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The Role of Opioid-Sparing Anesthesia and Analgesia Strategies in Urological Surgery

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Abstract. ***Background:*** Opioid-sparing anesthesia and analgesia are being increasingly incorporated into perioperative care in urological surgery because of concerns regarding opioid-related adverse effects and the need to facilitate early postoperative recovery.

Objective: The aim of this narrative review was to summarize recent evidence regarding the effectiveness, safety, and clinical applicability of opioid-sparing and multimodal analgesic strategies in adult patients undergoing urological procedures, with particular attention to the pharmacological and regional techniques used during the intraoperative and postoperative periods.

Materials and Methods: A narrative literature review was conducted using the *PubMed* and *Cochrane Library* databases. Publications from 2021 to 2026 were considered. The search strategy included combinations of the terms 'opioid-sparing anesthesia', 'opioid-free anesthesia', 'multimodal analgesia', 'enhanced recovery after surgery', 'postoperative pain', and 'opioids', combined with urology-related terms such as 'urology', 'nephrectomy', 'prostatectomy', 'cystectomy', and 'ureteroscopy'. Following the application of publication type filters, 111 records were identified in *PubMed* and 159 in the *Cochrane Library*. After assessment of relevance and eligibility, 25 publications were included in the narrative synthesis. The selected literature comprised randomized controlled trials, observational studies, systematic reviews, meta-analyses, and guidelines addressing perioperative analgesic management and opioid-reduction strategies in urological surgery.

Results: The available evidence indicates that multimodal opioid-sparing strategies can reduce opioid exposure at different stages of perioperative care while maintaining adequate postoperative analgesia in several urological procedures. The evaluated approaches differed in their timing and components: some studies investigated intraoperative opioid-sparing anesthesia using agents such as ketamine, esketamine, dexmedetomidine, and lidocaine, whereas others focused on postoperative analgesia, opioid prescribing, or regional techniques. Urology-specific studies demonstrated that non-opioid multimodal regimens can provide pain control comparable to opioid-based approaches after robot-assisted radical prostatectomy, while opioid-limiting protocols may reduce opioid use after transurethral resection of the prostate. Regional techniques, including transversus abdominis plane (TAP), quadratus lumborum (QL), and erector spinae plane (ESP) blocks, as well as local anesthetic infiltration, may further reduce early postoperative pain and opioid requirements. Evidence concerning dexmedetomidine, ketamine, and other non-opioid agents suggests potential opioid-sparing effects in selected urological procedures, although the available evidence remains heterogene-

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ous across surgical settings and analgesic protocols. Opioid reduction may also be associated with less nausea and vomiting, earlier functional recovery, and reduced opioid prescribing at discharge. However, current evidence does not demonstrate consistent superiority of complete opioid-free anesthesia over individualized opioid-sparing strategies, particularly for procedures associated with substantial postoperative pain.

Conclusions: Opioid-sparing multimodal analgesia represents a useful component of perioperative care in urological surgery. The available evidence supports reducing unnecessary opioid exposure through combinations of systemic non-opioid medications, regional anesthesia techniques, and individualized rescue analgesia. Interpretation of the findings requires consideration of whether the investigated interventions were administered intraoperatively, postoperatively, or throughout the perioperative period. The optimal analgesic regimen should be individualized according to the surgical procedure, expected pain intensity, comorbidities, previous opioid exposure, and contraindications to individual analgesic agents. Complete opioid avoidance should not be considered an obligatory endpoint, and a limited amount of rescue opioid therapy may remain appropriate when clinically indicated. Further procedure-specific randomized trials are required to establish optimal combinations and dosing strategies.

Keywords: opioid-sparing anesthesia, urology, multimodal analgesia.

Opioidus tausojančių ir analgezijos strategijų pritaikymas urologinėms operacijoms

Santrauka. ***Įvadas:*** Opioidų poreikį mažinantys anestezijos metodai tampa vis svarbesne urologinės chirurgijos perioperacinės priežiūros dalimi dėl siekio sumažinti nepageidaujamą opioidų vartojimo poveikį ir pagerinti pacientų pooperacinį atsistatymą.

Tikslas: Šios naratyvinės apžvalgos tikslas – apibendrinti naujausius duomenis apie opioidus tausojančių ir multimodalinių analgezijos strategijų efektyvumą, saugumą bei klinikinį pritaikymą suaugusiems pacientams, kuriems atliekamos urologinės operacijos, ypatingą dėmesį skiriant intraoperaciniu ir pooperaciniu laikotarpiu naudojamiems farmakologiniams bei regioninės anestezijos metodams.

Tyrimo medžiaga ir metodai: Atlikta naratyvinė literatūros apžvalga, naudojantis „PubMed“ ir „Cochrane Library“ duomenų bazėmis. Buvo vertinamos 2021–2026 m. publikacijos, naudojant raktažodžių *„opioid-sparing anesthesia“, „opioid-free anesthesia“, „multimodal analgesia“, „enhanced recovery after surgery“, „postoperative pain“* ir *„opioids“* derinius su urologija susijusiais raktažodžiais *„urology“, „nephrectomy“, „prostatectomy“, „cystectomy“* ir *„ureteroscopy“*. Pritaikius publikacijų tipų filtrus, „PubMed“ duomenų bazėje identifikuota 111 įrašų, o „Cochrane Library“ – 159 įrašai. Įvertinus publikacijų tinkamumą ir atitiktį atrankos kriterijams, į naratyvinę sintezę įtrauktos 25 publikacijos. Atrinktą literatūrą sudarė atsitiktinių imčių kontroliuojamieji tyrimai, stebėjimo tyrimai, sisteminės apžvalgos, metaanalizės ir gairės, nagrinėjančios perioperacinės analgezijos valdymą ir opioidų vartojimo mažinimo strategijas urologinėje chirurgijoje.

Rezultatai: Turimi duomenys rodo, kad multimodalinės opioidus tausojančios strategijos gali sumažinti perioperacinį opioidų vartojimą ir kartu užtikrinti adekvačią pooperacinio skausmo kontrolę atliekant įvairias urologines operacijas. Tirtos strategijos skyrėsi pagal taikymo laiką ir sudėtį: dalyje tyrimų vertinti intraoperaciniai opioidų poreikį mažinantys anestezijos metodai, apimantys ketamino, esketamino, deksmedetomidino ar lidokaino vartojimą, o kituose tyrimuose daugiausia analizuota pooperacinė analgezija, opioidų skyrimas arba regioninės anestezijos metodai. Urologijoje atlikti randomizuoti tyrimai parodė, kad po robotinės radikaliosios prostatektomijos neopioidinės multimodalinės strategijos gali užtikrinti skausmo kontrolę, panašią į opioidais pagrįstų metodų, o po transuretrinės prostatos rezekcijos opioidų vartojimą ribojantys protokolai gali sumažinti jų suvartojimą. Regioninės anestezijos metodai, įskaitant skersinio pilvo raumens plokštumos (angl. *transversus abdominis plane,* TAP), kvadratinio juosmens raumens (angl. *quadratus lumborum,* QL) ir nugaros tiesiamojo raumens plokštumos (angl. *erector spinae plane,* ESP) blokadas bei vietinių anestetikų infiltraciją, taip pat gali sumažinti ankstyvą pooperacinį skausmą ir opioidų poreikį. Duomenys apie deksmedetomidiną, ketaminą ir kitus neopioidinius medikamentus rodo opioidų poreikio sumažėjimą atliekant tam tikras urologines procedūras, nors esami įrodymai išlieka prieštaringi ir priklauso nuo chirurginių metodų ir nuskausminimo protokolų. Mažesnis opioidų vartojimas taip pat gali būti susijęs su retesniu pykinimu ir vėmimu, ankstesniu funkcijų atkūrimu bei mažesniu opioidų skyrimu išrašant iš stacionaro. Vis

dėlto dabartiniai duomenys neleidžia teigti, kad anestezija be opioidų vartojimo yra pranašesnė už opioidus tausojančią strategiją, ypač atliekant operacijas, susijusias su didesniu pooperaciniu skausmu.

Išvados: Opioidus tausojanti multimodalinė analgezija yra naudinga perioperacinės priežiūros dalis urologinėje chirurgijoje. Turimi duomenys pagrindžia galimybę sumažinti nereikalingą opioidų vartojimą derinant sisteminius neopioidinius analgetikus, regioninės anestezijos metodus ir individualizuotą gelbstinčiąją analgeziją. Vertinant tyrimų rezultatus svarbu atsižvelgti į tai, ar analgezijos intervencijos buvo taikytos intraoperaciniu, pooperaciniu, ar visu perioperaciniu laikotarpiu. Optimali analgezijos schema turėtų būti individualizuojama atsižvelgiant į operacijos pobūdį, numatomą skausmo intensyvumą, gretutines ligas, ankstesnį opioidų vartojimą ir konkrečių analgetikų kontraindikacijas. Visiškas opioidų atsisakymas neturėtų būti privalomas analgezijos tikslas. Tais atvejais, kai neopioidinės skausmo malšinimo priemonės neužtikrina pakankamos skausmo kontrolės, kliniškai pagrįstas papildomas opioidų skyrimas išlieka tinkama ir pagrįsta gydymo strategija. Reikėtų tolesnių tyrimų, siekiant nustatyti optimalius analgetikų derinius ir jų dozavimo strategijas.

Raktažodžiai: opioidų poreikį mažinanti anestezija; urologija; multimodalinė analgezija.

Introduction

Postoperative pain management is an important component of contemporary anesthesiology and perioperative medicine. Inadequate analgesia may impair mobilization and functional recovery, whereas excessive exposure to opioids may result in nausea, vomiting, gastrointestinal dysfunction, urinary retention, and other adverse effects [1]. These considerations are particularly relevant in urological surgery, where the spectrum of procedures ranges from minimally invasive endoscopic interventions to extensive robotic and open oncological operations.

Opioid-sparing anesthesia aims to reduce perioperative opioid exposure while maintaining adequate analgesia. Rather than relying on a single analgesic class, this approach generally combines agents with different mechanisms of action and, when appropriate, regional anesthesia techniques [2,3]. The rationale is to achieve adequate analgesia through complementary mechanisms while reducing the dose and potential adverse effects of individual drugs.

The concept of opioid-sparing analgesia is closely related to *Enhanced Recovery After Surgery* (ERAS) pathways. Within ERAS pathways, opioid-sparing analgesic strategies have been associated with reduced opioid use and, in some urological procedures, a shorter hospital stay [4]. Nevertheless, analgesic management represents only one component of ERAS, and improvements in postoperative outcomes cannot necessarily be attributed to analgesic therapy alone.

Urological surgery provides an appropriate setting in which to evaluate opioid-sparing strategies because procedures differ considerably in surgical trauma and expected postoperative pain [1,2]. Transurethral procedures may require relatively limited postoperative analgesia, whereas radical prostatectomy, radical cystectomy, nephrectomy, and complex reconstructive procedures may result in more substantial pain and functional impairment. Therefore, a single analgesic protocol is unlikely to be optimal for all urological procedures.

The increasing use of laparoscopic and robotic approaches has further changed perioperative analgesic requirements. Although minimally invasive surgery generally reduces tissue trauma and accelerates recovery, clinically relevant postoperative pain may still occur. Regional anesthesia techniques and multimodal pharmacological approaches have consequently become increasingly relevant in minimally invasive urological surgery.

The aim of this narrative review was to evaluate current evidence on opioid-sparing anesthesia and analgesia in urological surgery, with a particular focus on the timing and components of analgesic interventions, including intraoperative pharmacological strategies, regional anesthesia techniques, and postoperative pain management.

Materials and Methods

Study Design

A narrative literature review was performed because the available evidence regarding opioid-sparing anesthesia in urological surgery is heterogeneous with respect to surgical procedures, analgesic interventions, study populations, and outcome measures. The review focused primarily on adult patients undergoing urological procedures in whom multimodal, opioid-sparing, or opioid-free analgesic strategies were evaluated.

Literature Search

The literature search was performed using *PubMed* and the *Cochrane Library*. Publications from 2021 to 2026 were considered. The search strategy included combinations of the terms 'opioid-sparing anesthesia', 'opioid-free anesthesia', 'multimodal analgesia', 'enhanced recovery after surgery', 'postoperative pain', and 'opioids', together with urology-related terms, including 'urology', 'nephrectomy', 'prostatectomy', 'cystectomy', and 'ureteroscopy'. Boolean operators AND and OR were used to combine the search terms.

After applying the selected publication type filters, 270 records were retrieved from the two databases: 111 from *PubMed* and 159 from the *Cochrane Library*. The search aimed to identify randomized controlled trials, systematic reviews, meta-analyses, and observational studies evaluating opioid-sparing strategies in adult patients undergoing urological surgery. Relevant perioperative guidelines were also considered when they provided additional clinical context for the interpretation of urology-specific evidence.

Eligibility and Evidence Selection

Studies were considered relevant when they evaluated adult patients undergoing urological surgery and assessed at least one clinically relevant outcome, including postoperative pain, opioid consumption, opioid prescribing, opioid-related adverse effects, recovery, mobilization, gastrointestinal recovery, the length of hospital stay, or the quality of recovery.

Studies evaluating interventions administered during different phases of perioperative care were considered. These included preoperative or intraoperative administration of non-opioid medications, regional anesthesia techniques performed before or during surgery, local anesthetic infiltration, and postoperative analgesic regimens or opioid-prescribing strategies. The timing of each intervention was considered when interpreting and comparing study findings.

Urology-specific studies involving adult patients undergoing surgical procedures were prioritized. Pediatric studies, individual case reports, conference abstracts, and publications without sufficient information for interpretation were excluded.

A total of 25 publications were used in the narrative synthesis. Due to the fact that the studies differed substantially in surgical procedures, interventions, patient populations, comparators, and outcome measures, no quantitative meta-analysis was performed.

Results and Discussion

Opioid Consumption and Postoperative Pain

The most consistent finding across the available literature is that opioid-sparing interventions can reduce perioperative opioid exposure without necessarily compromising postoperative analgesia. Importantly, evidence directly derived from urological populations supports this conclusion.

A randomized controlled trial involving patients undergoing transurethral resection of the prostate evaluated an opioid-limiting multimodal protocol incorporating ibuprofen, opioid-use education, and avoidance of routine opioid prescription at discharge. The study demonstrated that opioid use could be reduced through a structured multimodal approach without deterioration in clinically relevant pain outcomes [5]. Unlike studies comparing different anesthetic regimens, this intervention primarily targeted postoperative opioid prescribing and use after discharge. These findings are particularly relevant for procedures in which postoperative opioid requirements are relatively low, and routine opioid prescribing may result in unnecessary exposure.

More extensive evidence is available from robot-assisted radical prostatectomy. Lee et al. compared a non-opioid multimodal analgesia protocol with morphine-based patient-controlled analgesia in 80 patients undergoing robot-assisted radical prostatectomy. The non-opioid protocol included pregabalin, intravenous paracetamol, bilateral quadratus lumborum block, and pudendal nerve block. Pain scores were not significantly different between groups, demonstrating non-inferiority of the multimodal approach, while more than half of the patients in the non-opioid group did not require opioid agonists during the initial 48 hours [6]. This intervention combined systemic medication with regional anesthesia and evaluated postoperative analgesia and opioid requirements. It should therefore be distinguished from protocols primarily targeting intraoperative opioid administration.

The findings are supported by a systematic review and meta-analysis of interventions designed to reduce opioid prescription following urological surgery. The analysis included more than 8,000 patients and demonstrated a significant reduction in opioid prescriptions and opioid consumption following implementation of various interventions, without a significant deterioration in patient satisfaction with analgesia. Importantly, the interventions included not only pharmacological changes but also provider-directed prescribing strategies and patient education [7]. This suggests that opioid reduction in urology is not exclusively a pharmacological issue, and that prescribing practices themselves represent an important target.

A further distinction is necessary between reducing opioid administration during surgery and reducing opioid use during postoperative recovery. Some studies assess intraoperative opioid consumption as an indicator of anesthetic requirements, whereas others evaluate postoperative pain scores, rescue analgesia, or opioid prescriptions after discharge. These outcomes reflect different aspects of pain management and should not be considered interchangeable. Importantly, the clinical approach should focus on avoiding unnecessary opioid exposure while retaining rescue opioids when non-opioid analgesia is insufficient [8].

Multimodal Analgesia in Urological Surgery

Multimodal analgesia involves the combination of analgesic interventions with complementary mechanisms of action. In urological surgery, commonly used components include paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, regional anesthesia techniques, and selected intravenous agents such as ketamine or dexmedetomidine [9].

The evidence suggests that the effectiveness of multimodal analgesia is determined more by the overall combination and appropriate patient selection than by any single drug. This is particularly apparent in robot-assisted radical prostatectomy, where the combination of systemic non-opioid medication and regional blocks was able to provide analgesia comparable to opioid-based patient-controlled analgesia (PCA) [6].

Paracetamol is commonly included because of its established analgesic effect and relatively favorable safety profile when administered within recommended dosing limits. NSAIDs can provide additional opioid-sparing effects through inhibition of prostaglandin synthesis. However, their use should be individualized in patients with impaired renal function, gastrointestinal disease, bleed-

ing risk, or other contraindications [10]. Evidence from broader surgical populations suggests that perioperative NSAIDs administration does not necessarily result in a clinically important increase in operative bleeding, although patient selection remains important.

The role of ketamine is more selective. Perioperative ketamine acts primarily through N-methyl-D-aspartate (NMDA) receptor antagonism and may be particularly useful in patients at increased risk of substantial postoperative pain or in those with previous opioid exposure. Therefore, ketamine may be best considered as an adjunct rather than a universal component of opioid-sparing anesthesia [11,12]. In urological surgery, an esketamine-based opioid-sparing anesthesia protocol was associated with improved early postoperative recovery following laparoscopic partial or unilateral nephrectomy [11]. This study evaluated an intraoperative anesthetic protocol, while early postoperative recovery was assessed as an outcome. Esketamine has also been studied in elderly patients undergoing ureteroscopy, where its addition reduced the propofol required for successful ureteroscope insertion [13]. This finding relates primarily to intraoperative anesthetic requirements and should not be interpreted as direct evidence of reduced postoperative opioid consumption.

Dexmedetomidine may serve as an adjunct to multimodal analgesia owing to its sedative and analgesic effects. It was incorporated into an intraoperative multimodal regimen alongside ketorolac and rectus sheath blocks in patients undergoing robot-assisted prostatectomy [14]. However, its use requires careful dose individualization because of the potential for bradycardia and hypotension.

Regional Anesthesia Techniques

Regional anesthesia represents another important component of opioid-sparing strategies in urological surgery. TAP blocks, quadratus lumborum blocks, and local anesthetic wound infiltration have all been investigated in laparoscopic, robotic, and open urological procedures [3,4,15,16,17]. Depending on the procedure and study protocol, these techniques may be performed before or during surgery so that to provide perioperative analgesia and reduce the need for systemic opioids.

The available evidence suggests that regional techniques may reduce early postoperative pain and opioid requirements in selected urological procedures, although their effectiveness is not uniform across surgical approaches and block techniques. Borys et al. reported that quadratus lumborum block reduced postoperative opioid consumption in patients undergoing open and laparoscopic nephrectomy and was also associated with lower persistent postoperative pain severity [15]. The randomized design of this study provides evidence for the use of QL block in the perioperative analgesic management of nephrectomy patients, although the results should be interpreted in the context of the specific surgical approaches and analgesic protocol investigated.

Similarly, studies evaluating TAP blocks and local anesthetic infiltration have demonstrated potential benefits after robot-assisted prostatectomy [16,17]. The UROTAP randomized trial compared robot-assisted TAP block, ultrasound-guided TAP block and local anesthetic infiltration in patients undergoing urological surgery [16]. A separate randomized trial compared wound infiltration with the TAP block after laparoscopic radical prostatectomy [17]. These studies are relevant because they assess alternative regional or local analgesic techniques rather than comparing regional anesthesia with a systemic opioid regimen alone.

However, regional blocks should not be interpreted as complete substitutes for systemic analgesia. Fascial plane blocks primarily provide somatic analgesia, whereas visceral pain may persist. Their effectiveness may also depend on the exact surgical approach, block technique, local anesthetic administration, and provider experience. Consequently, the available evidence favors integration of regional anesthesia into a broader multimodal pathway rather than use of a regional technique as an isolated intervention [3,10].

Overall, the studies of regional anesthesia differ in the block performed, the comparator used, the timing of administration and the accompanying systemic analgesia. Consequently, their findings

cannot be directly compared without considering these methodological differences. The choice of a technique should be based on the surgical approach, expected pain distribution, patient characteristics, and available expertise.

Opioid-Sparing Versus Opioid-Free Anesthesia and Analgesia Approaches

Opioid-sparing and opioid-free approaches differ primarily in the extent to which opioids are used during perioperative care. Opioid-free protocols exclude opioids from the specified anesthetic or analgesic regimen, whereas opioid-sparing protocols aim to minimize opioid requirements through multimodal analgesia while allowing their use when necessary [6,11,12,18,19]. This distinction is important because an opioid-free intraoperative protocol does not necessarily mean that opioids will not be required after surgery. Similarly, a postoperative opioid-free analgesic regimen does not establish that opioids were avoided during anesthesia.

Opioid-free postoperative strategies after ureteroscopy or retrograde intrarenal surgery have been associated with reduced opioid use and favorable postoperative outcomes [18]. These findings relate specifically to postoperative analgesic management and should not be interpreted as evidence for the superiority of opioid-free intraoperative anesthesia. They suggest that complete opioid avoidance may be feasible for selected minimally invasive procedures. Moreover, the evidence is characterized by substantial heterogeneity in surgical procedures, analgesic protocols, outcome definitions, and comparator regimens. Therefore, the observed benefits cannot automatically be extrapolated to every urological operation.

Evidence regarding intraoperative opioid-free anesthesia is provided by a randomized controlled trial in patients undergoing retroperitoneoscopic renal surgery. Gao et al. compared opioid-free anesthesia combined with a QL block with opioid-based anesthesia combined with the same regional technique. The opioid-free group demonstrated better early postoperative quality of recovery, lower postoperative opioid consumption, and faster mobilization and readiness for discharge [19]. As both groups received a QL block, the comparison primarily addressed the contribution of the anesthetic regimen to outcomes within a regional analgesia protocol.

Nevertheless, major urological procedures may involve greater surgical trauma and more complex pain mechanisms. In such patients, insisting on complete opioid avoidance could potentially result in undertreated pain if the non-opioid regimen is insufficient. However, the available evidence favors an approach in which opioids are reserved for rescue treatment rather than routinely administered or prescribed [20].

Postoperative Recovery

Reduction of perioperative opioid exposure may support postoperative recovery by facilitating early mobilization, oral intake, and participation in ERAS pathways. Multimodal analgesia may therefore contribute to recovery through improved pain control while minimizing reliance on systemic opioids.

Liposomal bupivacaine injected at the time of fascial closure has been investigated in patients undergoing radical cystectomy and was associated with reduced opioid use and shorter hospital stay compared to epidural analgesia [21]. However, the hospital length of stay should be interpreted cautiously because it is influenced by numerous factors beyond analgesia, including the surgical technique, postoperative complications, ERAS implementation, mobilization, nutritional management, and institutional discharge criteria.

When interpreting these results, the timing of the intervention should be considered. Some studies evaluated an intraoperative anesthetic strategy and subsequently assessed postoperative opioid consumption, pain intensity or recovery, whereas others investigated interventions specifically targeting postoperative analgesia. In addition, postoperative recovery is influenced by regional blocks,

systemic analgesics and other ERAS components. Therefore, improvements in recovery cannot always be attributed solely to reduced intraoperative opioid administration.

Opioid-Related Adverse Effects and Safety

Perioperative opioid administration is associated with a range of dose-dependent adverse effects that are relevant to patient safety. These include nausea, vomiting, sedation, respiratory depression, gastrointestinal dysfunction, and urinary retention [1]. The incidence and clinical significance of these complications may vary according to opioid dose, route of administration, concomitant medications, and patient-related factors.

Urological patients represent a particularly relevant population because postoperative urinary function is an important clinical outcome. Although urinary retention is multifactorial and may be influenced by the surgical procedure, anesthetic technique, fluid management, and catheterization, intraoperative opioid exposure has also been identified as a potential predictor of postoperative urinary retention [22]. However, this association does not establish that a reduction of opioid administration will independently prevent urinary retention, as other perioperative factors may contribute to this outcome.

Respiratory depression is an important consideration when opioids are used in the perioperative management of patients undergoing urological surgery. In patients undergoing robot-assisted laparoscopic nephrectomy, the use of neuraxial opioids has been associated with an increased risk of respiratory depression, particularly when combined with systemic opioids [23]. Therefore, limiting systemic opioid exposure and incorporating multimodal analgesic strategies may help reduce opioid-related respiratory complications.

In urological surgery, NSAIDs are being increasingly used as part of multimodal analgesia to reduce postoperative opioid requirements, although their use requires careful consideration of renal function and the individual risk of acute kidney injury. A recent retrospective propensity score-matched cohort study included 3,359 adult patients undergoing partial or radical nephrectomy and analyzed 739 matched pairs of patients who did or did not receive NSAIDs. The study found that perioperative NSAID administration was not associated with an increased risk or severity of postoperative acute kidney injury. It also discovered shorter postoperative hospitalization among patients receiving NSAIDs [24]. These findings provide supportive evidence for the use of NSAIDs as part of opioid-sparing analgesia in appropriately selected urological patients, while emphasizing the need for individualized assessment of renal risk.

Ketamine and dexmedetomidine are also used as components of opioid-sparing anesthesia in urological surgery. In a randomized study of patients undergoing laparoscopic nephrectomy, a low-dose combination of ketamine, lignocaine, and dexmedetomidine provided analgesia and hemodynamic control comparable with fentanyl-based anesthesia, although changes in heart rate and blood pressure were observed during treatment [12]. Therefore, the safety of opioid-sparing anesthesia depends on selecting an appropriate combination of agents according to the patient's clinical characteristics rather than simply replacing opioids with multiple alternative medications. Renal function, cardiovascular status, concomitant medications, and the type and extent of the planned urological procedure should be considered when developing an individualized analgesic strategy.

Clinical Implications

The available evidence supports a procedure-specific approach to opioid-sparing analgesia in urological surgery. Analgesic regimens should be selected according to the expected intensity and duration of postoperative pain, the extent of surgical trauma, and relevant patient characteristics rather than applied uniformly across procedures [25]. The selection of an opioid-sparing strategy should also take into account the phase of perioperative care being targeted. Intraoperative approaches may

include ketamine-, lidocaine- and dexmedetomidine-based regimens, as well as esketamine-based protocols [11,12,14]. Postoperative management may include paracetamol, NSAIDs and pregabalin as components of multimodal analgesia, alongside regional techniques and individualized rescue medication [5,6,9,25]. Regional techniques can complement both phases by providing analgesia extending into the postoperative period [15–17].

The clinical objective is not complete opioid elimination in every patient, but, instead, adequate analgesia with the minimum necessary opioid exposure. Table 1 summarizes the main procedure-specific considerations for implementing opioid-sparing strategies in urological surgery.

Table 1. Procedure-specific considerations for opioid-sparing anesthesia and analgesia in urological surgery

Surgical setting	Opioid-sparing strategies	Potential clinical benefits	Main considerations
Transurethral procedures	NSAIDs, paracetamol, structured opioid-use education, avoidance of routine opioid prescription [5,25]	Reduced opioid prescribing and consumption while maintaining adequate pain control [5]	Routine opioids may be unnecessary in selected patients; NSAID use should be individualized according to renal and bleeding risk [5,25]
Robot-assisted radical prostatectomy	Multimodal non-opioid analgesia, paracetamol, regional blocks, selected adjunctive agents [6,9,14]	Reduced opioid exposure with comparable postoperative pain control; possible reduction in PONV and faster bowel recovery [6]	The analgesic combination should be adapted to the surgical approach and patient characteristics
Laparoscopic and robotic renal surgery	QL/TAP blocks, local anesthetic infiltration, ketamine/esketamine, dexmedetomidine [2,3,11,12,15,16]	Reduction of early postoperative pain and opioid requirements; potential improvement in early recovery [11,12,15,16]	Choice of technique should consider renal function, cardiovascular status, surgical approach and provider experience
Radical cystectomy	Regional/local analgesia, multimodal ERAS-based analgesia, selected use of liposomal bupivacaine [4,21]	Reduced opioid use and potential improvement in postoperative recovery [4,21]	Length of stay is influenced by multiple perioperative factors and should not be attributed to analgesia alone
Ureteroscopy / RIRS	NSAIDs/paracetamol, multimodal non-opioid analgesia, selected opioid-free postoperative regimens [18,25]	Opioid-free postoperative management may be feasible in selected minimally invasive procedures [18]	Rescue opioids should remain available when non-opioid analgesia is insufficient [18,25]
Major urological surgery with substantial expected pain	Multimodal analgesia, regional techniques, appropriately titrated rescue opioids [8,18,20]	Reduction of unnecessary opioid exposure while maintaining adequate analgesia	Complete opioid avoidance should not be considered mandatory; treatment should be individualized according to expected pain, previous opioid exposure, and comorbidities [8,20]

Abbreviations in use: NSAIDs, nonsteroidal anti-inflammatory drugs; QL, quadratus lumborum; TAP, transversus abdominis plane; PONV, postoperative nausea and vomiting; ERAS, enhanced recovery after surgery; RIRS, retrograde intrarenal surgery.

Limitations

This review has several limitations. First, it was designed as a narrative review rather than a systematic review or meta-analysis, and therefore the selection and interpretation of the available literature may be subject to selection bias.

Second, the included publications were heterogeneous with respect to surgical procedures, patient populations, analgesic protocols, comparators, and outcome measures. The interventions also

differed in their timing and purpose: some studies investigated intraoperative anesthetic regimens and intraoperative opioid consumption, whereas others assessed postoperative analgesia, opioid prescribing, or outcomes across the perioperative period. Furthermore, the pharmacological combinations and regional anesthesia techniques varied between studies. This heterogeneity makes direct comparison between individual analgesic interventions difficult.

Third, the literature search was restricted to publications from 2021 to 2026. This approach was chosen to emphasize contemporary evidence but may have excluded earlier studies that still remain relevant to established regional anesthesia and multimodal analgesia techniques.

Finally, postoperative recovery is influenced by multiple components of perioperative care, including surgical approach, ERAS implementation, patient characteristics, nutritional management, mobilization, fluid therapy, prevention of postoperative nausea and vomiting, and discharge practices. Consequently, the independent contribution of opioid-sparing anesthesia to outcomes such as the length of stay or the overall recovery cannot always be established.

Conclusions

Current evidence supports opioid-sparing multimodal analgesia as an effective component of perioperative care in urological surgery. Urology-specific studies indicate that multimodal non-opioid strategies can reduce perioperative opioid requirements while maintaining adequate postoperative pain control. Regional techniques may provide additional opioid-sparing benefits in selected procedures.

Reduced opioid exposure may contribute to improved early postoperative recovery and lower opioid-related adverse effects, although evidence regarding hospital length of stay, postoperative complications, and longer-term outcomes remains heterogeneous.

The available evidence encompasses different types of interventions, including intraoperative opioid-sparing anesthetic regimens, postoperative multimodal analgesia, regional anesthesia and opioid-prescribing interventions. Their effects should be interpreted according to the timing and components of each strategy, as well as the outcomes evaluated in individual studies.

Complete opioid avoidance should not be regarded as a universal perioperative endpoint. The appropriate goal is to minimize unnecessary opioid exposure while maintaining effective, patient-centered analgesia. Analgesic regimens should therefore be individualized according to the surgical procedure, expected pain intensity, comorbidities, previous opioid exposure, and contraindications to specific agents. Further procedure-specific randomized controlled trials are needed to determine optimal analgesic combinations, dosing, timing, and regional anesthesia techniques.

Author contributions

B. J.: Conceptualization, Data Curation, Visualization, Writing – Original Draft Preparation.

K. M.: Conceptualization, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Review & Editing.

References

1. Chang C, Nikolavsky D, Ong M, Simhan J. Pain management strategies in urethral reconstruction: a narrative review. *Transl Androl Urol*. 2022;11(10):1442-1451. doi:10.21037/tau-22-363
2. Shim JW, Shin D, Hong SH, Park J, Hong SH. Efficacy of Multimodal Analgesia with Transversus Abdominis Plane Block in Comparison with Intrathecal Morphine and Intravenous Patient-Controlled Analgesia after Robot-Assisted Laparoscopic Partial Nephrectomy. *J Clin Med*. 2024;13(14):4014. doi:10.3390/jcm13144014
3. Róziewska A, Klukowski M, Jureczko L. New techniques of regional anaesthesia for renal laparoscopic surgeries. *Urologia*. 2022;89(4):610-615. doi:10.1177/03915603211048741

4. Roebuck E, Beano H, Robinson M, Edwards D, Worrilow WM, Sinks A, et al. Surgeon-administered Transversus Abdominis Plane (TAP) Block is Associated With Decreased Opioid Usage and Length of Stay Following Radical Cystectomy. *Urology*. 2022;161:135-141. doi:10.1016/j.urology.2021.11.023
5. Donahue RP, Stamm AW, Daily AM, Kozlowski PM, Porter CR, Govier FE, et al. Opioid-Limiting Pain Control After Transurethral Resection of the Prostate: A Randomized Controlled Trial. *Urology*. 2022;166:202-208. doi:10.1016/j.urology.2022.03.010
6. Lee JE, Oh J, Lee JN, Ri HS, Lee CS, Yeo J. Comparison of a Non-Opioid Multimodal Analgesia Protocol with Opioid-Based Patient-Controlled Analgesia for Pain Control Following Robot-Assisted Radical Prostatectomy: A Randomized, Non-Inferiority Trial. *J Pain Res*. 2023;16:563-572. doi:10.2147/JPR.S397529
7. Carnes KM, Singh Z, Ata A, Mian BM. Interventions to Reduce Opioid Prescriptions following Urological Surgery: A Systematic Review and Meta-Analysis. *J Urol*. 2022;207(5):969-979. doi:10.1097/JU.0000000000002447
8. Micali M, Cucciolini G, Bertoni G, Gandini M, Lattuada M, Santori G, et al. Analgesic Strategies for Urologic Videolaparoscopic or Robotic Surgery in the Context of an Enhanced Recovery after Surgery Protocol: A Prospective Study Comparing Erector Spinae Plane Block versus Transversus Abdominis Plane Block. *J Clin Med*. 2024;13(2):383. doi:10.3390/jcm13020383
9. Sisa K, Huoponen S, Ettala O, Antila H, Saari TI, Uusalo P. Effects of pre-emptive pregabalin and multimodal anesthesia on postoperative opioid requirements in patients undergoing robot-assisted laparoscopic prostatectomy. *BMC Urol*. 2021;21(1):14. doi:10.1186/s12894-021-00785-9
10. Oodit R, Biccard BM, Panieri E, Alvarez AO, Sioson MRS, Maswime S, et al. Guidelines for Perioperative Care in Elective Abdominal and Pelvic Surgery at Primary and Secondary Hospitals in Low–Middle-Income Countries (LMIC's): Enhanced Recovery After Surgery (ERAS) Society Recommendation. *World J Surg*. 2022;46(8):1826-1843. doi:10.1007/s00268-022-06587-w
11. Qi Y, Li W, Ren Y, Sun J, Zhu Y, Wang L, et al. Effect of Esketamine-Based Opioid-Sparing Anesthesia Protocol on the Quality of Early Recovery After Urological Surgery: A Randomized Clinical Trial. *Drug Des Devel Ther*. 2025;19:2005-2016. doi:10.2147/DDDT.S511112
12. Arun TC, Karim HMR, Singha SK, Biswal DK. A Comparison of Analgesic and Recovery Profiles of Ketamine, Lignocaine, and Dexmedetomidine (KeLiDex) Versus Fentanyl-Based Anesthesia in Laparoscopic Nephrectomies: A Randomized, Single-Blind, Pilot Study. *Cureus*. 2024;16(6):e63380. doi:10.7759/cureus.63380
13. Luo X, Hao WW, Zhang X, Qi YX, An LX. Effect of esketamine on the ED50 of propofol for successful insertion of ureteroscope in elderly male patients: a randomized controlled trial. *BMC Anesthesiol*. 2024;24(1):195. doi:10.1186/s12871-024-02580-z
14. Shim JW, Jun EH, Bae J, Moon HW, Hong SH, Park J, et al. Intraoperative multimodal analgesic bundle containing dexmedetomidine and ketorolac may improve analgesia after robot-assisted prostatectomy in patients receiving rectus sheath blocks. *Asian J Surg*. 2022;45(3):860-866. doi:10.1016/j.asjsur.2021.07.043
15. Borys M, Szajowska P, Jednakiewicz M, Wita G, Czarnik T, Mieszkowski M, et al. Quadratus Lumborum Block Reduces Postoperative Opioid Consumption and Decreases Persistent Postoperative Pain Severity in Patients Undergoing Both Open and Laparoscopic Nephrectomies—A Randomized Controlled Trial. *J Clin Med*. 2021;10(16):3590. doi:10.3390/jcm10163590
16. Rosen DC, Winoker JS, Mullen G, Moshier E, Sim A, Pathak P, et al. Robot-assisted vs ultrasonography-guided transversus abdominis plane (TAP) block vs local anaesthesia in urology: results of the UROTAP randomized trial. *BJU Int*. 2022;130:815-822. doi:10.1111/bju.15833
17. Tejedor A, Deiros C, Bijelic L, García M. Wound infiltration or transversus abdominis plane block after laparoscopic radical prostatectomy: a randomized clinical trial. *Anesth Pain Med (Seoul)*. 2023;18(2):190-197. doi:10.17085/apm.23005
18. Terada BD, Gonçalves FG, Porto BC, Duarte Silva B, Passerotti CC, Sanderberg RA, et al. Unveiling the impact of opioid-free postoperative regimens in ureteroscopy: a comprehensive systematic review and meta-analysis. *Minerva Urol Nephrol*. 2024;76(5):545-553. doi:10.23736/S2724-6051.24.05824-5
19. Gao H, Xu Z, Zhang L, Liu Y, Jiang Y, Wang Q, et al. Superiority of opioid free anesthesia with regional block over opioid anesthesia with regional block in the quality of recovery after retroperitoneiscopic renal surgery: a randomized controlled trial. *Minerva Anestesiol*. 2024;90:845-854. doi:10.23736/S0375-9393.24.18186-2
20. Lee G, Patel HV, Srivastava A, Ghodoussipour S. Updates on enhanced recovery after surgery for radical cystectomy. *Ther Adv Urol*. 2022;14:17562872221109022. doi:10.1177/17562872221109022

21. Chu CE, Law L, Zuniga K, Lin TK, Tsourounis C, Rodriguez-Monguio R, et al. Liposomal Bupivacaine Decreases Postoperative Length of Stay and Opioid Use in Patients Undergoing Radical Cystectomy. *Urology*. 2021;149:168-173. doi:10.1016/j.urology.2020.11.036
22. Zhu P, Yang Y. An anesthesia-integrated model for predicting postoperative urinary retention after transurethral resection of the prostate: A retrospective cohort study. *J Int Med Res*. 2026;54(8):3000605261477855. doi:10.1177/03000605261477855
23. Meineke MN, Losli MV, Sztain JF, Swisher MW, Abramson WB, Martin EI, et al. Robot-assisted laparoscopic nephrectomy: early outcome measures with the implementation of multimodal analgesia and intrathecal morphine via the acute pain service. *World J Urol*. 2024;42(1):117. doi:10.1007/s00345-024-04801-z
24. Ye CY, Li LY, Yang MJ, et al. Nonsteroidal anti-inflammatory drug use and acute kidney injury in nephrectomies: A retrospective propensity score-matched cohort study. *Anaesth Crit Care Pain Med*. 2025;44(6):101581. doi:10.1016/j.accpm.2025.101581
25. Koo K, Winoker JS, Patel HD, Faisal F, Gupta N, Metcalf MR, et al. Evidence-Based Recommendations for Opioid Prescribing After Endourological and Minimally Invasive Urological Surgery. *J Endourol*. 2021;35:1838-1843. doi:10.1089/end.2021.0250