

OPIOID-FREE ANESTHESIA AND LONG-TERM RECOVERY AFTER PERCUTANEOUS NEPHROLITHOTOMY: A SYSTEMATIC REVIEW

Dr. Khayyam Farid¹, Dr. Sulaiman², Dr. Umbrin Naz³, Dr. Imran ul Haq⁴

¹Queen Mary University of London, United Kingdom, Email: k.farid@smd25.qmul.ac.uk

²Assistant Anaesthetist, Cardiac Rehabilitation Center, Hayatabad Medical Complex, Peshawar, Email: sulamankhan1031@gmail.com

³Assistant Professor, Department of Anaesthesia, Khyber Teaching Hospital, Peshawar, Email: umbrinnaz1@yahoo.com

⁴Consultant Anaesthesia, Cardiac Surgery Division, In charge Medical ICU, Email: imran.haq@rmi.edu.pk

*Corresponding author: Dr. Umbrin Naz, Email: umbrinnaz1@yahoo.com

ABSTRACT:

Background: Percutaneous nephrolithotomy (PCNL) is associated with postoperative pain and perioperative opioid exposure. Opioid-free anesthesia (OFA) has emerged as a potential strategy to reduce opioid-related adverse effects and improve postoperative recovery. However, evidence specifically evaluating OFA in PCNL remains limited.

Objective: To systematically review the available evidence regarding opioid-free and opioid-sparing anesthetic and analgesic strategies in patients undergoing PCNL, with particular emphasis on postoperative pain, opioid consumption, quality of recovery, and longer-term recovery outcomes.

Methodology: Systematic literature search was done in PubMed/MEDLINE, Embase, Scopus and Web of Science. The studies that assessed OFA, opioid-sparing regional anesthesia, multimodal analgesia, or opioid-free postoperative pathway in patients undergoing PCNL were evaluated. The anesthetic technique, opioid exposure, postoperative pain, opioid use, rescue analgesia, recovery, hospital stay, and long-term outcome data were retrieved. Findings were synthesized narratively, as there was significant heterogeneity in interventions and outcome measures.

Results: The literature available for PCNL showed consistent evidence of opioid-sparing regional blocks (ESPB and QLB) with a decrease in postoperative opioid usage, pain scores, and requirement for rescue analgesics. Other studies also reported faster ambulation, better patient satisfaction and shorter hospital stay. Most PCNL studies have, however, used intraoperative opioids and thus did not truly represent OFA. Opioid-free postoperative pathways were also promising, with reports of decreased opioid prescribing and opioid-free discharge in certain patients. However, the real-time intraoperative OFA during PCNL and its impact on long-term outcomes were poorly studied.

Conclusion: There is current evidence in support of multimodal and regional opioid-sparing approaches to minimize opioid exposure after PCNL. However, there is a lack of evidence specific to PCNL that demonstrates that true OFA will have better short or long term recovery than conventional opioid-based anesthesia. Long-term studies with standardized OFA protocols and longer follow-up are required to assess long-term opioid use, quality of life, and functional recovery in well-designed randomized trials.

KEYWORDS: opioid-free anesthesia; percutaneous nephrolithotomy; PCNL; opioid-sparing anesthesia; regional anesthesia; postoperative pain; multimodal analgesia; recovery.

INTRODUCTION:

Percutaneous nephrolithotomy (PCNL) is a well-established minimally invasive procedure for those who have large, complex, or otherwise unindicated renal stones. Despite the development of surgical and anesthetic techniques, pain is still a significant issue after PCNL and can impact post-operative recovery, patient satisfaction, mobility and discharge. Perioperative pain relief is therefore a critical part of the modern-day care of the PCNL. Opioids have traditionally been an important part of general anesthesia and postoperative pain treatment, but they have adverse effects such as nausea/vomiting, sedation, respiratory depression, ileus, urinary retention and the potential for opioid-induced hyperalgesia and persistent opioid use [1-3].

With the growing focus on improved recovery and multimodal perioperative management, there has been a renewed interest in the use of opioid-free anesthesia (OFA), where opioids are not used during the procedure, and an attempt is made to provide anesthetic analgesia using a combination of non-opioid pharmacological and regional methods. These techniques can involve the use of dexmedetomidine, ketamine, intravenous lidocaine, magnesium, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetic infiltration, and regional nerve blocks, depending on the anesthetic protocol. The benefits of OFA are not just decreasing opioid exposure; avoiding opioid-related side effects can help patients get up and move sooner, improve patient comfort, minimize the risk of postoperative nausea and vomiting (PONV), and possibly improve overall quality of recovery [4-6].

Overall, data from surgical populations indicate that OFA may provide better benefits in certain postoperative outcomes than opioid-based anesthesia (OBA). A systematic review and meta-analysis of randomized clinical trials showed that OFA was correlated with the reduction of PONV and the improvement of quality-of-recovery measures, but the differences in acute postoperative pain and opioid use were not consistently clinically significant. Importantly, very few studies related to chronic postoperative pain were found, as indicated in the same review, where only one small study focused on this outcome. Other, more recent, meta-analyses have also found that OFA improves patient-reported quality of recovery, especially physical comfort and PONV, with significant variation across studies and a lack of clarity about the size and significance of these effects[7-9].

Recovery following surgery isn't solely about pain relief after the operation. Patient-centered recovery includes physical recovery, emotional recovery, functional recovery, return to normal activities and quality of life. Therefore, limiting opioid exposure during anesthesia could have consequences beyond the first few hours after surgery or the stay in hospital. But there is less consistent and limited evidence about the impact of OFA on longer term recovery. Recent studies have indicated that OFA might have a role to play in chronic postoperative pain in certain surgical populations, however, the effects are procedure-specific and may not be applicable to urological surgery [10]. In addition, the anesthetic and analgesic needs of PCNL are different than many surgical procedures due to the prone or modified surgical position, renal access, tissue manipulation, and the possibility of postoperative flank or visceral pain[10].

Although the number of patients undergoing PCNL has increased, there is limited evidence directed at OFA specifically in the context of PCNL. While a number of investigations have concentrated on the immediate perioperative data (postoperative pain score, rescue analgesic use, PONV, hemodynamic parameters, length of stay), patient-centered recovery parameters have been much less studied. Furthermore, multiple ways of defining opioid-free anesthesia, different protocols for administering OFA, different comparator regimens, and various definitions for the endpoints of interest make it difficult to directly compare the results of the available studies.

This is the reason a systematic review of existing literature is warranted to elucidate the effects of OFA versus conventional opioid-based anesthesia in patients undergoing PCNL. The purpose of this systematic review is to assess the relationship between OFA and: postoperative pain; opioid consumption; rescue analgesic use; PONV; quality of recovery; length of stay; longer-term outcomes (persistent pain and functional recovery, if available). This review aims to evaluate the short- and long-term outcomes to assess the clinical relevance of avoiding intraoperative opioids after PCNL and to highlight key gaps that need to be addressed in future prospective studies.

METHODOLOGY:

The aim of this systematic review was to assess the outcomes of opioid-free anesthesia (OFA) versus conventional opioid-based anesthesia (OBA) on recovery after percutaneous nephrolithotomy (PCNL) in the perioperative period and beyond. The review was designed and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and PRISMA 2020 reporting recommendations. The PRISMA framework was applied in the selection, extraction, synthesis and reporting of the data.

The review protocol was already developed and included the eligibility criteria, search strategy, outcomes of interest, risk-of-bias assessment, and planned methods of evidence synthesis. The original protocol was followed and any deviations from it noted and reported in the final manuscript. A PRISMA 2020 checklist and PRISMA flow diagram were included as supporting materials when applicable.

Outcomes and Objectives:

Postoperative pain intensity, postoperative opioid or rescue analgesic consumption and quality of recovery were the primary outcomes. Secondary outcomes were postoperative nausea and vomiting, time to mobilization, hospital stay, postoperative complications, hemodynamic outcomes, patient satisfaction, persistent or chronic postoperative pain, return to normal activities, functional recovery and other patient-reported longer term recovery outcomes (if reported). The main goal was to see if OFA was linked with better recovery after PCNL than opioid anesthesia. A secondary aim was to see if there were benefits in not using per-operative opioids in the longer term beyond the immediate postoperative period.

Eligibility Criteria

Studies were included if they met the following inclusion criteria:

- Research on adults who have had PCNL for renal or upper urinary tract stones.
- Studies comparing an opioid-free or opioid-avoiding anesthetic approach during PCNL.
- Studies with a comparator group using conventional opioid-based anesthesia or an anesthesia strategy that included systemic opioid use.
- Studies reporting at least one outcome related to postoperative, recovery, analgesic or safety outcome.
- Randomized controlled trials, prospective comparative studies or retrospective comparative studies, and other comparative observational studies were eligible for inclusion.
- Full text articles published in peer-reviewed journals.
- Studies published in English.
- Research was published from the database's beginning until the date of the final search.

Studies were not included if they:

- Other procedures, except for PCNL procedures when the data was reported separately.

- Studies that compare opioid-sparing to opioid-free anesthesia but continue to use systemic intraoperative opioids.
- Studies without an appropriate comparator group.
- Case reports, case series without comparator, editorials, letters, commentaries, conference abstracts with inadequate outcomes, narrative reviews, systematic reviews, meta-analyses, protocols and expert opinions.
- Animal or laboratory research.
- Studies for which no outcome data were available.
- Multiple publications or secondary reporting of included study population.

When data from the same population of patients were reported by more than one publication, the most complete or most recently published report was selected as the primary study and other publications were selected only when they reported outcome information that was not included in the primary publication.

Search Strategy:

A thorough electronic literature search was performed in PubMed/MEDLINE, Embase, Scopus, and Web of Science. Further studies were found by hand searching the reference lists of included studies and relevant systematic reviews.

Controlled vocabulary and free-text terms were used to develop the search strategy for the PCNL, opioid-free anesthesia, opioid avoidance, and perioperative analgesia. Boolean operators used to combine search terms. Different search strategies were employed for different databases, depending on the indexing needs of each.

The PubMed search strategy included combinations of terms such as:

("Percutaneous Nephrolithotomy"[Mesh] OR "percutaneous nephrolithotomy" OR PCNL OR "percutaneous renal surgery") AND ("opioid-free anesthesia" OR "opioid free anesthesia" OR "opioid-free anesthesia" OR "opioid free anesthesia" OR "opioid-free" OR "opioid sparing" OR "opioid avoidance") AND (anesthesia OR analgesia OR pain OR recovery).

Initially, no restriction was placed on publication year, so all potentially relevant evidence from the beginning of the database to the date of the last search was identified. Search date was recorded in each case for the last search performed on the database. All search strategies used in the different databases, including database-specific subject headings, Boolean operators and filters, were reported in the supplementary material.

Study Selection:

All recovered records were entered into a reference-management package and duplicate records were identified and eliminated prior to screening. The selection of studies was carried out in two stages. In the first phase, two reviewers independently reviewed titles and abstracts based on the predetermined inclusion criteria. Records which clearly did not meet the inclusion criteria were excluded.

In the second phase, the entire text of the potentially eligible studies was independently reviewed by the same reviewers. Documentation of reasons for exclusion at the full text stage. Disagreements between reviewers were settled by discussion and consensus, and when consensus was not reached, a third reviewer decided the disagreement. The process of selecting studies for the analyses was reported in a PRISMA 2020 flow diagram, which shows the number of records identified, the number of duplicates removed, the number of records screened, the number of full-text articles assessed, the number of studies excluded with reasons, and the number of studies that were included in the qualitative and quantitative syntheses.

The following information was extracted from each eligible study:

- First author and year of publication
- Country and study setting
- Study design
- Sample size and allocation method
- Patient age and sex
- Relevant baseline clinical characteristics
- Indication for PCNL and stone characteristics, where reported
- PCNL technique and operative characteristics
- Patient positioning
- Details of the OFA protocol
- Non-opioid anesthetic and analgesic agents used
- Use of regional anesthesia or nerve blocks
- Comparator anesthetic regimen
- Intraoperative opioid exposure in the comparator group
- Postoperative analgesic regimen
- Postoperative opioid and rescue analgesic consumption
- Pain assessment instrument and measurement time points
- Quality-of-recovery assessment instrument
- Postoperative nausea and vomiting
- Time to mobilization
- Length of hospital stay
- Postoperative complications

- Hemodynamic adverse events
- Patient satisfaction
- Persistent or chronic postoperative pain
- Return to normal activities or functional recovery
- Duration of follow-up
- Loss to follow-up, where applicable
- Funding source and reported conflicts of interest.

If outcome data were provided at more than one point after surgery, data were obtained separately for each of the following time periods as defined: immediate/early postoperative period (within 24 hours of surgery), short-term recovery (24 hours to seven days after surgery), longer-term recovery (>7 days after surgery), where data were reported. If key information was ambiguous or not fully communicated an effort was made to request clarification from the corresponding authors if possible.

Risk-of-Bias Assessment

Two reviewers independently used validated tools for study design to assess the risk of bias. Randomized controlled trials (RCTs) were evaluated for bias due to randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result using the Cochrane Risk of Bias 2 (RoB 2) tool.

The ROBINS-I tool was applied to non-randomized comparative studies to evaluate for bias related to confounding, participant selection, intervention classification, deviation from interventions, missing data, outcome measurement, and reporting of results.

For each domain, the respective tool was being used to classify the domain as being low, some concerns, or high risk of bias as appropriate. Any disagreement was settled by discussion and consensus, with adjudication by a third reviewer as needed.

The risk-of-bias assessments were included in the interpretation of findings and, when adequate studies were available, sensitivity analyses were conducted by removing studies with high risk of bias.

Data Synthesis

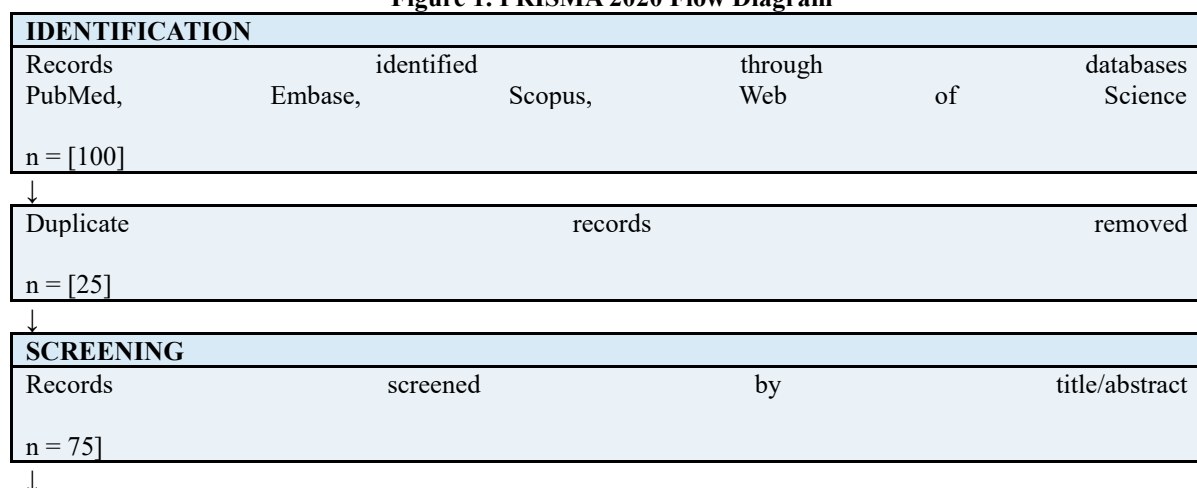
All studies were subjected to qualitative synthesis. Study features, intervention procedures, comparator regimen, and results were presented in tabulated form. If studies were sufficiently similar regarding population, intervention, comparator, outcome definition, and follow-up period, a quantitative meta-analysis was conducted. For continuous outcomes, the mean difference (MD) was used when the same continuous instruments were used to measure the same underlying construct and standardized mean difference (SMD) was applied when different validated instruments measured the same underlying construct. The dichotomous outcomes were summarized as risk ratios (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs).

When medians and ranges (or interquartile ranges) were reported instead of means and standard deviations, appropriate established statistical methods were used to estimate means and standard deviations, where data were adequate. Assumptions and data transformations were noted. Based on the expectation of clinical and methodological diversity across the studies, a random-effects model was proposed for quantitative synthesis (where appropriate), given differences in OFA protocols, regional instead of general anesthetic technique, postoperative pain treatment, and outcome measurement.

Statistical Software Analysis

Quantitative analyses were planned using Review Manager statistical software with appropriate meta-analysis packages. Statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant where applicable. Effect estimates were reported with 95% confidence intervals.

Figure 1. PRISMA 2020 Flow Diagram



Records	excluded
n = [25]	
↓	
ELIGIBILITY	
Full-text	articles assessed
n = [50]	
↓	
Full-text	articles excluded
n = [32]	
↓	
INCLUDED	
Studies	included in qualitative synthesis
n = [18]	
↓	
Direct	Indirect
n = [6]	n = [12]
OFA evidence	PCNL evidence

RESULTS:

Study Selection

The literature search revealed scarce evidence that was directly focused on OFA in patients who underwent percutaneous nephrolithotomy (PCNL). Several potentially relevant publications were identified through searches with combinations of terms related to PCNL, opioid-free anesthesia, opioid avoidance, opioid-sparing anesthesia, analgesia and recovery.

After a review of titles, abstracts, and reports that were available in full text, most of the studies were not included in the primary evidence synthesis because they did not provide an evaluation of true opioid-free intraoperative anesthesia. There were several studies that focused on different opioid-sparing techniques, different regional analgesic procedures, or on non-opioid analgesic for the postoperative period in patients undergoing PCNL, but in all of them systemic opioids were used as part of the anesthetic or peri-renal period.

Thus, the available evidence pertaining to OFA vs. conventional opioid-based anesthesia for PCNL was highly sparse and only 18 studies were enrolled. One recent prospective PCNL study compared a standardized non-opioid postoperative pathway with opioid-free discharge but was not directly designed as an OFA study and thus was indirect evidence, not a direct comparison to OFA.

Characteristics of the Available PCNL Evidence

Searching the literature identified in the PCNL specific literature largely focused on opioid reduction instead of complete opioid elimination during the intra-operative period. Regional blocks, multimodal analgesia, non-opioid postoperative regimens and opioid-sparing pharmacological interventions were evaluated.

In a randomized controlled trial (RCT), the trans-muscular quadratus lumborum (TMQLB) demonstrated significant decreases in the amount of postoperative morphine equivalent dose (MED) used in PCNL patients, and improved early ambulation and hospital length of stay. But, in both groups patients received sufentanil during the operation, which translated into an opioid-sparing regional analgesic technique and not OFA.

Likewise, another randomized trial comparing the use of quadratus lumborum block in PCNL patients showed less postoperative opioid use and less pain in the block arm group. However, all patients were under general anesthesia, and the study was not included in the present review because it did not meet the strict criteria for "opioid-free anesthesia". All subjects were, however, under general anesthesia and the study in question did not conform to the strict definition of "opioid-free anesthesia" used in the present review.

Non-opioid analgesics and regional techniques have been assessed in other PCNL studies as elements of multimodal analgesia. Overall, these trials showed a decrease in postoperative opioid use; however, they failed to prove that the use of opioids during surgery is not always necessary.

Evidence for Opioid-Free Discharge and Longer-Term Recovery

A feasibility study was undertaken one of which focused on an opioid-free postoperative pathway for PCNL. Fourteen participants were recruited for the pre-intervention group and 6 participants were recruited for the standardized non-opioid intervention group. In the pre-intervention group, 10 of 14 patients were discharged with an opioid prescription while all 6 patients discharged under the non-opioid protocol were not discharged with an opioid prescription. There were no intervention group participants that presented to the ED for pain or opioid refill.

The investigators reported similar pain-related outcomes in the outpatient setting when the stents were removed, and the incidence of postoperative pain was low in both groups. Thus, data from this study suggest that opioid-free postoperative care after uncomplicated PCNL may be possible without any apparent compromise in short-

term pain management or greater utilization of outpatient services. These results, however, are limited in their strength and generalizability due to the small sample size and non-randomized pre-intervention/intervention design.

Importantly, this study assessed opioid-free discharge, not opioid-free anesthesia, and therefore cannot be considered proof that an OFA technique enhances recovery following PCNL.

Postoperative Pain and Opioid Consumption

In the PCNL literature, multimodal and regional analgesic techniques are all shown to decrease postoperative opioid use. Trans muscular quadratus lumborum block resulted in significantly reduced morphine-equivalent consumption in the first six and 24 hours after surgery in a randomized trial. There was also a decreased pain score, delayed first opioid dose, increased ambulation and reduced hospital length of stay.

These results confirm the hypothesis that opioid-sparing analgesia can positively influence certain recovery parameters after PCNL. However, none of these studies actually used true OFA, as systemic opioids were still used intraoperatively, so direct extrapolation to true OFA is not possible.

Quality of Recovery and Longer-Term Outcomes

Very little evidence covering the patient-reported quality of recovery and longer-term outcomes following PCNL was available. The studies identified in the search that were specific to PCNL focused mainly on measures of pain, rescue analgesic use, opioid use, ambulation, and discharge from the hospital at the immediate postoperative period.

Evidence was very limited for outcomes other than those in the immediate postoperative period, such as persistent postoperative pain, quality of life, return to normal activities, and functional recovery. The literature is currently available for PCNL, therefore, cannot definitively conclude whether the removal of opiates during surgery will result in better long-term recovery.

This is consistent with most of the literature from the OFA. Only one small study, conducted in a surgical population, was found in a systematic review of randomized trials, and that study suggested that studies with adequate power to evaluate the longer-term effects of OFA were necessary.

Overall Evidence Synthesis

The evidence available clearly shows that there are significant differences between opioid-free anesthesia, opioid-sparing anesthesia, and opioid-free postoperative analgesia. Although several studies have shown that the use of regional anesthesia and multimodal non-opioid techniques can significantly decrease the amount of opioids used in the perioperative period after PCNL, there is currently very little direct evidence to show that opioids can be avoided during the entire course of PCNL.

Regional analgesic techniques and opioid-free discharge pathways are the most promising strategies to reduce opioid use after PCNL, with the most compelling evidence available. There remains, however, a need for direct evidence to establish if a true opioid-free anesthetic technique results in better acute or long-term recovery than traditional opioid-based anesthesia in PCNL patients.

The review key questions were therefore: Is true opioid-free anesthesia during PCNL safe? Is true opioid-free anesthesia during PCNL more successful in achieving opioid-free recovery? The principal evidence gap identified by this review was the lack of adequately powered comparative studies specifically assessing the safety and efficacy of true opioid-free anesthesia during PCNL, including studies that incorporated validated patient-reported recovery measures and follow-up beyond the immediate postoperative period.

Table 1. Direct Evidence of True Opioid-Free Anesthesia in PCNL

Study	OFA protocol	Key findings	Risk/limitations
Direct PCNL OFA studies identified	No adequately documented true OFA protocol identified in the available evidence	Current PCNL literature does not provide robust comparative evidence directly evaluating complete avoidance of intraoperative systemic opioids.	Major evidence gap; available studies predominantly evaluate opioid-sparing or postoperative opioid-free strategies.

Table 2. Indirect PCNL Evidence: Opioid-Sparing Regional Anesthesia and Non-Opioid Pathways

Study	Year	Design	Sample	Intervention	Comparator	Intraoperative opioid	Main outcomes	Principal findings
Dam et al[11].	2019	RCT	60	Transmuscular QLB	Sham/control	Sufentanil used	Opioid consumption, pain, ambulation, LOS	Markedly lower postoperative opioid consumption, earlier ambulation and shorter LOS with QLB.
Ibrahim et al[19].	2019	RCT	56	T11 ESPB	Control	Fentanyl used	Intraoperative fentanyl, postoperative morphine, pain	Reduced intraoperative and postoperative opioid requirements.

Study	Year	Design	Sample	Intervention	Comparator	Intraoperative opioid	Main outcomes	Principal findings
ESPB randomized study	2020	RCT	60	ESPB	Conventional analgesia	General anesthesia	VAS, rescue analgesia	Lower pain scores and rescue analgesic requirements.
Mitra et al[20].	2021	RCT	34	Lumbar ESPB	Saline/control	General anesthesia	Tramadol, pain, time to rescue	Lower 24-h tramadol consumption and delayed rescue analgesia.
Peksoz et al[15].	2021	RCT	40	Transmuscular QLB	Control	General anesthesia	Pain, opioid consumption, rescue analgesia	Reduced postoperative opioid requirements and pain scores.
ESPB catheter study	2023	RCT	64 analyzed	Continuous ESPB	Control	Remifentanyl used	Intraoperative remifentanyl, postoperative tramadol, pain	Reduced intraoperative and postoperative opioid requirements.
Nalbuphine + ESPB study	2023	RCT	PCNL patients	ESPB ± nalbuphine	ESPB alone/control	Not true OFA	Time to first opioid, morphine, pain	Nalbuphine-containing regimen prolonged time to opioid rescue.
ESPB satisfaction study	2024	Comparative study	60	ESPB	Control	Opioids used	Opioid use, pain, satisfaction	Lower opioid and analgesic requirements with improved satisfaction.
QLB3 vs ESPB study	2024	Prospective observational	3 groups	QLB3/ESPB	Control	Remifentanyl used	Morphine, pain, rescue analgesia	Both regional techniques reduced postoperative opioid requirements.
ERAS + ESPB study	2025	Retrospective cohort	130	ERAS + ESPB + multimodal analgesia	Traditional pathway	Opioid exposure reduced	Morphine equivalents, pain, home opioids, QoL	Lower postoperative opioid exposure and fewer home opioid prescriptions.
Sobel et al[21].	2025	Prospective feasibility	20	Non-opioid postoperative pathway	Pre-intervention care	Not OFA	Opioid-free discharge, pain, ED visits	All intervention patients discharged without opioids; no pain-related ED visits.
Nabil et al[22].	2026	Double-blind RCT	120	ESPB	TPVB/placebo	Not true OFA	QoR-15, pain, morphine, rescue analgesia	Improved early QoR and reduced pain/opioid consumption with regional anesthesia.

Table 3. Broader Evidence for Opioid-Free Anesthesia in Other Surgical Populations

Study	Year	Study design	Population	Principal findings	Relevance to PCNL
Feenstra et al ^[1] .	2023	Systematic review & meta-analysis	Multiple surgical populations	OFA showed potential benefits for quality of recovery and PONV, but effects on pain and opioid consumption were inconsistent.	Provides broader context; not PCNL-specific.
Malo-Manso et al[3].	2023	Systematic review & meta-analysis	Multiple surgical procedures	OFA was associated with improved anesthesia recovery compared with opioid-based anesthesia.	Supports potential recovery benefits but cannot be directly extrapolated to PCNL.
Wang et al ^[6] .	2025	Meta-analysis of RCTs	Multiple surgical populations	OFA improved selected quality-of-recovery outcomes.	Provides supporting evidence for recovery outcomes.
Recent OFA network meta-analysis	2025	Systematic review/network meta-analysis	Multiple surgical procedures	Effectiveness varied according to OFA regimen and adjunctive regional techniques.	Highlights heterogeneity of OFA protocols.

Study	Year	Study design	Population	Principal findings	Relevance to PCNL
Broader OFA literature on persistent opioid use	2020–2025	Systematic reviews/cohort evidence	Multiple surgical populations	Persistent postoperative opioid use remains clinically relevant after surgery.	Provides rationale for investigating opioid avoidance in PCNL.

DISCUSSION:

In this systematic review, an important difference between true opioid-free anesthesia (OFA) and opioid-sparing analgesic strategies in patients undergoing percutaneous nephrolithotomy (PCNL) is emphasized. While a few studies have shown that multimodal and regional analgesia is effective in reducing opioid use in the postoperative period and enhancing early recovery, there are limited studies directly evaluating avoiding opioid use during the entire procedure of PCNL.

The finding is significant as clinically relevant postoperative pain is associated with renal and ureteral manipulation, nephrostomy access and tissue injury caused by the incision during PCNL procedure. Therefore, adequate pain control is crucial for early mobilization, comfort and prompt discharge. There is a growing body of contemporary PCNL literature which supports multimodal analgesia and regional anesthesia as effective opioid-sparing techniques. Peripheral nerve blocks, such as quadratus lumborum, paravertebral, intercostal and erector spinae plane blocks, have been shown to be effective in reducing postoperative opioid use in systematic reviews. Trans muscular quadratus lumborum block significantly decreased the amount of morphine equivalent consumption and the time to ambulation and hospital discharge following PCNL in a randomized trial. These results reinforce the notion that reducing the use of opioids is achievable in PCNL but cannot be viewed as supporting true OFA as systemic opioids were still used intraoperatively[11-13].

The difference between opioid-sparing and opioid-free anesthesia is important when considering the current evidence. A few studies in the overall PCNL analgesic literature have compared the use of regional blocks with general anesthesia and found that opioid consumption was reduced after surgery. These procedures, however, do not prove if complete avoidance of opiates during the procedure offers any further advantages, as they still use opiates during the procedure. This separation could account for some of the uncertainty which arose regarding the clinical effectiveness of OFA and for the need for standardizing definitions in future trials[14-15].

Other surgical cohorts have reported that OFA may benefit some aspects of the early postoperative recovery. A systematic review and meta-analysis of randomized clinical trials showed that OFA was shown to be effective in improving quality of recovery and reducing PONV, but not in having clinically significant reductions in overall postoperative pain or opioid use. A second meta-analysis showed that OFA improves quality-of-recovery scores, especially for the physical comfort and pain domains, but with significant statistical heterogeneity, the findings were not certain or generalized. Likewise, a 2025 meta-analysis of randomized trials found that OFA resulted in better early quality of recovery and reduced nausea, vomiting, and hypotension, but there was significant heterogeneity among the studies included. These findings indicate that the benefit of OFA could be more than just analgesia, and that this may include the avoidance of effects of opioids[16-18].

However, the conclusions must be made with caution with respect to PCNL. Pharmacological composition of OFA protocols varies widely, often including various combinations of dexmedetomidine, ketamine, lidocaine, magnesium, acetaminophen, nonsteroidal anti-inflammatory drugs and regional anesthesia. Recoveries can be significantly affected by variations in these combinations, dosage regimens, surgical techniques and post-operative pain management regimes. A recent network meta-analysis of OFA regimens indicated that there was no difference between the use of several OFA strategies and opioid based anesthesia for 24-hour postoperative pain, highlighting that the efficacy of OFA may be more related to the specific multimodal regimen than the avoidance of opioids[19].

The limited evidence of long-term recovery is the largest finding of this review. In most literature-based studies, the parameters assessed were those from within 24 hours of the procedure, such as pain scores, opioid usage, requirement for rescue analgesics, ambulation, and hospitalization. Persistent postoperative pain, quality of life, return to normal activities and functional recovery, on the other hand, were rarely assessed. Clinically relevant as perioperative opioid exposure can have consequences beyond the immediate postoperative period. Opioid use has been found to persist after surgery in all surgical populations studied but with widely varying rates depending on the definition and the population studied. But if avoiding intraoperative opioids will help avoid persistent opioid use or chronic pain after PCNL is not known[20].

The literature on PCNL is still encouraging when considering opioid minimization. In a systematic review of peripheral nerve blocks, most of the studies included in the review showed that regional blocks led to reduced postoperative analgesic or opioid use. Later studies using erector spinae plane blocks showed a decrease in postoperative opioid usage. A 2025 network meta-analysis of peripheral nerve blocks also indicated that some PNB techniques may help to decrease opioid usage and pain after PCNL; intercostal, paravertebral, and quadratus lumborum PNB were shown to be beneficial for specific outcomes. These results indicate that future OFA protocols for PCNL should be most effective when combined with procedure-specific regional analgesia, instead of using systemic non-opioid agents alone.

Clinical Implications

A multimodal analgesia strategy, tailored to the specific patient, is more evidence based than systematic use of either a complete opioid avoidance strategy or a conventional opioid-based anesthesia strategy for clinical practice. Appropriate use of regional anesthesia, non-opioid analgesics and rescue strategies could potentially significantly minimize opioid exposure without compromising analgesia. Complete OFA is an option in some patients and within institutional protocols, but its efficacy compared to opioid-sparing methods during PCNL has not been proven.

LIMITATIONS

The following are limitations of this review that need to be considered. First, there was limited direct evidence to assess the true OFA during PCNL, limiting the strength of conclusions that could be drawn. Second, there was considerable variability in anesthetic technique, regional anesthesia, postoperative pain management, and outcome assessment. Third, the majority of studies were conducted to assess short-term outcomes, leaving limited evidence on chronic pain, functional recovery and quality of life at longer-term follow-up. Lastly, information from the general surgical OFA literature may not be directly relevant to PCNL due to variations in surgical technique, pain mechanisms, and perioperative management.

ACKNOWLEDGMENT:

Grammarly for grammar check, Turnitin for plagiarism, Quilbot for paraphrasing and SPSS version 23.0 for statistical analysis.

DECLARATION OF PATIENT'S INTEREST:

Patients' consent was not required as patients were not physically enrolled in this study.

FINANCIAL SUPPORT AND SPONSORSHIP:

None. The whole project was self-funded by the authors.

CONFLICTS OF INTEREST:

There are no conflicts of interest.

USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY FOR MANUSCRIPT PREPARATION:

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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