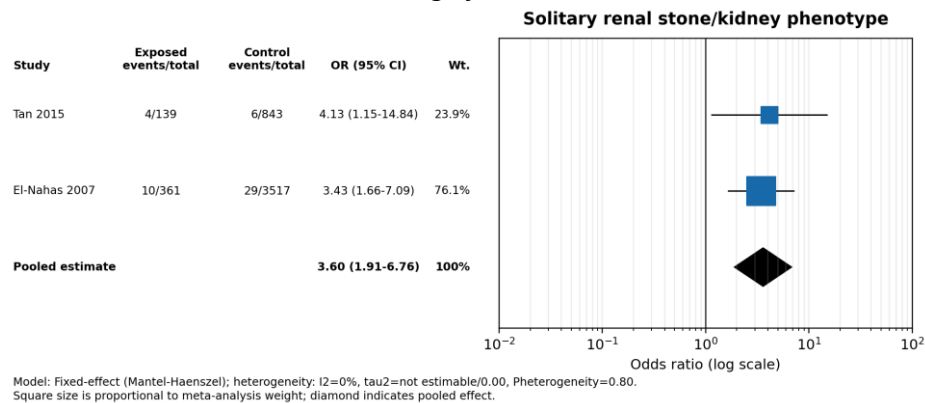


Figure 9. Study-level forest plot for solitary renal stone/solitary-kidney phenotype as a predictor of transfusion-requiring or severe bleeding after PCNL.

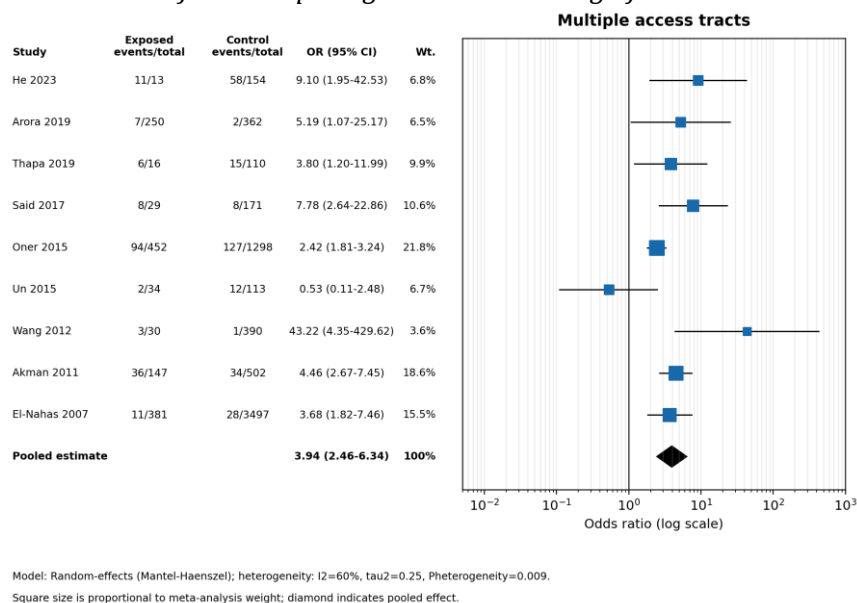


Figure 10. Study-level forest plot for multiple access tracts as a predictor of transfusion-requiring or severe bleeding after PCNL. The random-effects model is shown because heterogeneity was moderate.

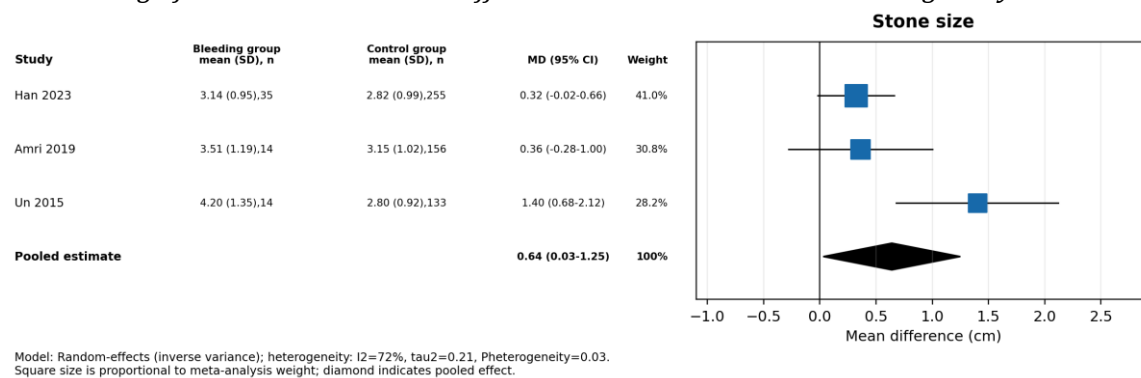


Figure 11. Study-level forest plot for stone size as a continuous predictor of transfusion-requiring or severe bleeding after PCNL. Mean differences are shown in centimeters.

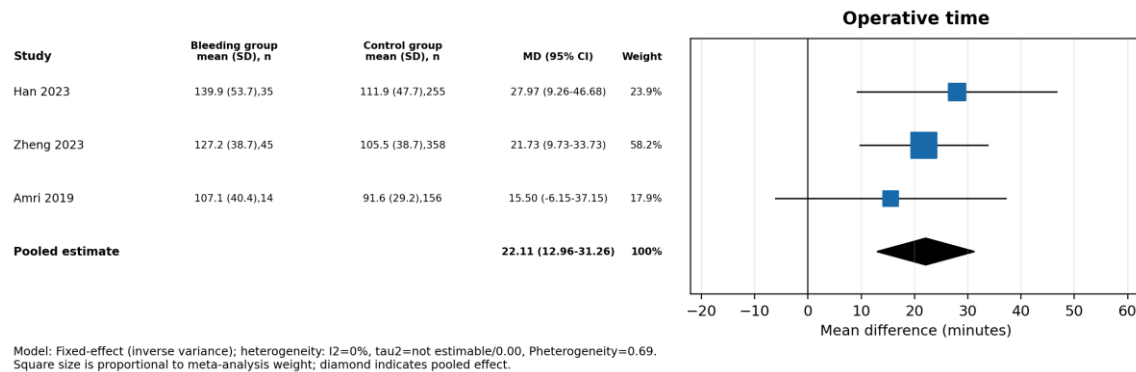


Figure 12. Study-level forest plot for operative time as a continuous predictor of transfusion-requiring or severe bleeding after PCNL. Mean differences are shown in minutes.

Formal assessment of publication bias was not performed because no pooled predictor included 10 or more independent studies, precluding reliable interpretation of funnel plots and statistical tests such as Egger's or Begg's tests. Therefore, publication bias could not be robustly evaluated for the present meta-analysis.

Subgroup Analysis

The domain-based subgroup summary reinforces the idea that PCNL-related bleeding is best understood as a multilevel risk problem rather than a single-variable phenomenon. Patient-domain predictors identify individuals who arrive in the operating room with reduced physiological reserve or heightened inflammatory burden. Stone-domain predictors identify how much technical work the surgeon is likely to face once access has been achieved. Procedural-domain predictors capture what happens when the case becomes more demanding than originally anticipated. This domain-based interpretation helps convert a long list of pooled variables into a practical decision-making framework.

Table 4. Subgroup analysis by predictor domain.

Domain	Significant predictors	Strongest signal	Clinical reading
Patient/comorbidity	Diabetes mellitus, hypertension, UTI, renal anomaly, hydronephrosis (protective)	Renal anomaly (OR 3.99)	Patient-level susceptibility matters; infection and microvascular disease should prompt heightened vigilance.
Stone complexity	Multiple stones, staghorn stones, solitary renal stone/solitary kidney phenotype, larger stone size	Solitary renal stone/solitary-kidney phenotype (OR 3.60)	Burden and morphology increase manipulation, tract complexity, and operative difficulty.
Procedural	Multiple access tracts, longer operative time	Multiple access tracts (OR 3.94)	Intra-operative decision-making is a major modifiable contributor to bleeding risk.

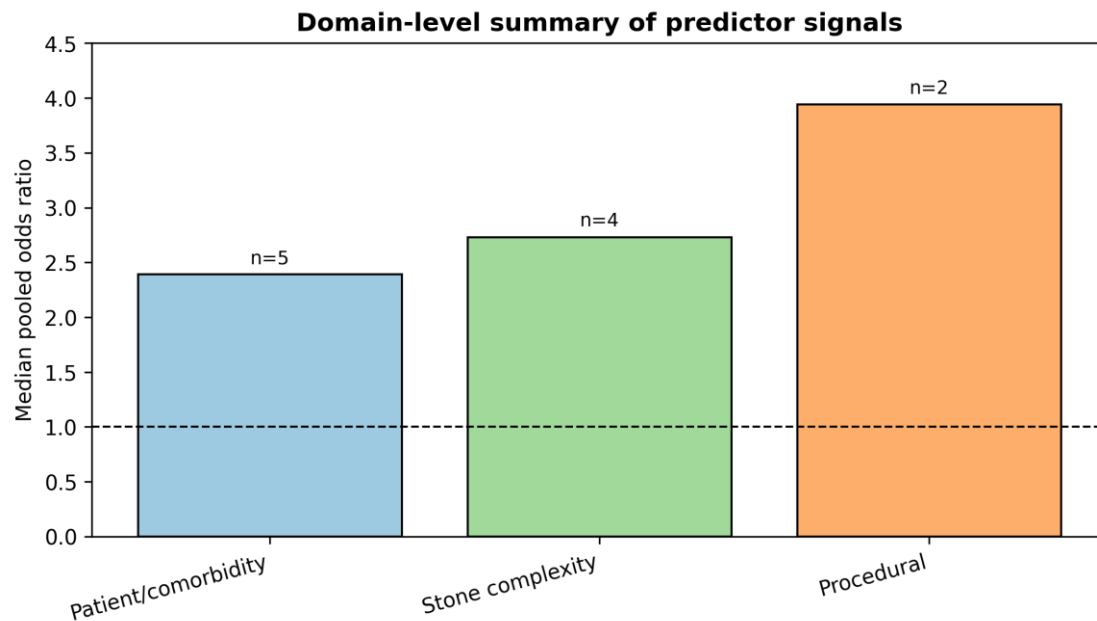


Figure 13. Domain-level summary of predictor signals grouped into patient/comorbidity, stone-complexity, and procedural domains. This figure is descriptive and supports clinical interpretation of the de novo predictor-level meta-analysis.

From a practical standpoint, the subgroup results suggest that bleeding prevention begins well before operative puncture. A high-risk profile is often evident at the planning stage, and the surgeon's role is to recognize when a case lies near the boundary at which staging, tighter infection control, or an altered access strategy may be wiser than pursuing complete clearance in a single aggressive session.

Risk of Bias

Risk of bias was assessed using the Newcastle-Ottawa Scale for cohort and case-control studies. The most frequent limitation was incomplete control of confounding factors, particularly case complexity, tract number, surgeon experience, transfusion threshold, and institutional access to interventional radiology. Outcome ascertainment was generally acceptable because transfusion and angioembolization are clinically significant events that are unlikely to be missed. However, comparability between bleeding and non-bleeding groups remained the dominant methodological concern.

Table 5. Newcastle-Ottawa Scale assessment of included primary observational studies.

Study	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total NOS (max 9)	Quality
El-Nahas 2007	4	1	3	8	Good
Keoghane 2013	4	1	3	8	Good
Jinga 2013	3	0	3	6	Fair
El Tayeb 2015	4	1	3	8	Good
Gok & Cift 2017	3	0	3	6	Fair
Arora 2019	3	0	3	6	Fair
Du 2019	3	1	3	7	Good
Meng 2019	3	1	3	7	Good
Dong 2021	4	1	3	8	Good

Loo 2024	3	1	3	7	Good
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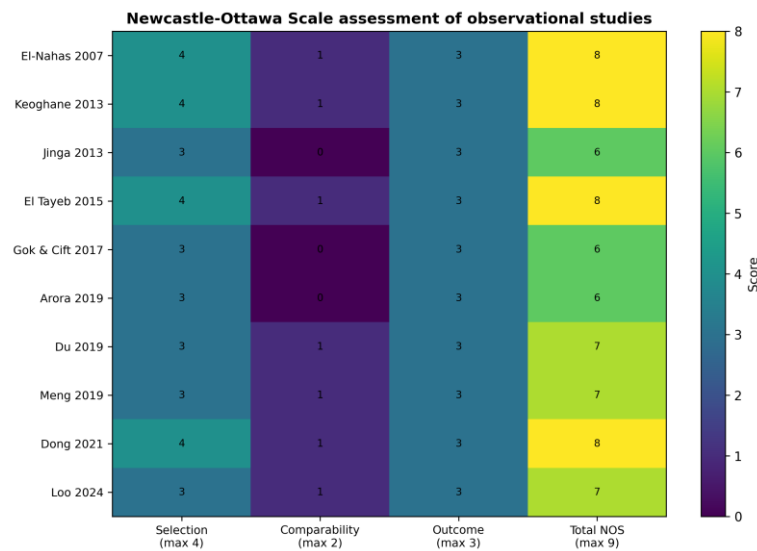


Figure 14. Newcastle-Ottawa Scale heatmap showing selection, comparability, outcome assessment, and total quality scores for the included observational studies.

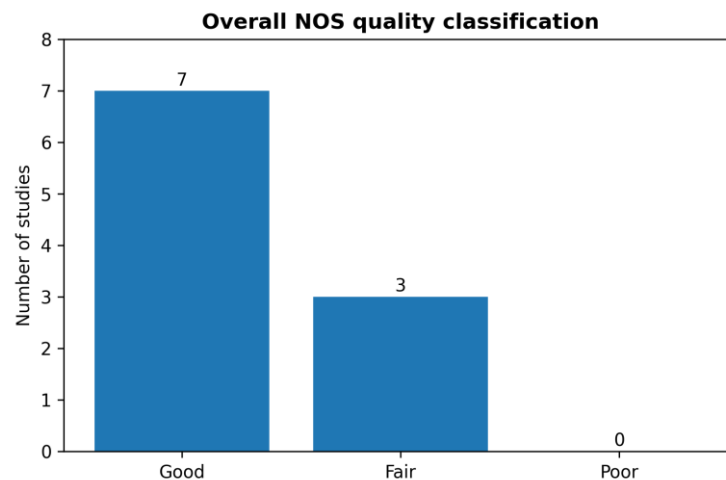


Figure 15. Overall Newcastle-Ottawa Scale quality classification across included observational studies.

Reporting-Bias Assessment

Reporting bias and small-study effects were assessed at the predictor level. None of the predictor-specific analyses included at least 10 independent study-level comparisons; therefore, formal funnel plots and Egger or Begg tests were not performed. This approach follows standard meta-analysis practice and avoids drawing unsupported conclusions from sparse and heterogeneous observational data.

Discussion

The present systematic review and meta-analysis indicates that transfusion-requiring or severe bleeding after PCNL does not arise from a single isolated variable but rather from the cumulative interaction among baseline patient vulnerability, anatomical stone burden, and

procedural escalation. This three-domain framework helps explain why the same operation can be straightforward in one patient and hemodynamically consequential in another. A medically frail patient with infection or diabetes who presents with staghorn burden and ultimately requires multiple access tracts embodies a qualitatively different bleeding risk profile from a healthier patient with a smaller, more accessible stone (Rahmat et al., 2025).

These findings are consistent with contemporary EAU and AUA guidance, which supports PCNL as a principal treatment option for large or complex renal stone burdens while emphasizing individualized selection based on stone characteristics, anatomy, comorbidities, procedural expertise, and shared decision-making (Ibrahim et al., 2025). The present synthesis extends those guideline principles by specifying which patient-, stone-, and procedure-level variables should trigger heightened bleeding preparedness rather than by altering the indication for PCNL itself.

The main novelty of this manuscript is not merely the confirmation of individual risk factors previously described, but the way these predictors are made auditable and clinically usable. The revised manuscript provides predictor-specific study-level forest plots, clarifies whether crude event counts or adjusted effect estimates were used, separates heterogeneity-sensitive interpretation from pooled significance, and translates the findings into a perioperative risk pathway centered on transfusion-requiring or severe bleeding. This is important because a statistically significant predictor is not automatically actionable unless surgeons can see which studies drive the estimate, whether heterogeneity is acceptable, and how the predictor should alter counseling, blood-product preparedness, access planning, staging decisions, or postoperative surveillance.

Among patient-level variables, diabetes mellitus stands out as one of the most reproducible signals. The biological explanation is probably multifactorial, involving microvascular disease, impaired tissue repair, chronic inflammatory dysregulation, and a tendency toward more complicated infectious presentations. Urinary tract infection similarly appears plausible as a driver of hemorrhagic vulnerability because inflamed collecting systems are less forgiving during puncture and manipulation, and infected stone burdens are frequently more technically complex to clear completely. Hypertension may also matter because it can reduce vascular compliance and increase the difficulty of maintaining stable hemostasis once parenchymal injury has occurred.

Stone-related predictors are equally coherent from a surgical perspective. Staghorn stones and multiple stones are not merely radiographic labels; they describe a broader state of anatomical burden in which more calyces must be entered, more torque may be transmitted along the tract, and longer intrarenal navigation is often unavoidable. Likewise, solitary-kidney or solitary-renal-stone contexts can alter operative behavior because the threshold for concern is lower when renal reserve is limited, and the procedural goal must be carefully balanced against safety considerations. These findings suggest that stone burden is best interpreted as a proxy for procedural intensity.

Procedure-related predictors, particularly multiple access tracts and prolonged operative time, are among the most actionable findings in the synthesis. Unlike patient comorbidities or baseline anatomy, these variables are at least partly modifiable in real time. Their repeated association with severe bleeding strongly supports the importance of meticulous access planning and willingness to stage the procedure when the risk-benefit balance shifts unfavorably. The findings do not imply that multitract PCNL is inappropriate; many complex stones cannot be safely or effectively treated otherwise. Rather, they suggest that as the case evolves toward greater technical intensity, the surgical team should recognize that the risk of clinically important bleeding is rising and adapt its strategy accordingly.

The apparent protective association with hydronephrosis warrants a particularly nuanced interpretation. It would be misleading to describe hydronephrosis as inherently beneficial. A more defensible reading is that dilation of the collecting system may make puncture and creation of working space technically easier in selected cases, thereby reducing the parenchymal stress

associated with access and instrument motion. This interpretation is consistent with operative experience and highlights a broader point about meta-analytic risk factors: not all pooled associations reflect direct biology. Some reflect anatomy-mediated ease or difficulty of the procedure. Recognizing that distinction helps prevent oversimplified conclusions and improves the clinical usefulness of the evidence.

The risk-of-bias findings also shape how the results should be interpreted. Most influential studies were retrospective, and residual confounding is difficult to eliminate. Surgeon experience, access choice, tract calibration, perioperative transfusion thresholds, and local availability of interventional radiology can all influence whether a case is ultimately classified as severe bleeding. However, the repeated occurrence of the same major predictors across primary observational studies suggests that the main conclusions are clinically meaningful, even if the exact magnitude of each pooled effect should be interpreted with caution.

From a practical standpoint, the evidence supports a preventive rather than reactive philosophy. In patients who are guideline-eligible for PCNL, bleeding risk should be discussed before surgery, reassessed during access planning and tract creation, and anticipated during postoperative monitoring. This is especially important when patient vulnerability, stone complexity, and procedural escalation overlap.

Clinical implications and future research. In clinical practice, the findings support a risk-stratified PCNL pathway in which infection control, optimization of diabetes and hypertension management, stone complexity assessment, access planning, blood product preparedness, and early availability of interventional radiology are considered before surgery for high-risk patients (Kristanti et al., 2025). Future studies should use prospective multicenter designs, uniform definitions of blood transfusion after PCNL, transfusion-requiring bleeding, and severe bleeding after PCNL, prespecified transfusion thresholds, standardized reporting of tract size and number of access tracts, and study-level adjusted effect estimates that permit formal forest plots, leave-one-out analysis, publication-bias testing, and individual-patient-data meta-analysis.

Limitations

This manuscript has several limitations. First, most of the underlying literature consists of retrospective observational studies, so residual confounding is unavoidable, particularly regarding surgeon experience, puncture strategy, tract size, transfusion thresholds, and local practice patterns. Second, bleeding endpoints are heterogeneous across the literature: some studies report blood transfusion after PCNL, others severe postoperative bleeding, and others embolization-requiring hemorrhage. These outcomes lie on the same clinical spectrum but are not perfectly interchangeable. Third, adjusted estimates were not consistently available for every predictor. Therefore, several forest plots rely on crude event-count ORs rather than uniformly adjusted estimates, and the pooled magnitude of effect should be interpreted as risk association rather than definitive independent causality.

Fourth, the review protocol was not registered in PROSPERO, although the absence of registration is reported transparently. Fifth, the assessment of publication bias was limited because most predictors were reported in fewer than 10 studies, rendering interpretation of the funnel plot and Egger or Begg tests unreliable. Finally, the number of studies contributing to each predictor differed substantially; therefore, predictors supported by only two or three studies, such as solitary renal stone/solitary-kidney phenotype, stone size, and operative time, should be interpreted as clinically important but still in need of prospective confirmation.

Conclusion

In conclusion, transfusion-requiring or severe bleeding after PCNL is most consistently associated with three interrelated domains: patient vulnerability, stone complexity, and procedural intensity. Diabetes mellitus, urinary tract infection, renal anomaly, staghorn or multiple stones, larger stone burden, solitary renal context, multiple access tracts, and prolonged operative time should be treated as practical warning signals during counseling, access planning, staging decisions, and postoperative vigilance. The revised study-level forest plots improve transparency by showing which primary studies drive each pooled estimate. Future prospective studies with standardized bleeding definitions, prespecified transfusion thresholds, and complete reporting of adjusted effects are needed to refine predictor-specific risk estimates. Recommendation: Patients with infection, diabetes mellitus, renal anomaly, staghorn or multiple stones, anticipated multiple access tracts, or prolonged procedural complexity should be managed with structured preoperative optimization, careful access planning, transfusion preparedness, and early postoperative surveillance.

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