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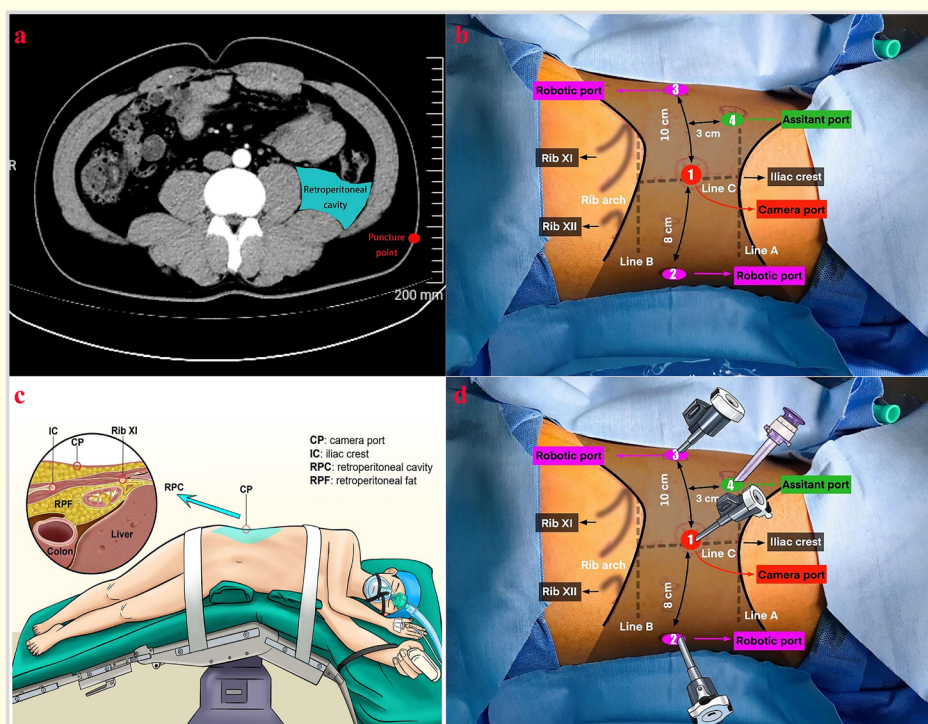
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**Figure 2** - Procedures. 2a) Retroperitoneal cavity and puncture point; 2b) Trocars location; 2c) Patient position; 2d), Port placement. e20260042



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# Robot-Assisted Partial Nephrectomy is the Hot Topic in this Number of International Brazilian Journal of Urology

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The July-August number of International Brazilian Journal of Urology presents original contributions with a lot of interesting papers in different fields: Prostate cancer, Robotic Surgery, Kidney cancer, Neonatal circumcision, Telesurgery, Vesicoureteral Reflux, Bladder Cancer, Neuroblastoma, Endourology and Reconstructive Urology. The papers came from many different countries such as Brazil, China, USA, Palestina, Tunisia, France and Germany, and as usual the editor's comment highlights some of them. The editor in chief would like to highlight the work about Robot-assisted Partial Nephrectomy, the cover in this edition.

Dr. Liang and colleagues from China, presented in page e20260042 (1) a nice study about the Tubeless Retroperitoneal Robot-assisted Partial Nephrectomy (TLRRPN) and concluded that TLRRPN is a safe, efficient, innovative, cost-effective, and selective surgical procedure. This operation fundamentally reduces the adverse effects associated with tubes in patients and significantly facilitates rapid recovery.

Robotic surgery has revolutionized the surgical treatment of urogenital cancer, resulting in better outcomes and faster recovery (2-9). The present study is interesting and will greatly assist the urologist in diagnosing this disease.

The Editor-in-chief expects everyone to enjoy reading.

## CONFLICT OF INTEREST

None declared.

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# Surgical Treatment of Adrenal Neuroblastoma in Children – A Narrative Review

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## ABSTRACT

**Objective:** To analyze the role of surgical treatment in pediatric adrenal neuroblastoma and the operative methods employed according to staging and risk stratification based on patient-related and tumor biological factors.

**Materials and Methods:** A narrative literature review was conducted through a structured search of the PubMed/MEDLINE, Scopus, and Web of Science databases. Studies published in English between 2020 and 2025 were included, while classical references were used to contextualize staging and risk stratification systems. Letters, editorials, case reports, and studies not providing specific insight into the topic were excluded.

**Results:** Surgical treatment represents a key component in the management of pediatric adrenal neuroblastoma. Staging and risk stratification determine both the timing of surgery and its role in achieving local disease control. In low-risk neuroblastoma, surgery alone may be curative. In intermediate-risk patients, neoadjuvant chemotherapy precedes resection, reducing surgical complexity and facilitating tumor removal. In high-risk patients, tumor resection exceeding 90% may contribute to improved overall survival (OS). Image-Defined Risk Factors (IDRFs) are essential for staging and surgical planning, as they define the anatomical relationship between the tumor and adjacent vascular and organ structures. Surgical approaches include open surgery and minimally invasive surgery, the latter being appropriate in carefully selected cases.

**Conclusion:** Surgical treatment remains fundamental in pediatric adrenal neuroblastoma, and operative strategies should be guided by clinical, biological, and radiologic parameters to achieve maximal oncologic safety.

## ARTICLE INFO

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## INTRODUCTION

Neuroblastoma (NB) is the most common extracranial solid malignancy in children, with an annual incidence rate of 13.2 per 1,000,000 children per year. It originates from neural crest cells. Its most frequent location is the adrenal medulla. Bilateral presentation is rare and is generally associated with a worse prognosis compared to NB located in other anatomical sites along the paravertebral sympathetic chain. The biological heterogeneity of NB influences spontaneous regression, prognosis, and the possibility of cure (1–3).

Nong et al. (2025), in a comprehensive global epidemiological study on NB in the pediatric population, concluded that despite fluctuations in trends of incidence, mortality, and disability-adjusted life years (the sum of years of life lost due to premature death and years lived with disability), the disease burden remains considerable in regions with low, lower-middle, and middle socioeconomic development indices (4).

An important retrospective study conducted by Zhang et al. (2023) demonstrated a higher prevalence of adrenal NB in male children (56.0%), right-sided unilateral location (66.7%), and tumor size greater than 4 cm (85.3%), with most cases presenting in advanced stages and with distant metastases. For radiologic diagnosis, computed tomography proved to be the method of choice compared with ultrasonography ( $p < 0.05$ ) (5).

For nearly five decades, criteria for NB staging have been established. The Children's Cancer Group (CCG), a North American cooperative group, developed and updated staging systems, including the International Neuroblastoma Staging System (INSS) and the International Neuroblastoma Risk Group Staging System (INRGSS) (6, 7).

Risk stratification guides the treatment of these patients. Research strategies dedicated to understanding the biological profile of NB have contributed to increasingly precise risk classification, resulting in therapeutic approaches proportional to tumor complexity (8).

The role of the pediatric oncologic surgeon in adrenal NB ranges from obtaining tissue for diagnosis to performing tumor resection with therapeutic intent and has been progressively influenced by the transition from the INSS system to the INRGSS, as well as by the

consolidation of minimally invasive techniques. Spencer et al. (2022), in a 20-year retrospective analysis, demonstrated a significant reduction in open biopsies after 2009 (45% vs. 26%,  $p = 0.04$ ), reflecting greater incorporation of percutaneous methods. However, the increase in minimally invasive surgeries (MIS) during the same period did not reach statistical significance (3% vs. 9%,  $p = 0.14$ ), suggesting that changes in diagnostic practice preceded definitive consolidation of minimally invasive approaches in surgical treatment (9).

In low-risk adrenal NB, treatment strategies range from observation to surgical resection aimed at complete removal of the tumor mass and regional lymph nodes. Chemotherapy is typically reserved for patients with adverse biological characteristics. Contemporary risk-adapted management has resulted in a 5-year OS of nearly 98%. (10).

In intermediate-risk adrenal NB (INRG L2 with IDRFs), without MYCN amplification, neoadjuvant chemotherapy aims to reduce tumor volume and technical complexity of resection, with duration and intensity adjusted according to clinical response and tumor biological factors. After satisfactory response, complete macroscopic resection is pursued. Partial resection may be acceptable when IDRFs persist involving major vessels or critical structures and when radicality would imply disproportionate morbidity, considering that oncologic control in this group is predominantly systemic (11, 12).

The treatment of high-risk adrenal NB is multimodal, intensive, and sequential. It begins with systemic induction chemotherapy, during which surgical resection of the primary tumor is performed after adequate volumetric reduction. During induction, hematopoietic stem cell collection is also carried out for subsequent autologous transplantation. The consolidation phase includes high-dose chemotherapy followed by autologous bone marrow transplantation and external beam radiotherapy directed to the tumor bed and any residual metastatic sites. Finally, the post-consolidation phase includes immunotherapy based on anti-GD2 antibody combined with isotretinoin, a strategy that has demonstrated significant gains in event-free survival (EFS) and OS (13, 14).

Favorable surgical outcomes following systemic disease control are reported in a South African

study conducted by van Heerden et al. (2022), which included 204 high-risk NB patients, 105 of whom underwent surgery and 82 with adrenal tumors. In univariate prognostic analysis, patients who achieved remission of metastatic disease — 45/56 (80.4%) — had their tumors resected ( $p < 0.001$ ) (15).

Pediatric adrenalectomy may be performed via open surgery or, in selected cases, by minimally invasive surgery (MIS), including transperitoneal laparoscopic adrenalectomy (TLA), posterior retroperitoneoscopic adrenalectomy (PRA), and robot-assisted surgery. TLA is the most widely adopted approach and is considered safe in children without IDRFs, particularly in small, well-delimited tumors without vascular invasion. The choice of approach should be based on tumor size, presence of IDRFs, and relationship with vascular structures, reserving open surgery for extensive lesions or those with significant vascular involvement (16, 17). Zhong et al. (2021) reported that PRA is a feasible and safe surgical approach for the management of pediatric adrenal oncologic diseases, including NB. In this comparative study between TLA and PRA, the authors primarily assessed pathological outcomes, operative time, transfusion requirements, conversion to open surgery, time to resumption of oral intake, and length of hospital stay (18).

Van Uitert et al. (2025) published a Dutch national multicenter study (2011–2022) including 137 pediatric patients who underwent adrenalectomy, of whom 87 (64%) had suspected NB. Among the 86 histologically confirmed NB cases, open surgery was used in 73 patients (85%), whereas 13 (15%) underwent TLA, with no cases treated by PRA (19).

Considering the marked biological heterogeneity and consequent diversification in the clinical presentation of adrenal NB in children, the objective of this narrative review is to highlight the role of surgical techniques employed, considering risk stratification systems based on patient-related factors and tumor biological characteristics.

## MATERIALS AND METHODS

This narrative review aimed to provide a comprehensive and updated analysis of the evidence regarding the surgical treatment of primary adrenal NB in pediatric

patients. A structured literature search was conducted to support the thematic discussion; however, the study design followed an interpretative and integrative approach, consistent with the narrative review model.

The search was performed in the PubMed/MEDLINE, Scopus, and Web of Science databases, including publications indexed within the last six years (2020–2025). The strategy combined controlled descriptors (DeCS/MeSH): “Neuroblastoma,” “Adrenal Glands,” “Surgical Procedures, Operative,” and “Adrenalectomy.” Additionally, a manual review of the reference lists of selected studies was conducted to identify potentially relevant publications not captured by the initial electronic search strategy.

Although the structured database search supported the identification of contemporary studies, additional publications were included based on their clinical relevance, cooperative group guidelines, and contributions considered fundamental for contextualizing staging systems and surgical decision-making models. This approach is consistent with the interpretative and integrative nature of narrative reviews.

Given the narrative design of this study, no formal systematic review protocol, quantitative synthesis, or PRISMA flow diagram was applied. Study selection was guided by thematic relevance and clinical applicability to the proposed conceptual and surgical axes.

Eligible studies included those involving pediatric patients that addressed aspects related to surgical strategy, operative timing (primary surgery or post-neoadjuvant chemotherapy), extent of tumor resection, perioperative morbidity, or oncologic outcomes. Multicenter cooperative studies were also included, given their relevance in standardizing risk stratification and guiding therapeutic decisions.

Excluded were letters to the editor, editorials, case reports, studies focused exclusively on extra-adrenal NBs, duplicate publications, and articles published in languages other than English.

Data were organized through qualitative thematic synthesis, structured according to analyses related to surgical indication, operative planning based on radiologic risk factors, degree of resection radicality, role of minimally invasive approaches, operative morbidity, and prognostic impact.

## RESULTS

With the evolution of multimodal systemic therapies, the isolated relevance of surgery in NB has decreased, without eliminating its therapeutic necessity. Pediatric oncologic surgeons are responsible for defining the therapeutic strategy based on a correct understanding of tumor biological behavior, while maintaining the perspective of improved prognosis (20).

Tumors located in the adrenal gland may be classified into two major groups: adrenocortical tumors – including adenoma and adrenocortical carcinoma – and tumors of the adrenal medulla, such as NB and pheochromocytoma (21).

In the presence of clinical and/or laboratory suspicion of a cortical tumor or pheochromocytoma, tumor biopsy should generally be avoided due to potential hormonal repercussions and hemodynamic complications. Conversely, in suspected NB, tumor biopsy is recommended for diagnostic purposes, since histological analysis and molecular characterization of the tumor are prerequisites for adequate risk stratification and therapeutic definition (22).

Historically, NB staging was initially structured according to the INSS (Table-1), later replaced by the INRGSS (Table-2), which incorporated preoperative criteria

based on radiologic and biological factors. Recent advances in research have been directed toward the identification and validation of genes associated with tumor staging according to the INSS, highlighting their potential as biomarkers in prognostic models for NB. (6, 7, 23).

Risk grouping depends on demographic (age at diagnosis) and clinical factors (stage, MYCN gene amplification, histopathology, chromosomal aberrations, and cellular ploidy). Proper staging and accurate risk stratification lead to treatment strategies associated with improved outcomes (Table-3) (12, 24).

Liukitithara et al. (2022) reported a cohort of 37 pediatric patients (2007–2016), 19 of whom had adrenal NB (51.3%), with 73.0% classified as high risk and nearly all (18/19) presenting with INSS stage IV and metastatic disease, reflecting late diagnosis (21). Similar findings were reported by Khan and Verma (2025) in a cohort of 53 patients (2016–2022), including 31 (58.5%) with adrenal NB. Among those staged according to INRGSS (49/53), more than half were diagnosed at M or MS stages, indicating metastatic disease (25).

Certain critical elements related to adrenal NB surgery deserve particular attention. When technically feasible and safe, resection exceeding 90% of tumor volume is recommended, extending to the limits of contiguous structures, with preservation of major involved vessels.

**Table 1 - Staging according to the International Neuroblastoma Staging System (INSS).**

| INSS | Definition                                                                                                                    | Key Characteristics                      |
|------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| 1    | Localized tumor with complete gross excision, with or without microscopic residual disease; ipsilateral lymph nodes negative. | Complete resection; negative LNs         |
| 2A   | Localized tumor with incomplete gross excision; ipsilateral lymph nodes negative.                                             | Incomplete resection; negative LNs       |
| 2B   | Localized tumor with or without complete excision; ipsilateral lymph nodes positive; contralateral negative.                  | Ipsilateral positive LNs                 |
| 3    | Tumor crossing the midline or unilateral tumor with contralateral regional lymph node involvement.                            | Midline crossing or contralateral LNs    |
| 4    | Primary tumor with distant metastasis (except stage 4S).                                                                      | Distant metastasis                       |
| 4S   | Localized primary tumor with limited metastasis to skin, liver, and/or bone marrow in infants <1 year.                        | Localized + limited metastasis (<1 year) |

**Table 2 - Staging according to the International Neuroblastoma Risk Group Staging System (INRGSS).**

| INRGSS | Definition                                                                             | Key Characteristics      |
|--------|----------------------------------------------------------------------------------------|--------------------------|
| L1     | Locoregional tumor without image-defined risk factors (IDRFs).                         | Localized; no IDRFs      |
| L2     | Locoregional tumor with one or more IDRFs.                                             | Localized; IDRFs present |
| M      | Distant metastatic disease.                                                            | Metastasis (except MS)   |
| MS     | Metastatic disease confined to skin, liver, and/or bone marrow in patients <18 months. | Infants <18 months       |

**Table 3 - Patient-related and tumor biological factors associated with risk stratification.**

| Risk Factor             | Type          | Relevance and Impact                                                    |
|-------------------------|---------------|-------------------------------------------------------------------------|
| Age at diagnosis        | Demographic   | Diagnosis <18 months: lower risk; >18 months: higher risk, reduced EFS. |
| MYCN amplification      | Cytogenetic   | Associated with poor prognosis and high-risk disease.                   |
| Ploidy                  | Cytogenetic   | Diploid tumors associated with worse outcomes.                          |
| Chromosomal alterations | Cytogenetic   | 17q gain; 1p/11q deletion linked to aggressive disease.                 |
| Histology               | Morphological | Poor differentiation associated with high risk.                         |

EFS = Event-Free Survival

En bloc resection of adjacent organs is not routinely recommended. Lymph node dissection should include the renal pedicle chains, azygos vein chains, intercavaortic chains, and pericaval chains. Above all, the primary recommendation is preservation of patient integrity (26, 27).

An important biological tumor factor to be evaluated is MYCN gene amplification in tumor tissue obtained by diagnostic biopsy. When gene amplification is present, recommended surgical resection often becomes unfeasible at presentation. Neoadjuvant chemotherapy aims to reduce tumor volume, minimize the effects of proximity to critical structures, decrease the

risk of injury to vital structures, and optimize surgical outcomes (28).

To expand surgical understanding through standardized data collection, pediatric surgeons from cooperative pediatric oncology groups developed the first detailed and structured surgical report for NB, including adrenal tumors, under the premise of establishing an international consensus adaptable to different local realities (29).

Tumor volume represents an important predictive prognostic factor, with tumors larger than 4 cm associated with unfavorable evolution (30). Conversely, in

neonates and infants — an age group generally associated with better prognosis — serial magnetic resonance imaging may justify initial nonoperative management, known as a “watch-and-wait” strategy (31).

Identification of IDRFs through computed tomography or magnetic resonance imaging constitutes a central element in assessing resectability of adrenal NB (Figure-1). These radiologic parameters reflect the anatomical relationship between the tumor and critical

adjacent structures, particularly major abdominal vessels — such as the aorta and inferior vena cava — as well as the celiac axis and renal pedicle. The presence of IDRFs is associated with greater technical complexity and lower likelihood of complete macroscopic resection, whereas their absence facilitates extensive tumor excision with oncologic safety. Under such circumstances, unresected tumors are associated with worse oncologic prognosis (Table-4) (32–34).

**Figure 1 - Radiological aspects of adrenal neuroblastoma.**



A) Computed Tomography (CT) scan of a 1-year-old male patient. Arrows indicate a positive Image-Defined Risk Factor (IDRF), characterized by tumor encasement of the right renal hilar vessels. B) CT scan of a 1-year-old female patient. Arrow indicates absence of IDRF, with the tumor merely abutting the right renal hilar vessels without vascular encasement.

**Table 4 - Image-Defined Risk Factors (IDRFs) related to adrenal topography.**

| IDRF Attribute | Radiological Definition and Criteria                                                                                                                                                               |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Contact        | Absence of a visible fat plane between the tumor and adjacent normal tissue and/or involvement of <50% of the vessel circumference.                                                                |
| Encasement     | Absence of a visible fat plane between the tumor and the adjacent vessel with >50% circumferential arterial involvement. Venous flattening and obliteration of the vascular lumen may be observed. |
| Infiltration   | Tumor extension into adjacent organs. Direct involvement of the renal artery, renal vein, or renal pelvis is technically classified as renal invasion.                                             |



A systematic review and meta-analysis by Parhar et al. (2020) aimed to quantify the predictive capacity of IDRFs assessed at pretreatment (before neoadjuvant chemotherapy) in relation to surgical outcomes and patient survival. The authors concluded that the presence of IDRFs increased the risk of incomplete surgical resection and postoperative complications, as well as reduced five-year EFS and OS (35).

Espinoza et al. (2024), in a multicenter study, demonstrated a lower probability of complete resection (>90%) in children with a higher number of IDRFs, both at diagnosis and at the time of surgical treatment ( $p = 0.0004$ ) (36). In contrast, a single-center study by Liu et al. (2024) demonstrated that the number of IDRFs significantly decreased after four cycles of neoadjuvant chemotherapy ( $p = 0.034$ ). The study showed that both the quantity and quality of preoperative IDRFs may predict secondary surgical outcomes beyond simple presence or absence (37).

With the aid of information technology, using radiomics-based machine learning (application of advanced algorithms to extract large quantitative datasets from medical images), surgical risk in children with adrenal NB may be predicted based on criteria including major vascular involvement (celiac axis, superior mesenteric artery, iliac vessels, inferior vena cava), tumor crossing the midline, retroperitoneal lymph node metastasis, renal pedicle invasion, and hepatic, pancreatic, or duodenal invasion (38).

Avanzini et al. (2025), in a collaborative study, stratified and assigned relevance scores to each IDRF using data collected between 2016 and 2020, correlating them with surgical risks. The study aimed to provide more precise definitions of surgical objectives and ideal conditions favoring macroscopic tumor resection (39).

In high-risk adrenal NB, surgery is incorporated during the induction phase, with a possible role also during consolidation. OS and EFS appear to be positively impacted by significant tumor resections (>90%) (13, 14, 40).

In rare cases of bilateral adrenal NB, a more conservative surgical approach on the less affected side should be considered. Prognosis in these patients is more dependent on disease extent and tumor biological profile, such as MYCN gene amplification (40).

Anesthetic management, an integral component not only of the operative procedure but also of tumor biopsy and postoperative pain control, requires thorough preoperative clinical evaluation. Anesthetic considerations depend largely on tumor location, operative approach, and extent of surgical dissection. Particular attention should be given, even in previously healthy patients, to tumor- or chemotherapy-induced physiopathological alterations affecting cardiovascular, gastrointestinal, and immune systems (42).

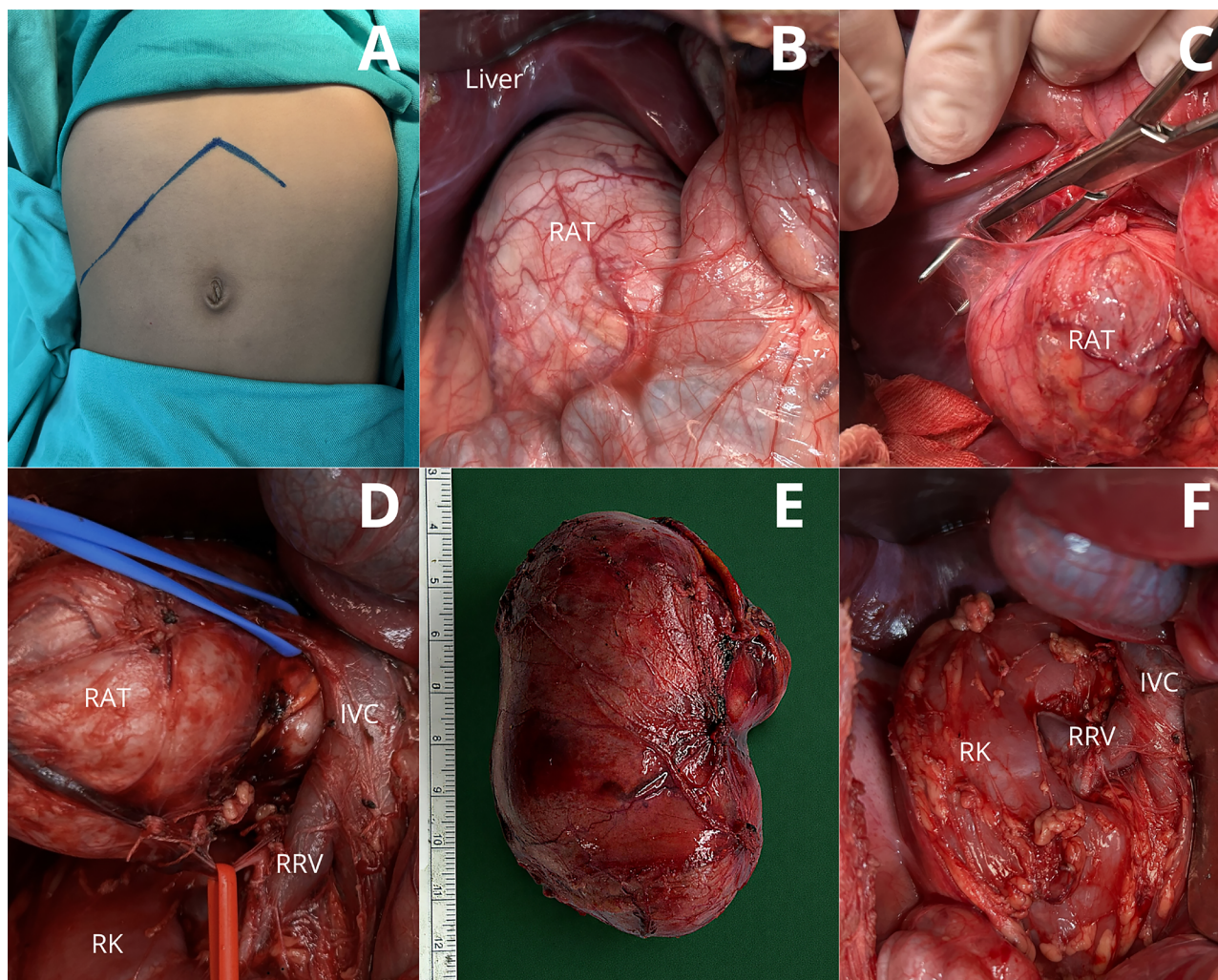
Open transperitoneal surgery has been employed for decades as an alternative to excise adrenal NB infiltrating adjacent tissues — especially vessels or lymph nodes — and tumors crossing the midline. Incisions may be combined according to the required exposure when the tumor extends superiorly or medially. This surgical technique remains a solid strategy to achieve complete tumor excision (Figure-2) (43).

Fiori et al. (2020) recommend laparoscopy as first choice for benign adrenal tumors measuring 6–8 cm and possibly extending to 10–12 cm in the absence of radiologic signs of malignancy. Extension of traditional size limits has been associated with favorable outcomes in centers with specific expertise in minimally invasive adrenal surgery (44).

Uttinger et al. (2022), in a retrospective analysis of pediatric adrenalectomies in Germany (2009–2017), reported a prevalence of NB (56%) among malignant adrenal tumors, predominantly in children younger than five years. The number of open surgeries exceeded MIS in all participating hospitals, regardless of surgical volume ( $p = 0.015$ ) (45).

Initially, MIS was used for diagnostic procedures and subsequently extended to tumors such as adrenal NBs. The same oncologic principles of open surgery — negative margins, prevention of tumor rupture, and extensive lymphadenectomy when indicated — must be replicated in MIS to ensure excellent oncologic outcomes (46).

The main laparoscopic approaches include transperitoneal and posterior retroperitoneoscopic techniques. The transperitoneal route is preferred due to anatomical familiarity, wider operative field, and easier simultaneous abdominal exploration. The surgical setup and trocar positioning are illustrated in Figure-3 (A and B). The posterior

**Figure 2 - 3-year-old male patient.**

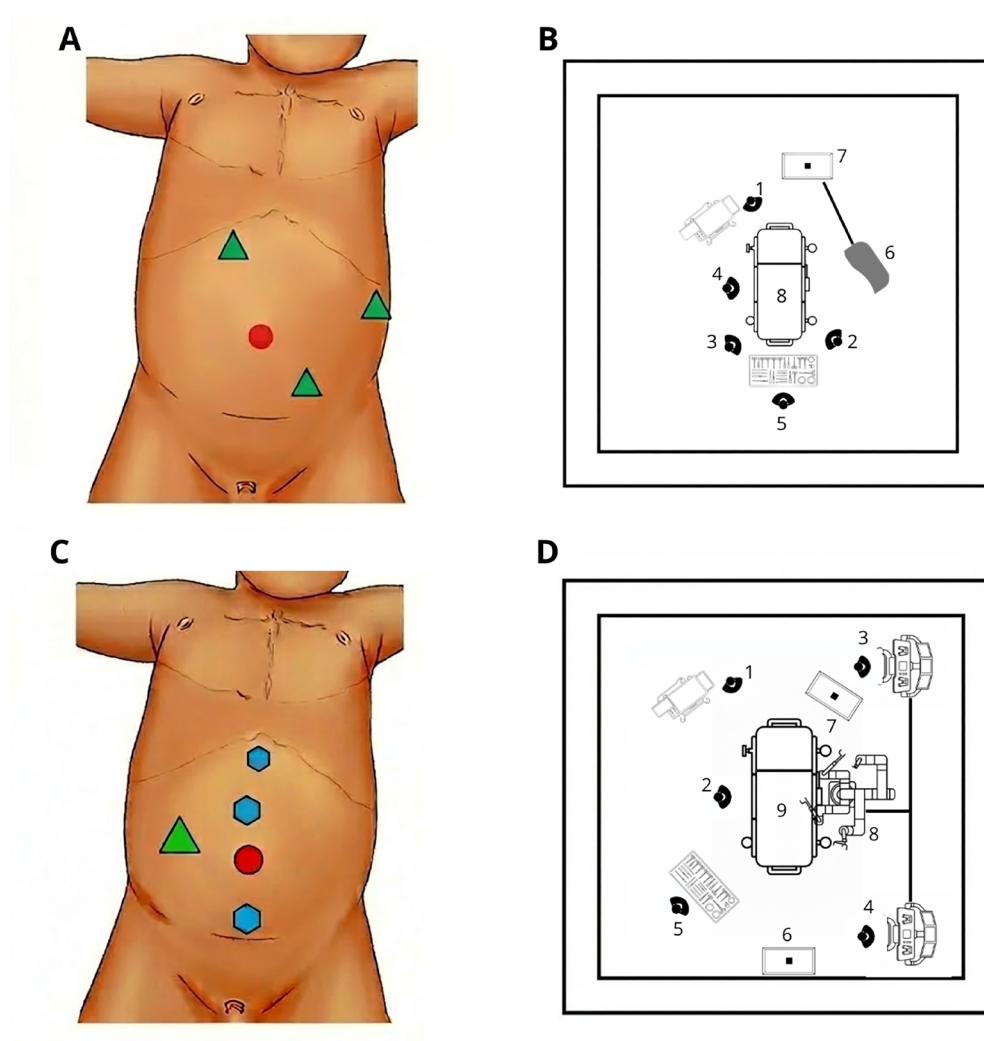
A) Skin marking for the surgical incision in right open adrenalectomy. B) Right adrenal tumor (RAT) corresponding to adrenal neuroblastoma. C) Dissection of adhesions between the right adrenal tumor and the liver. D) Right adrenal tumor and its anatomical relationships with the inferior vena cava (IVC), right renal vein (RRV), and right kidney (RK). Blue vessel loop: right adrenal vein. Red vessel loop: inferior right adrenal artery (branch of the right renal artery). E) Resected right adrenal tumor specimen. F) Surgical bed following right adrenalectomy, demonstrating the inferior vena cava, right renal vein, and right kidney.

retroperitoneoscopic approach allows direct gland access without violation of the peritoneal cavity, reducing postoperative pain, operative time, and hospital stay, albeit with a more restricted operative field (17).

Regarding robotic surgery, increasing evidence suggests that its structural advantages translate into intraoperative technical benefits and consequently faster postoperative recovery and po-

tentially lower morbidity. The surgeon operates from a dedicated robotic console, which enables precise control of articulated instruments and high-definition three-dimensional visualization of the surgical field. The robotic surgical setup adopted for adrenal tumor resection is illustrated in Figure-3 (C and D). Relative contraindications include the presence of one or two IDRFs. Formal contraindications include more than two IDRFs or any number involv-



**Figure 3 - Minimally Invasive Surgery (MIS) setup for adrenal neuroblastoma resection.**

A) Ports positioning for transperitoneal laparoscopic left adrenalectomy. Green triangles indicate laparoscopic working ports; the red circle indicates the camera port. B) Operating room layout for laparoscopic procedure. 1 – Anesthesiologist; 2 and 3 – Assistant surgeons; 4 – Laparoscopic surgeon; 5 – Scrub nurse; 6 – Laparoscopic tower; 7 – Video monitor; 8 – Operating table. C) Ports positioning for robot-assisted left adrenalectomy. The green triangle indicates the assistant port, including the pneumoperitoneum insufflation system. Blue hexagons indicate robotic ports. The red circle indicates the camera port. D) Operating room layout for robotic surgery. 1 – Anesthesiologist; 2 – Assistant surgeon; 3 and 4 – Surgeons at robotic consoles; 5 – Scrub nurse; 6 and 7 – Video monitors; 8 – Robotic patient cart; 9 – Operating table.

ing unpaired vessels — such as the celiac artery or superior mesenteric artery — and/or bilateral renal pedicle involvement (47, 48).

As highlighted by Matthyssens et al. (2021), standardization of complication reporting through the International Neuroblastoma Surgical Report Form (INSRF) reduces variability in operative documentation and allows more consistent comparison among surgical strategies. Complications within 30

postoperative days are classified according to the Clavien-Dindo system, ranging from grade I (minor interventions) to grade V (death) (29).

Surgical morbidity remains a critical factor in defining the ideal extent of resection in pediatric adrenal NB, particularly in tumors with vascular involvement. Perioperative complications such as lymphatic leakage, hypertension, massive hemorrhage, important structural injury, inadvertent re-

section of non-infiltrated organs and minor complications (hypoglycemia, intestinal obstruction, abdominal infection, incision-related complication) reflect this technical complexity. These events may compromise functional preservation, delay continuation of multimodal therapy, and negatively impact oncologic outcomes (49).

Chylous ascites represents a relevant complication following adrenal NB resection due to the intimate anatomical relationship with retroperitoneal lymphatic channels and the thoracic duct pathway (50). Froeba-Pohl et al. (2020), in a cohort of 204 patients, 98 (48%) with adrenal NB, reported lymphatic leakage in 40% of cases, correlated with greater extent of resection ( $p = 0.005$ ), advanced stage ( $p = 0.0001$ ), and MYCN amplification ( $p = 0.019$ ) (51).

Postoperative pleural effusion is another significant complication following adrenal NB resection. Hu et al. (2025) reported an incidence of 21.8%. Adrenal origin ( $aOR = 16.20$ ;  $p = 0.035$ ), operative time  $\geq 4.33$  hours ( $aOR = 180.20$ ;  $p = 0.001$ ), and early hypoalbuminemia ( $aOR = 17.13$ ;  $p < 0.001$ ) were independent predictors. These findings suggest that the complication is predominantly related to surgical trauma magnitude and systemic inflammatory response (52).

Alikärri et al. (2023), in a systematic review, demonstrated that sympathetic denervation resulting from subadventitial vessel resection in NB involving the superior mesenteric artery may cause intestinal parasympathetic hyperactivity, accelerating bowel transit. This diarrhea, distinct from that associated with excessive vasoactive intestinal peptide secretion by NB, is typically prolonged and requires pharmacologic and dietary management (53).

Laparoscopic and robot-assisted approaches have demonstrated feasibility and safety in localized tumors, with perioperative benefits such as reduced blood loss and shorter hospital stay. However, consistent evidence of oncologic superiority over open surgery is lacking, reinforcing the need

for individualized indication based on strict anatomical criteria. Major studies evaluating MIS in pediatric adrenal NB are summarized in Table-5. Predominantly, these are retrospective, single-center series with carefully selected patients, generally without IDRFs (46, 54–62).

Regarding prognosis, surgical resection is associated with improved oncologic outcomes, particularly in children with NB. Even in high-risk adrenal NB, improvements in one-, three-, and five-year OS are observed in patients undergoing surgical resection. Late diagnosis and large tumors with distant metastases represent independent risk factors when analyzing cancer-specific survival (CSS) (63, 64). A nomogram proposed by Zheng et al. (2020), supporting predictive clinical analysis, proved consistent in evaluating OS and CSS in children undergoing surgery for adrenal NB (65).

As synthesized in Table-6, studies reinforce that surgical treatment should be understood as a strategic component of multimodal therapy, with individualized indication based on the biological profile of the disease, including MYCN amplification, age at diagnosis, and risk category. Importantly, these studies consistently demonstrate that such biologically guided surgical integration translates into meaningful differences in OS outcomes, underscoring the impact of risk-adapted surgical decision-making on long-term prognosis (49, 54, 66–68).

This review presents limitations inherent to its narrative design. The methodological heterogeneity of included studies, predominantly retrospective and single center, limits direct comparability among series. Careful patient selection in minimally invasive surgery studies may overestimate perioperative benefits. Furthermore, the absence of randomized clinical trials comparing extent of resection and operative approach precludes definitive conclusions regarding oncologic superiority. Nevertheless, qualitative synthesis allows integration of contemporary evidence and delineation of consistent trends in the surgical management of pediatric adrenal NB.

**Table 5 - Studies evaluating minimally invasive surgery (MIS) for adrenal neuroblastoma in children.**

| Author                         | Study Design                                | Population                                        | Objective                                       | Method                                      | Results / Conclusion                                                                                           |
|--------------------------------|---------------------------------------------|---------------------------------------------------|-------------------------------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Oesterreich et al. (2022)(54)  | Retrospective, descriptive, single center   | 28 patients; 17 adrenal NB (60.7%)                | Analyze role of laparoscopic adrenalectomy (LA) | Retrospective MIS analysis (2003–2020)      | LA is safe for biopsy when percutaneous access is not feasible; appropriate for localized small-volume tumors. |
| Blanc et al. (2022) (46)       | Prospective, multicenter                    | 100 tumors; 12 adrenal NB (12%)                   | Evaluate first 100 robotic procedures           | Feasibility and safety study (2016–2020)    | Robotic surgery is feasible and safe; 8% conversion rate; no adrenal NB complications.                         |
| Chang et al. (2023) (55)       | Retrospective, comparative, single center   | 87 abdominal NB without IDRFs; 67 adrenal (77.0%) | Assess laparoscopic safety and efficacy         | Open (54) vs LA (33), 2016–2021             | Less blood loss ( $p=0.013$ ) and earlier feeding ( $p=0.002$ ); no oncologic difference.                      |
| Sugita et al. (2023) (56)      | Retrospective, comparative, single center   | 22 patients; 19 adrenal NB (86.3%)                | Compare biopsy and curative resection           | Surgical/histopathological comparison       | Laparoscopy feasible and safe; open biopsy shorter operative time ( $p=0.02$ ).                                |
| Pio et al. (2023) (57)         | Retrospective, comparative, single center   | 33 patients; 25 adrenal NB (75.7%)                | Compare PR vs TP approach                       | Perioperative analysis                      | PR approach reduced opioid use ( $p=0.02$ ) and hospital stay ( $p=0.008$ ).                                   |
| Kawakubo et al. (2024) (58)    | Retrospective, single center                | 24 peripheral neuroblastic tumors; 11 adrenal NB  | Clarify endoscopic indications                  | Preoperative CT IDRF assessment (2007–2022) | Safe without IDRFs; IDRF status crucial.                                                                       |
| Mora Fritis et al. (2024) (59) | Retrospective, observational, single center | 14 patients; 7 adrenal NB (50%)                   | Report on MIS outcomes                          | Observational review (2012–2023)            | MIS safe; no intraoperative mortality; mean stay 1 day.                                                        |
| Tian et al. (2024) (60)        | Retrospective, descriptive, single center   | 27 patients; 16 adrenal NB (59.2%)                | Describe single-incision PR technique           | Technical evaluation (2020–2023)            | Requires expertise; excellent postoperative outcomes.                                                          |
| Taghavi et al. (2024) (61)     | Prospective, observational, single center   | 39 robot-assisted cases; 23 NT, 20 adrenal NB     | Evaluate robot-assisted adrenalectomy (RAA)     | Six-year prospective study                  | RAA safe and effective; macroscopically negative margins achieved.                                             |
| Liu et al. (2025) (62)         | Retrospective, comparative, single center   | 22 adrenal NB (12 LA; 10 robotic)                 | Compare robotic vs laparoscopic                 | Retrospective analysis (2012–2024)          | Robotic group: lower blood loss ( $p=0.036$ ), shorter drainage ( $p=0.031$ ), shorter stay ( $p=0.021$ )      |

NB = Neuroblastoma; MIS = Minimally Invasive Surgery; LA = Laparoscopic Adrenalectomy; PR = Posterior Retroperitoneoscopic; TP = Transperitoneal; IDRFs = Image-Defined Risk Factors; RAA = Robot-Assisted Adrenalectomy; NT = Neuroblastic Tumor

**Table 6 - Overall survival (OS) outcomes in pediatric adrenal neuroblastoma (NB).**

| Author (Year)                  | Study Design                  | Population                       | Main Findings in Overall Survival (OS)                                                                                           |
|--------------------------------|-------------------------------|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Temple et al. (2021) (66)      | Surgical retrospective cohort | 76 NB/GNB                        | Infiltration of adjacent organs associated with worse OS (HR=8.90; p=0.007).                                                     |
| Gabra et al. (2022) (67)       | Surgical multicenter (SIOPEN) | 222 NB (54% adrenal); MIS cohort | 10-year OS 91.8%. Extent of resection did not impact OS. MYCN amplification, age >18 months, and high-risk status determined OS. |
| Oesterreich et al. (2022) (54) | Surgical single center        | 17 laparoscopic adrenal NB       | OS 86%; EFS 75%. No surgery-related mortality.                                                                                   |
| Bender et al. (2023) (68)      | Cooperative study (COG)       | NB <3 years (including adrenal)  | 5-year OS up to 94% after therapeutic de-escalation. Prognosis primarily driven by tumor biology.                                |
| He et al. (2024) (49)          | Surgical single center        | 571 retroperitoneal NB           | Perioperative mortality 0.53%. IDRFs associated with higher morbidity without demonstrated direct impact on OS.                  |

GNB = Ganglioneuroblastoma; SIOPEN = International Society of Paediatric Oncology European Neuroblastoma Group; MIS = Minimally Invasive Surgery; EFS = Event-Free Survival; COG = Children's Oncology Group; IDRFs = Image-Defined Risk Factors; HR = Hazard Ratio; OS = Overall Survival.

## CONCLUSIONS

Surgical treatment of pediatric adrenal NB remains a strategic component of multimodal management, with its indication and extent modulated by a complex interaction between biological risk stratification, radiologic anatomical characteristics, and response to systemic therapy. It thus constitutes not merely a technical intervention, but a prognostic-modulating element within the multimodal therapeutic framework.

In low-risk tumors, complete resection represents a potentially curative strategy, whereas in intermediate- and high-risk groups, surgery assumes an integrative role in local disease control, prioritizing maximal macroscopic resection while preserving functional integrity and maintaining oncologic safety.

Careful evaluation of IDRFs guides technical planning and operative approach selection, maintaining open surgery as the standard for complex tumors and reserving minimally invasive approaches for carefully selected cases.

Surgical decision-making should therefore be individualized, biologically oriented, and grounded in principles that balance radicality and morbidity, with the aim of optimizing long-term oncologic outcomes.

## ABBREVIATIONS

aOR = adjusted odds ratio  
CCG = Children's Cancer Group  
EFS = Event-Free Survival  
IDRFs = Image-Defined Risk Factors  
INRGSS = International Neuroblastoma Risk Group Staging System

INSS = International Neuroblastoma Staging System  
 INSRF = International Neuroblastoma Surgical Reporting Form  
 MIS = Minimally Invasive Surgery  
 NB = Neuroblastoma  
 OS = Overall Survival  
 PRA = Posterior Retroperitoneoscopic Adrenalectomy  
 PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
 TLA = Transperitoneal Laparoscopic Adrenalectomy

## CONFLICT OF INTEREST

None declared.

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# Which is the best laser for ureteroscopy? A Comprehensive Review

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## ABSTRACT

**Purpose:** The landscape of ureteroscopy has been transformed by rapid advancements in laser technology. The transition from the standard Holmium:YAG (Ho:YAG) to Thulium Fiber Laser (TFL) and emerging hybrid technologies (Magneto/Tm:YAG) creates decisional uncertainty. This review analyzes the physical principles, safety, and clinical outcomes of available lasers, proposing a context-based decision-making framework.

**Materials and methods:** A literature review using PubMed and Embase (2014-2025) yielded 1,902 records. Search terms included "holmium laser nephrolithotripsy," "thulium fiber laser," and "ureteroscopy laser." Fourteen seminal high-quality studies were selected for expert narrative synthesis, focusing on ablation efficiency, stone-free rates (SFR), complications, and cost-effectiveness.

**Results:** Literature heterogeneity, particularly inconsistent SFR definitions and imaging modalities, challenges comparative analysis. Clinically, TFL demonstrates superior ablation speeds and dusting capabilities compared to standard Ho:YAG, with equivalent safety. However, High-Power Ho:YAG remains unmatched in versatility for complex stones. Emerging pulsed Tm:YAG and Magneto Cyber Ho systems theoretically combine peak power with dusting efficiency but require further validation. Economically, TFL and High-Power systems demand significantly higher capital investment than Low-Power alternatives.

**Conclusions:** No universally superior laser exists; selection must be guided by institutional context. We propose a four-scenario framework: (1) Low-Power Ho:YAG is ideal for cost-sensitive, low-volume centers; (2) High-Power Ho:YAG is the standard for high-volume centers treating complex cases; (3) TFL is the choice for maximizing operative efficiency and dusting; and (4) Emerging Hybrid Technologies suit academic centers driving innovation. Future studies must prioritize standardized reporting to solidify the evidence base.

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## INTRODUCTION

In ureteroscopy, lasers have gained significant prominence. However, the diversity of laser types, characteristics, and applications can create decisional uncertainty. This review provides a comprehensive introduction to laser technology while updating specialists with recent advancements and insights in the field.

Since 1995, the Holmium Aluminum Garnet (Ho:YAG) laser has revolutionized lithotripsy, rapidly becoming the gold standard for urinary stone treatment due to its ability to fragment all stone types, high efficiency, and minimal tissue penetration (1). Building on the success of Ho:YAG, recent alternative laser technologies have emerged to enhance endoscopic lithotripsy performance, including thulium-based systems that demonstrate improved ablation characteristics and reduced stone retropulsion (2-4). Concurrent advancements in optical fiber delivery systems and pulse modulation technologies have further optimized energy transmission, improved safety profiles, and increased overall ablation efficiency (2).

These technological developments have expanded the available options for urologists. Indeed, recent literature continuously highlights how the refinement of retrograde intrarenal surgery (RIRS) techniques and equipment directly impacts clinical outcomes and patient safety (5, 6). The aim of this article is to present a literature review of the available options and provide a decision-making framework to assist urologists in selecting the appropriate device based on clinical reality.

While previous reviews have extensively compared standard Ho:YAG and TFL, literature lacks a pragmatic guide incorporating the newest hybrid and pulsed solid-state technologies (such as pulsed Tm:YAG and Magneto). Therefore, the novelty of this review lies in moving beyond a simple physical and clinical comparison. We provide an updated economic overview and propose a novel, context-based decision-making framework. This approach is highly important for the current urological literature as it assists surgeons, department heads, and healthcare managers in tailoring laser acquisition to their specific institutional realities, balancing budget constraints, surgical volume, and clinical needs (7).

## MATERIALS AND METHODS

A comprehensive review was conducted on PubMed and Embase. The search terms included: "holmium laser nephrolithotripsy", "thulium fiber laser lithotripsy", "thulium YAG laser lithotripsy", and "ureteroscopy laser". Articles published from 2014 to 2025 were included. Additionally, seminal works deemed fundamental to the topic were incorporated regardless of their publication date or the aforementioned inclusion criteria.

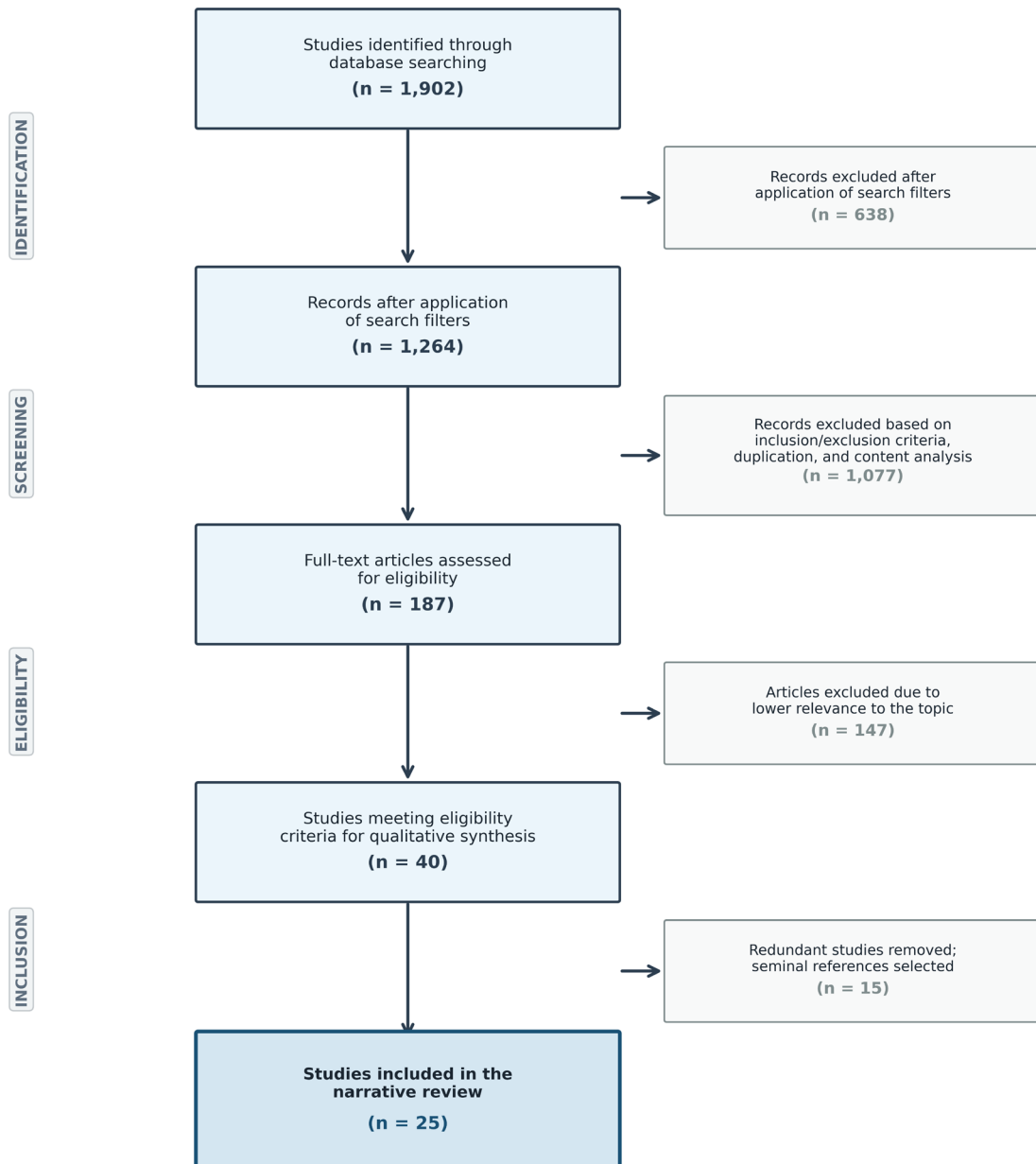
A total of 1,902 articles were identified in the searched databases. Of these, 1,264 articles published between 2014 and 2025 were assessed. Subsequently, 1,077 articles were excluded due to inappropriate or tangential content, lack of relevance, focus on the pediatric population, or unavailability in English, Portuguese, or Spanish. All relevant data were identified, selected, and summarized. Ultimately, 40 highly relevant articles were identified, from which 25 seminal studies were specifically selected to construct this expert review, as illustrated in our flowchart (Figure-1).

## RESULTS

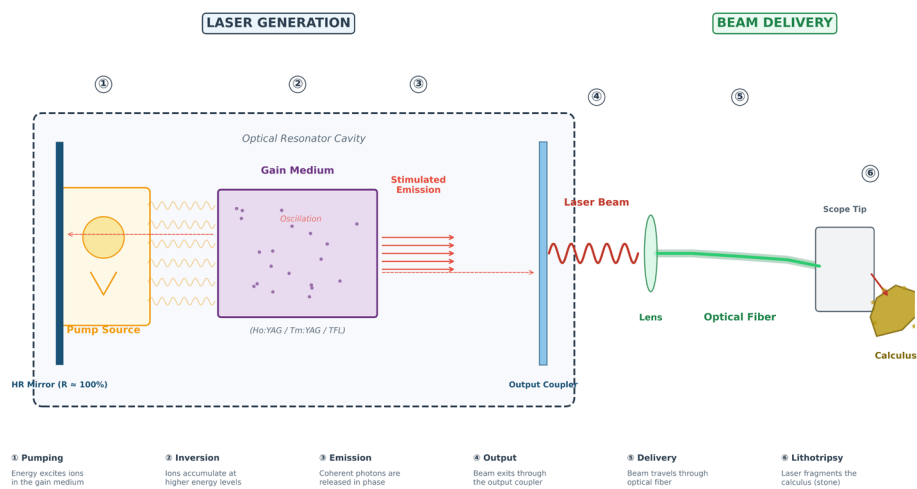
### Definition and Physical Principles

A laser device (Light Amplification by Stimulated Emission of Radiation) generates a highly directed and precise light beam characterized by photon coherence, where all photons share the same phase and direction, enabling stimulated emission (Figure-2). The mechanism by which lasers fragment urinary stones during lithotripsy is primarily photothermal, involving the direct conversion of laser energy into heat within the stone structure. When laser energy is absorbed by stone components, it generates intense localized heating that creates thermal conditions exceeding the molecular stability of stone materials. This thermal process causes decomposition of chemical bonds within the structure, resulting in stone fragmentation with efficiency dependent on the stone's absorption characteristics for the specific laser wavelength used. Additionally, vapor bubbles are generated through cavitation during the negative pressure phase of shock waves. These bubbles collapse violently within microseconds, producing secondary shock

**Figure 1 - Flow diagram of the study selection process for the narrative review. A total of 1,902 records were identified through electronic database searching. After the application of search filters, 1,264 records remained. Following screening based on predefined inclusion and exclusion criteria, removal of duplicates, and content analysis, 187 full-text articles were assessed for eligibility. Of these, 147 were excluded due to lower relevance to the topic. Among the 40 eligible studies, 15 redundant records were removed, and seminal references were preferentially retained, yielding a final sample of 25 studies included in the qualitative synthesis.**



**Figure 2 - Schematic representation of the fundamental components and operating principles of a solid-state laser system used in urological lithotripsy. The diagram illustrates six sequential stages: ① optical pumping, in which energy from a flashlamp or laser diode excites dopant ions ( $\text{Ho}^{3+}$  or  $\text{Tm}^{3+}$ ) within the gain medium (YAG crystal or silica fiber); ② population inversion, whereby excited ions accumulate at higher energy levels; ③ stimulated emission, where incident photons trigger the release of identical, phase-coherent photons; ④ beam output through the partially reflective output coupler of the optical resonator cavity; ⑤ coupling and delivery of the coherent laser beam through a flexible optical fiber (core diameter 200–550  $\mu\text{m}$ ); and ⑥ photothermal lithotripsy at the target calculus via ureteroscopy. The high-reflectance (HR) mirror ( $R \approx 100\%$ ) and the output coupler define the resonator cavity where photon amplification occurs through multiple oscillation cycles. Original figure; created by the authors.**



waves and microjets. The asymmetric collapse generates transient pressures near the stone surface. Cumulative microstructural damage from repeated cavitation events leads to stone disintegration.

Key laser properties include high intensity energy delivery to specific points, monochromaticity (single wavelength light), and low beam divergence (directionality) for precision applications. Lasers operate in continuous or pulsed modes, where continuous mode delivers energy constantly with gradual tissue heating that increases thermal damage risk, while pulsed mode emits energy in intermittent bursts with intervals allowing heat dissipation. Pulsed delivery is preferred for lithotripsy to minimize heat transfer to adjacent tissues, with duty cycle control being fundamental for maintaining thermal safety during stone fragmentation procedures.

The following are laser-related concepts that have implications in medical practice:

**Pulse Frequency:** The repetition rate measured in Hertz (Hz), determining how many pulses are emitted per second.

**Pulse Duration:** The time length of each individual pulse. Shorter pulses generally generate fewer thermal side effects but may increase retropulsion.

**Wavelength:** The distance between two consecutive electromagnetic wave peaks, measured in nanometers (nm), determining how laser light interacts with different tissues. Each tissue has specific absorption coefficients for different wavelengths, influencing penetration and therapeutic effects.

**Peak Power:** The maximum instantaneous laser power during pulse emission, measured in watts (W) or kilowatts (kW), calculated by dividing pulse energy by duration. This parameter directly influences tissue ablation capacity and stone fragmentation efficiency, with higher peak power values enabling more efficient fragmentation with lower total energy requirements.



**Absorption Rate:** The rate at which laser energy is absorbed by target tissue, determined by the tissue's absorption coefficient ( $\mu_a$ ) at the specific wavelength.

**Efficiency:** The relationship between useful energy delivered to target tissue and total system energy, considering transmission, scattering, and non-specific absorption losses, measured as ablated volume per energy unit ( $\mu\text{m}^3/\mu\text{J}$ ). Efficiency is influenced by wavelength, pulse duration, frequency, tissue optical properties, and application technique, with more efficient systems requiring less total energy and reducing collateral thermal damage and operative time.

These operational parameters are selected based on clinical context and surgeon preference.

### Currently Available Laser Types

The Holmium:YAG laser is considered the gold standard for lithotripsy due to its effectiveness in fragmenting all stone types. The laser emits pulses with a duration ranging from 350 to 700  $\mu\text{s}$ , classified as short-pulse (350  $\mu\text{s}$ ) or long-pulse (700  $\mu\text{s}$ ), and has a wavelength of 2120 nm with a tissue penetration depth of approximately 0.4 mm.

Ho:YAG lasers come in low-power (25-50 W) and high-power (80-120 W) configurations. Low-power systems use a single laser cavity directly aligned with fiber, typically operate at lower pulse energies (1.0 J), and offer cost-effectiveness. High-power systems incorporate multiple laser cavities requiring precise alignment, achieve higher pulse energies (up to 2.0 J) and frequencies (100 Hz), but demand sophisticated cooling systems and specialized electrical installations (e.g., a dedicated 50 A circuit), increasing costs. Both configurations achieve comparable success and complication rates, though high-power systems may reduce operative times for larger stones (2, 8).

The Moses™ technology enhances Holmium efficiency by delivering modulated pulses with two peaks: the first creates a water cavity facilitating more effective transmission of the second peak to the target stone. This reduces retropulsion and improves fragmentation efficiency, potentially shortening procedures. However, studies show no significant differences in stone-free rates and complications compared

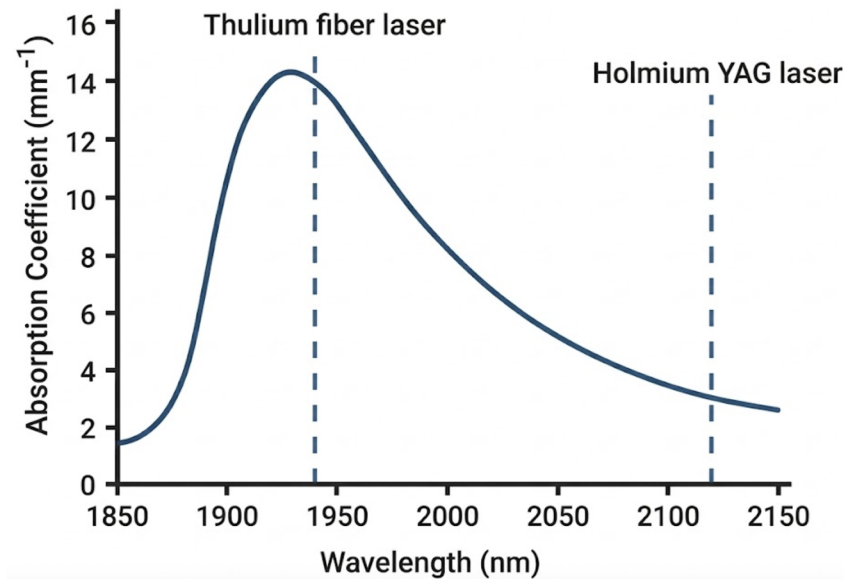
to conventional mode. In addition, these systems tend to produce higher noise levels and are generally bigger and heavier than their conventional counterparts, which can impact operating room logistics and ergonomics (2, 3).

Thulium lasers represent another important advancement in laser technology, comprising two main types: the Thulium Fiber Laser (TFL) and the pulsed Thulium:YAG (Tm:YAG) laser. The Thulium Fiber Laser operates at 1,940 nm, where water absorption of laser energy is higher, exhibiting significantly higher absorption with a coefficient of  $160\text{ cm}^{-1}$  (Figure-3). TFL consists of a long 10–20-micron silica fiber doped with Thulium that is characterized by adjustable pulse energies and frequencies, allowing for customization to meet specific clinical needs. Its key advantage lies in achieving high frequencies with lower energy (peak power), highlighting the TFL's potential for a different performance in lithotripsy.

The Thulium:YAG laser emits at 2,013 nm, offering intermediate absorption characteristics ( $\sim 100\text{--}150\text{ cm}^{-1}$ ), and features a Thulium crystal in the cavity which is stimulated by high-power laser diodes. Despite its higher peak power compared to the TFL—suggesting potential advantages in stone ablation—its clinical adoption remains limited when compared to Ho:YAG systems and TFL, due to its more recent release (2). The Thulium:YAG system offers various operational modes including Virtual Basket™, Bubble Blast™, and VaporTunnel™, each providing distinct advantages in stone fragmentation protocols.

Optical fibers consist of a high-purity silica core surrounded by a lower refractive index cladding that confines light through total internal reflection, with efficiency determined by the fiber's numerical aperture (NA). They transmit energy from lasers to stones, with 200 or 270  $\mu\text{m}$  fibers being most commonly used in urological lithotripsy practice. Smaller fibers enable better irrigation, reduced retropulsion, and greater endoscopic flexibility. Technical challenges include tip degradation from burnback and curvature radius effects, driving innovations such as detachable tips, automated vibratory fibers, and integrated pressure/temperature sensors to optimize procedure efficacy and safety.

**Figure 3 - Graph showing the variation of the absorption coefficient of the employed laser according to different wavelengths.**



### Safety and Endourological Use

Thermal safety is critical in endourological laser applications. Research demonstrates that proper continuous irrigation and ureteral access sheaths effectively maintain temperatures below tissue-damaging thresholds (2, 3). Appropriate power settings and irrigation rates are essential for thermal injury prevention. Recent ex-vivo and real-world temperature monitoring studies from 2024 and 2025 reaffirm that keeping intrarenal temperatures below the critical 43°C threshold is highly dependent on continuous fluid irrigation (at least 15–20 mL/min), especially when utilizing high-power settings in both Ho:YAG and modern TFL devices (9, 10).

While equipment-related complications occur (e.g., fiber tip degradation), clinically significant adverse events including ureteral perforations and strictures are well documented (2,4), highlighting the importance of precise technique and appropriate laser settings during lithotripsy and soft tissue procedures. Recent evidence reinforces that understanding the nuances of these evolving lithotripsy technologies and tailoring operative parameters are fundamental steps to reduce morbidity and improve the overall safety profile of ureteroscopy (11).

Several techniques can minimize thermal in-

juries during laser lithotripsy: reducing laser energy/frequency, limiting activation time, increasing irrigation flow, and using room temperature or cooled irrigation fluids (12). Ureteral access sheaths (UAS) facilitate irrigation outflow, reducing intrapelvic pressure and intrarenal temperature—particularly important with high-power laser settings (12). Low-power configurations prevent significant temperature increases and may not require high irrigation rates. Animal studies demonstrate that 15 mL/min irrigation is safe for 25 W lasers, while at least 30 mL/min is necessary for 48 W (13). Dusting strategies correlate with shorter procedures and lower ureteral injury risk, though residual fragments may increase future stone event probability (14).

### Comparative Cost Analysis and System Characteristics

The Holmium:YAG (Ho:YAG) laser is a well-established technology in endourology, widely used for its versatility and efficacy in treating urinary stones. The cost of Holmium laser systems generally ranges from USD 75,000 to USD 350,000, depending on their power output and specific functionalities. In contrast, the Thulium Fiber Laser (TFL) represents a newer option in lithotripsy, featuring a smaller, lighter device that

is easier to transport with high efficiency in stone pulverization. These features, however, come at a higher price, with TFL systems typically costing between USD 220,000 and USD 450,000. The Thulium:YAG emerges as an interesting option with great potential for achieving a high peak power, but it is still expensive with values between USD 250,000 to USD 500,000 and remains in early adoption stages. A comprehensive comparison of the technical specifications, advantages, limitations, and costs of these platforms is detailed in Table-1.

The consumables required for the systems, such as laser fibers, also contribute significantly to the overall cost of treatment. These fibers, available in different diameters, range from USD 200 to USD 1,000 per unit. Most fibers are designed for single use to ensure optimal sterility and performance. Nevertheless, some systems allow for the use of reusable fibers, which, while potentially reducing immediate costs, have a limited number of uses and must be replaced periodically.

### Challenges in Comparative Analysis and Standardization

A critical challenge in interpreting the current literature regarding laser lithotripsy lies in the lack of standardization across studies. The definition of “stone-free rate” (SFR) varies significantly, ranging from the complete absence of fragments to the presence of residual fragments <4mm, <2mm, or even dust, evaluated by different imaging modalities (CT scans vs. Ultrasound vs. KUB). Furthermore, laser settings (frequency, pulse width, and modulation) are often poorly reported or inconsistent between study arms. This heterogeneity makes direct meta-analytical comparisons difficult and highlights the urgent need for a consensus on definitions and reporting standards to solidify the theoretical ground for future comparative research.

### Clinical Decision-Making: A Context-Based Approach

Given the heterogeneity of the literature and the distinct advantages of each technology, the question is

**Table 1 - Comparative overview of laser technologies currently available for ureteroscopic lithotripsy.**

| Category                            | Parameter            | Low Power<br>Ho:YAG                                                                                                                    | High Power<br>Ho:YAG                                                                                                                                                               | Thulium Fiber<br>Laser (TFL)                                                                                                                                                             | Thulium YAG<br>(Tm:YAG)                                                                                                                                                             |
|-------------------------------------|----------------------|----------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Economic</b>                     | Estimated cost (USD) | 50,000–75,000                                                                                                                          | 150,000–300,000                                                                                                                                                                    | 150,000–300,000                                                                                                                                                                          | 80,000–160,000                                                                                                                                                                      |
| <b>Technical<br/>Specifications</b> | Wavelength (nm)      | 2,100                                                                                                                                  | 2,100                                                                                                                                                                              | 1,940                                                                                                                                                                                    | 2,013                                                                                                                                                                               |
|                                     | Peak power (W)       | 30                                                                                                                                     | > 2,000                                                                                                                                                                            | < 500                                                                                                                                                                                    | 3700                                                                                                                                                                                |
|                                     | Pulse frequency (Hz) | 5–20                                                                                                                                   | > 120                                                                                                                                                                              | > 2,000                                                                                                                                                                                  | 300                                                                                                                                                                                 |
| <b>Clinical<br/>Performance</b>     | Key advantages       | <ul style="list-style-type: none"> <li>• Low acquisition cost</li> <li>• High energy efficiency</li> </ul>                             | <ul style="list-style-type: none"> <li>• Faster ablation of large/hard calculi</li> <li>• Effective across all stone compositions</li> <li>• High peak-power capability</li> </ul> | <ul style="list-style-type: none"> <li>• Compact, lightweight, portable unit</li> <li>• Superior dusting at high frequency</li> <li>• Excellent fine fragmentation efficiency</li> </ul> | <ul style="list-style-type: none"> <li>• Combines high peak power with pulse modulation</li> <li>• Advanced programmable pulse profiles</li> </ul>                                  |
|                                     | Main limitations     | <ul style="list-style-type: none"> <li>• Longer operative times for large/hard stones</li> <li>• Limited dusting capability</li> </ul> | <ul style="list-style-type: none"> <li>• Requires dedicated infrastructure (50 A circuit, cooling)</li> <li>• Large, heavy, non-portable unit</li> </ul>                           | <ul style="list-style-type: none"> <li>• Reduced performance on large/hard calculi</li> </ul>                                                                                            | <ul style="list-style-type: none"> <li>• Highest acquisition cost</li> <li>• Lack of robust long-term comparative data</li> <li>• Still in early clinical adoption phase</li> </ul> |

Ho:YAG = holmium:yttrium-aluminum-garnet; TFL = thulium fiber laser; Tm:YAG = thulium:yttrium-aluminum-garnet; Cost estimates are approximate and may vary by region and vendor

not “which is the best laser,” but rather “which laser best fits a specific clinical reality.” We propose a decision-making framework based on four distinct institutional scenarios:

1. **Limited Budget and Low-Complexity Volume: The Low-Power Ho:YAG Solution.** For centers with budget constraints or lower surgical volume, the low-power Ho:YAG (20–35W) remains the most rational choice. It is a “workhorse” technology: reliable, cost-effective, and capable of treating the majority of ureteral and renal stones. Although it lacks the speed of high-frequency dusting, its proven efficacy and lower acquisition/maintenance costs offer the best cost-benefit ratio for standard cases.

2. **High Performance and Versatility: The High-Power Ho:YAG Solution.** For high-volume centers handling complex cases, high-power Ho:YAG systems represent the consolidated gold standard. While requiring significant infrastructure (specialized electrical circuits) and higher capital investment, they offer unmatched versatility for both lithotripsy and enucleation (HoLEP), making them ideal for comprehensive endourology departments.

3. **Efficiency and Maximized Dusting: The Thulium Fiber Laser (TFL) Solution.** For institutions focused on optimizing operative time and achieving high stone-free rates through dusting, TFL is the superior contender. Its ability to generate ultra-high frequencies allows for the production of fine dust, potentially reducing the need for basket retrieval and shortening procedure times. It is particularly advantageous for soft tissue ablation and precision lithotripsy, representing the modern standard for efficiency.

4. **Emerging Technologies and Future Potential: Tm:YAG and Magneto Technology.** New entries such as the pulsed Tm:YAG and the hybrid Magneto Cyber Ho represent the frontier of lithotripsy. They offer promising theoretical advantages—such as combining high peak power with TFL-like pulse trains. However, due to their high cost and the current scarcity of high-level comparative evidence, they are currently best suited for academic centers or early adopters aiming to investigate the limits of new lithotripsy modalities.

### **Cost-benefit in Relation to Clinical Application: Stone-Free Rate, Complications, Surgical Time**

Recent high-quality studies demonstrate that thulium fiber laser (TFL) generally achieves equivalent or superior stone-free rates (SFR) compared to standard Ho:YAG laser in ureteroscopy procedures. A pivotal randomized controlled trial revealed that overall 3-month SFR was significantly higher with TFL at 92% versus 67% with Ho:YAG ( $p=0.001$ ), with this advantage being particularly pronounced for renal stones (86% vs 49% SFR,  $p=0.001$ ) (15). Supporting meta-analyses have corroborated this benefit, with one comprehensive pooled analysis of 21 studies (totaling 3598 cases) demonstrating a modest but statistically significant SFR advantage for TFL (RR=1.09,  $p=0.01$ ) (16).

Regarding safety profiles, overall complication rates remain low and demonstrate broad similarity across laser modalities in ureteroscopy. Pooled analyses have identified no significant differences in total intraoperative or postoperative complications between TFL and Ho:YAG systems (17). Notably, randomized evidence indicates fewer adverse events with TFL, particularly regarding visually impairing bleeding, which occurred significantly less frequently with TFL compared to Ho:YAG (5% vs 22% of cases,  $p=0.014$ ) (15). While major complications like ureteral perforation and sepsis remain consistently low across all modalities, one meta-analysis found higher postoperative urosepsis rates with TFL (RR≈5.3) (16). However, overall evidence supports similar safety profiles for all three laser systems, with TFL potentially reducing intraoperative bleeding and stone retropulsion. These findings have been consistently corroborated by the most recent 2025 randomized controlled trials and systematic reviews, which confirm that TFL not only achieves comparable or higher stone-free rates but also significantly reduces operative and lithotripsy times when compared to conventional Ho:YAG systems (18, 19).

From an operational efficiency perspective, TFL consistently demonstrates shorter ureteroscopy duration compared to Ho:YAG laser. Both clinical trials and meta-analyses report significantly reduced operative

and lasing times with TFL implementation (15, 17). One randomized controlled trial documented mean URS time of 49 minutes with TFL versus 57 minutes with Ho:YAG ( $p=0.008$ ) (15), representing a clinically meaningful reduction in procedural duration. Retrospective cost analyses have translated these time savings into substantial economic benefits, with one institutional series finding that TFL reduced operating room time by approximately 13 minutes per case, equating to roughly \$440 in direct OR cost savings at \$34 per minute (20). Additionally, institutional costs per disposable fiber favor TFL at approximately \$320 compared to \$450 for Ho:YAG fibers (20). The aggregate evidence indicates that TFL, and potentially pulsed Thulium:YAG, can match or exceed Ho:YAG efficacy in ureteroscopy while simultaneously reducing operative time and associated healthcare costs. This continuous pursuit of enhanced surgical efficiency and optimized stone-free rates remains a central focus in contemporary endourological research, continuously shaping our clinical decision-making process (21).

### **Future Directions: Emerging Hybrid and Solid-State Technologies**

The Cyber Ho system with Magneto Technology combines controlled Holmium:YAG power with extended pulse trains similar to TFL. This creates a vapor channel intended to enable fine fragmentation ("dusting") with reduced retropulsion. A recent multicenter RCT (April 2025) evaluated 60 patients (Magneto vs. TFL). Results demonstrated that the Magneto group had significantly shorter lasing time (12.1 vs 17.3 min,  $p=0.04$ ) and reduced need for basket retrieval (13.3% vs 23.3%,  $p=0.04$ ), with similar stone-free rates (22). This technology represents a significant evolution, though further studies are needed to confirm cost-effectiveness.

Similarly, the pulsed solid-state Thulium:YAG (p-Tm:YAG) represents a novel category, distinct from both Ho:YAG and TFL. Panthier et al. (23) reported the initial clinical experience with this technology in 25 patients undergoing retrograde intrarenal surgery (RIRS). The study demonstrated that p-Tm:YAG is safe and feasible, achieving effective fragmentation with no major intra-operative complications. The device combines the peak power characteristics of solid-state lasers with the thulium

wavelength (2013 nm), theoretically offering a balance between the explosive power of Ho:YAG and the absorption efficiency of TFL. While Panthier et al. confirmed its clinical viability, they highlighted that specific parameter optimizations are still necessary to fully compete with established dusting standards. A subsequent prospective comparison of TFL and p-Tm:YAG during flexible ureteroscopy demonstrated comparable efficiency and safety profiles between the two technologies, reinforcing the clinical applicability of this emerging platform (24). Further comparative studies are required to strictly define its advantages over TFL in high-volume settings. Recent 2025 systematic reviews, including data from the EAU Section of Endourology, emphasize that p-Tm:YAG positions itself as a highly promising tool specifically for ureteroscopy. Preliminary clinical data for ureterolithotripsy demonstrate high stone-free rates and an excellent safety profile during retrograde approaches, owing to its stable pulse and high peak power (25).

## **CONCLUSIONS**

Laser technology in endourology has evolved from a one-size-fits-all approach to a diverse ecosystem of specialized tools. While TFL and emerging hybrid technologies demonstrate superior physical properties for dusting and speed, the Ho:YAG platform remains a robust standard. We conclude that no single laser is universally superior. The choice depends on the intersection of cost, stone complexity, and surgical volume. Low-power Ho:YAG serves cost-sensitive centers, while TFL and High-Power systems serve performance-driven institutions. Future research must prioritize standardized reporting of laser parameters and outcomes to allow for clearer comparative analyses.

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## **CONFLICT OF INTEREST**

None declared.

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# Ureterovesical Junction and Waldeyer's Sheath: A Narrative Review Applied to Vesicoureteral Reflux

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## ABSTRACT

The ureterovesical junction (UVJ) is a specialized anatomical and functional unit responsible for maintaining unidirectional urinary flow from the ureter into the bladder. Dysfunction at this junction may lead to vesicoureteral reflux (VUR), obstruction, recurrent infections, and potential renal damage. The aim of this review is to present a narrative overview of the historical evolution in the understanding of the UVJ and to summarize key surgical principles, techniques, and contemporary controversies in its management. A narrative analysis of historical anatomical literature, landmark surgical innovations, and contemporary management strategies for UVJ pathology was performed. Emphasis was placed on seminal contributors and the evolution of surgical techniques. Early anatomical descriptions established the importance of the intramural ureter and trigonal anatomy. With the advent of cystography, VUR became recognized as a major pediatric urologic condition. Despite technological advances, the fundamental surgical principles governing UVJ reconstruction remain unchanged: adequate submucosal tunnel length, preservation of vascularity, and tension-free reimplantation. Ongoing advances in minimally invasive surgery and biomaterials continue to refine management strategies.

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## INTRODUCTION

Primary vesicoureteral reflux (VUR) is a common pediatric condition that can lead to recurrent urinary tract infections, renal scarring, and reflux nephropathy (1). The ureterovesical junction (UVJ) is the point where each ureter enters the urinary bladder at its posterolateral aspect and traverses the bladder wall obliquely before opening at the ureteral orifice within the trigone. The ureterovesical junction plays a fundamental role in maintaining urinary continence and preventing VUR. The competence of the antireflux mechanism depends largely on the length of the intravesical ureter, its relationship to ureteral diameter, and the structural integrity of the bladder trigone (2). Developmental or structural abnormalities of this region have been associated with VUR and other functional disorders of the urinary tract (3).

The anatomical configuration of the distal ureter is fundamental to the competence of the antireflux mechanism. During fetal life, the relationship between intravesical ureteric length and ureteral diameter evolves, and shorter intravesical segments have been associated with VUR (4). Histological studies in patients with VUR have demonstrated smooth muscle disorganization, increased extracellular matrix deposition, and vascular alterations within the ureteral wall (5, 6).

This narrative review traces the historical milestones in the anatomical understanding of the UVJ and evaluates the importance of its embryological development and structural organization, including Waldeyer's sheath, with a focus on its role in vesicoureteral reflux and surgical innovation.

## EMBRYOLOGY APPLIED TO URETEROVESICAL JUNCTION

The primitive cloaca is divided by the urorectal septum from the fourth to the seventh week after conception (7-9). The cloaca is divided into two parts: the anorectal canal (posterior) and the urogenital sinus (anterior) (Figure-1). The cloacal membrane is also divided into two parts: anteriorly, the urogenital membrane, and posteriorly, the anal membrane. The urogenital sinus

that arises from the primitive cloaca is divided into three parts: the vesical, pelvic, and phallic portions.

The vesical part is the most superior and largest portion of the urogenital sinus. Initially, it is continuous with the allantois, whose lumen later closes, giving rise to the urachus (7-9). The second part of the urogenital sinus, located below the vesical portion, is the pelvic part, which gives rise to the prostate and the membranous part of the urethra (Figure 1). The distal part of the urogenital sinus is the phallic portion, which is externally closed by the urogenital membrane (Figure-1).

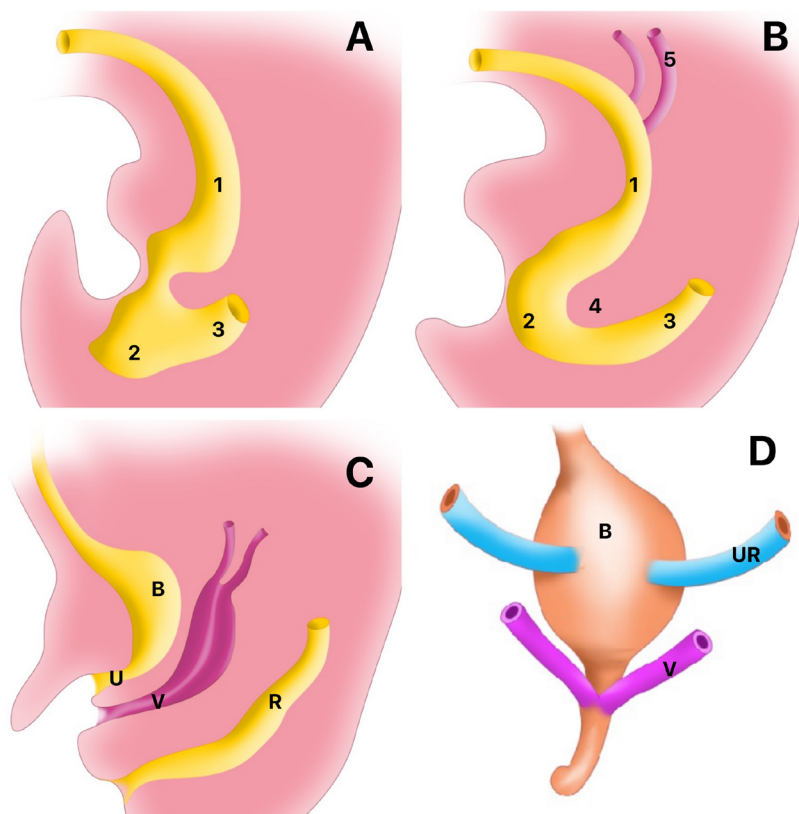
Around the fifth week of development, the distal part of the mesonephric duct in relation to the ureteric buds dilates and is absorbed into the region of the urogenital sinus (8). The mesonephric ducts merge at the midline and form a triangular region, the future bladder trigone (10).

The bladder is embryologically divided into two portions: the body and the trigone. The bladder body derives from the endoderm of the vesical region of the urogenital sinus. The epithelium of this region is derived from the urogenital sinus endoderm, whereas the lamina propria, muscular layers, and adventitia derive from the adjacent splanchnic mesenchyme (7-9).

The fetal bladder can be identified by the tenth week postconception, due to the onset of urine production (11). The bladder is formed from mesenchymal and endodermal cells (11). Most of the urinary bladder originates from the vesical part of the urogenital sinus, while the trigone results from the absorption of the caudal region of the mesonephric duct during bladder development (11, 12). During the second gestational trimester, the bladder undergoes a series of developmental changes, ultimately acquiring a urothelial lining and a well-developed muscular coat (11-13).

The bladder trigone originates from the incorporation of the mesonephric ducts at the base of the developing bladder (10). Initially, these ducts contribute to forming the bladder trigone mucosa. However, this epithelium is later replaced by the endodermal epithelium of the urogenital sinus (7-9).

From the beginning of development until the 35th day after conception, the ureter is patent along its en-

**Figure 1 - Embryological development of the cloaca and urogenital sinus.**

A) At the 5th week of gestation, the cloaca remains undivided, 1 – Urogenital sinus; 2 – Cloaca; 3 – Hindgut; B) At the 6th week, the cloaca is divided into the urogenital sinus and the hindgut, 1 – Urogenital sinus; 2 – Cloaca; 3 – Hindgut; 4 – Urorectal septum; 5 – Müllerian structures; C) By approximately the 12th week, the three openings—anus, vagina, and urethra are formed. B – Urinary bladder; U – Urethra; V – Vagina; R – Rectum and D) Final positions of the ureters and Wolffian ducts (ejaculatory ducts) in male embryos. UR – Ureter; V – Wolffian duct

tire length (8). However, between the 37th and 40th days after conception, the ureteral lumen closes, and only its middle portion remains patent (8). After the 40th day, the ureteral lumen rapidly reopens both cranially and caudally, and the ureter becomes fully patent again.

Anomalies in ureteral development occur in approximately 10% of urological patients (14). The most common anomalies include partial and complete duplication, ectopic orifices, ureterocele, ureterovesical junction incompetence causing ureteral reflux, and intrinsic ureteral obstruction. Congenital ureteral obstructions occur most frequently at the pyeloureteral and ureterovesical junctions. According to Alcaraz (15), congenital ureteral obstructions may be divided into two major groups: intrinsic ureteral

obstructions and obstructions of the ureterovesical junction. The latter occur due to the persistence of the ureterovesical membrane (Chwalla membrane), which temporarily obstructs this region between the 37th and 43rd days after conception (16).

Some bladder pathologies exhibit different patterns between the sexes, particularly primary vesicoureteral reflux, which is generally more severe in male fetuses and is associated with thickening of the bladder wall (17). The second trimester is particularly important in bladder embryonic development (11). The development of the prostate during the second gestational trimester, associated with hormone production by the fetal testes, may contribute to transient urethral obstruction in male fetuses (18, 19).

Muscle development in the region between the two ureteral orifices in the fetal bladder remains a subject of discussion, although it represents a fundamental morphological and functional component of the antireflux mechanism. This mechanism, which prevents urinary reflux, matures during the last trimester of gestation. The formation and proper configuration of this muscular network between the ureteral orifices and the bladder are essential for effective antireflux function (20).

## THE URETEROVESICAL JUNCTION

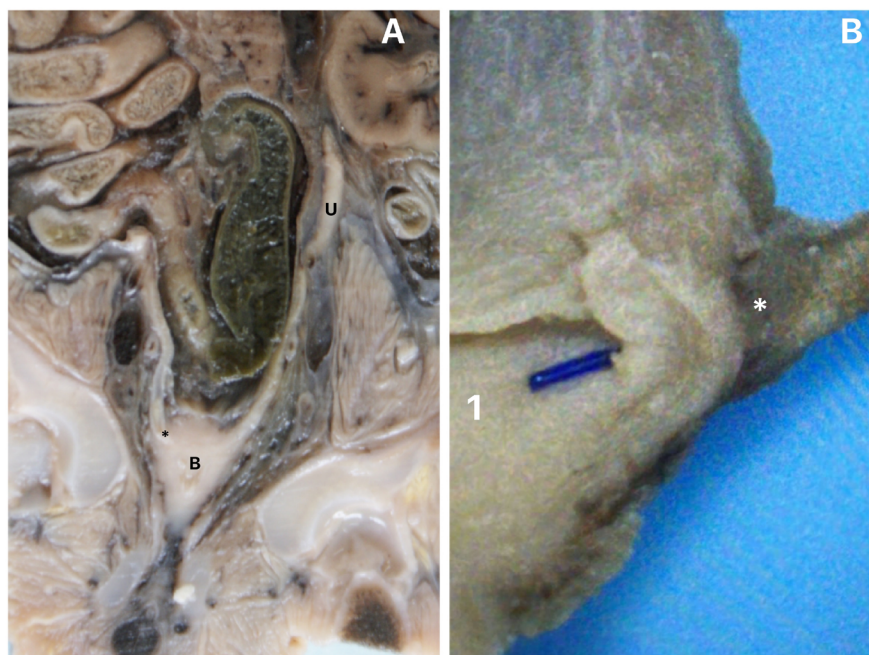
The ureterovesical junction represents the distal integration of the upper urinary tract into the bladder and functions as a dynamic antireflux mechanism (Figure-2). The portion of the ureter that passes through the bladder muscle layer is called the intramural segment; this portion of the ureter extends toward the bladder trigone. The bladder muscular layer that surrounds the intramural portion of the ureter, together with Waldeyer's

sheath (a fibrous sheath that envelops the distal portion of the ureter), compose the mechanism responsible for preventing vesicoureteral reflux (21). Several conditions may cause vesicoureteral reflux, and one of the most common is anomalous implantation of the intramural ureter within the bladder. In patients with reflux, the morphology of the ureteral ostium at the vesical trigone is altered (Figure-3) (21).

Functionally, the UVJ acts as a dynamic antireflux mechanism, protecting the kidneys from elevated bladder pressures. Pathology at this junction manifests primarily as VUR or obstruction, both of which may lead to renal injury if left untreated. The understanding of UVJ anatomy and function has progressed from early cadaveric descriptions to advanced imaging techniques and minimally invasive reconstructive surgery.

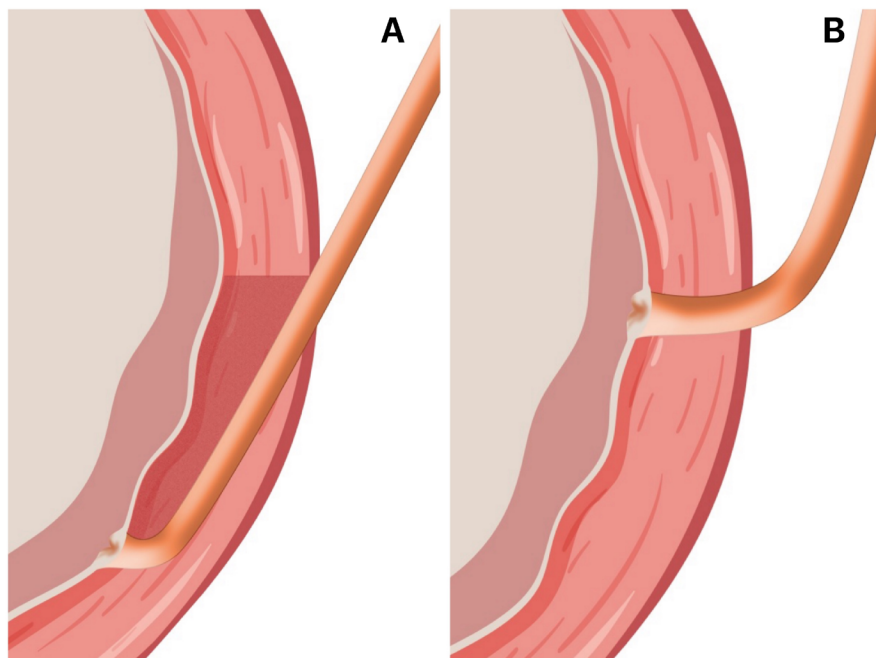
The anatomical configuration of the UVJ produces a physiological valve mechanism: during bladder filling, the ureter remains patent, and during micturition, detrusor contraction compresses the intramural ureter, thereby preventing vesicoureteral reflux. Therefore, his-

**Figure 2 - Ureterovesical junction (UVJ) in a human fetus.**



A) Frontal section showing the UVJ (\*) in a 24-week postconception fetus. B) Macroscopic view of the UVJ (\*) after dissection. The blue polypropylene suture indicates the ureteral lumen. 1 - Bladder trigone; B - Urinary bladder.

**Figure 3 - Schematic representation of the ureterovesical junction and the mechanism of vesicoureteral reflux. Defects of the ureterovesical junction may result in vesicoureteral reflux.**



A) Schematic illustration of a long submucosal tunnel providing adequate muscular support along the intramural ureter, preventing reflux. B) Schematic illustration of a short submucosal tunnel with deficient muscular support, resulting in vesicoureteral reflux.

tologically, it functions as a dynamic muscular, sphincter-like support rather than a true anatomical sphincter.

Previous studies have described the histology of the ureter during the fetal period, demonstrating that the arrangement of the urothelium and the musculature of the ureteral wall is clearly evident during development (22) (Figure-4). In our laboratory, we performed a histological study of the UVJ and demonstrated the relationship between the ureter and the detrusor muscle (Figure-5).

The caliber of the ureter along its course is not uniform, ranging from 2 to 10 millimeters in diameter. Along its course, there are three regions of physiological narrowing: the pyeloureteral junction, the crossing over the iliac vessels, and the intramural portion. These constriction points are common sites where calculi and blood clots may become lodged, and where the introduction of ureteroscopic instruments should be performed with caution to avoid perforation (23).

The blood supply to the ureter at the ureterovesical junction derives primarily from branches of pel-

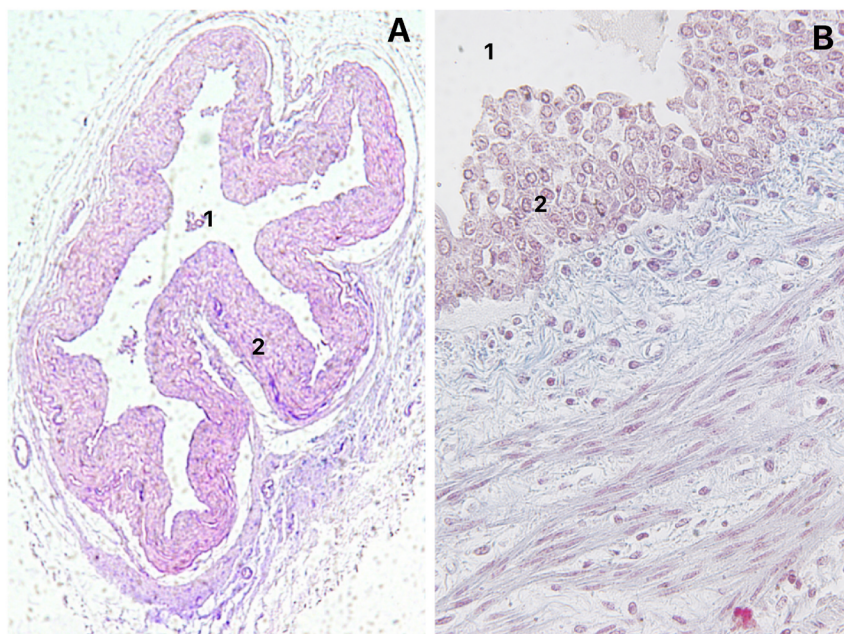
vic vessels. In males, these include the superior vesical artery (a branch of the internal iliac artery), the inferior vesical artery, and occasionally the middle rectal artery. In females, the vascular supply includes the superior vesical artery, the uterine artery, and the vaginal artery. These arteries form a longitudinal anastomotic network along the ureter.

Venous drainage of the UVJ occurs through a ureteric venous plexus that drains into the vesical venous plexus and, in females, into the uterine or vaginal plexus, ultimately reaching the internal iliac vein. Lymphatic drainage of the UVJ occurs primarily to the internal iliac lymph nodes, with additional drainage to the external iliac nodes (23).

The ureterovesical junction receives autonomic innervation from the inferior hypogastric (pelvic) plexus. Sympathetic fibers originate from the T11-L2 spinal segments and travel via the lumbar splanchnic and hypogastric nerves. These fibers function to facilitate ureteric peristalsis and mediate pain (ureteric colic). Parasympathetic fibers originate from the S2-S4 spinal segments



**Figure 4 - Histological features of the human ureter.**



A) Photomicrograph of the ureter in a 20-week postconception human fetus (H&E, x40). B) Higher-magnification photomicrograph of the same specimen (H&E, x400). 1 - Ureteral lumen; 2 - Urothelium.

and travel via the pelvic splanchnic nerves, assisting peristalsis of the distal ureter.

## HEINRICH VON WALDEYER

Heinrich Wilhelm Gottfried von Waldeyer-Hartz (1836–1921) was a German anatomist known for synthesizing neuron theory and for introducing the term "chromosome" (Figure-6). He is also remembered for anatomical structures of the human body that bear his name, including Waldeyer's tonsillar ring (the lymphoid tissue ring of the naso- and oropharynx) and Waldeyer's sheath. Waldeyer was one of the most prominent anatomists and scientists of his time and published 269 papers throughout his career. He also authored two important monographs, *The Pelvis and Ovary and Egg*. Numerous anatomical terms remain associated with his name (24).

In a brief report, Waldeyer described the presence of an injectable space beneath the musculature of the UJ that allows this layer to be easily separated from the ureter, and he referred to a sheath-like struc-

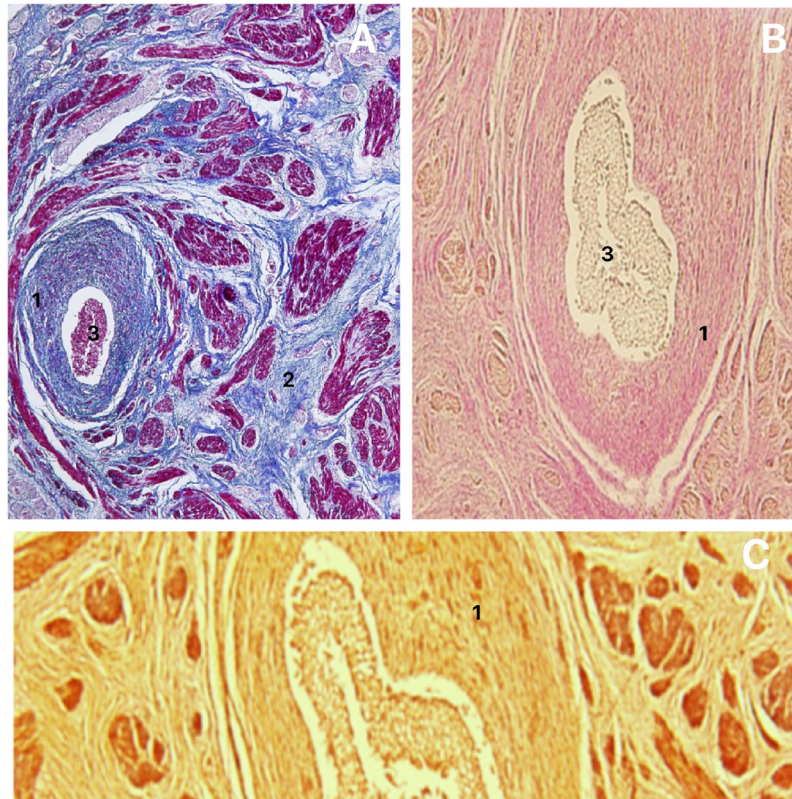
ture, suggesting a gradual origin for Bell's muscle and other muscular components (25). Tanagho and Pugh (26) described "Waldeyer's sheath" in detail, stating that the sheath forms an encircling layer around the distal 1.5 to 3 cm of the ureter and consists histologically of fibromuscular tissue.

## THE WALDEYER'S SHEATH

Waldeyer's sheath is a fibromuscular extension of the bladder detrusor muscle that surrounds the intramural ureter, anchoring the ureter within the bladder wall, contributing to the antireflux valve mechanism, and coordinating with detrusor contraction during voiding. Waldeyer's sheath develops as the detrusor muscle differentiates from the splanchnic mesoderm. As the trigone forms and the ureters are incorporated into the bladder wall, muscle fibers reorganize around the intramural segment, forming Waldeyer's sheath.

Waldeyer's sheath contains collagen and elastic fibers and is composed predominantly of detrusor-de-

**Figure 5 - Histological features of the ureterovesical junction (UVJ).**



A) Photomicrograph of the UVJ in a 20-week postconception human fetus (Masson's trichrome,  $\times 40$ ). B) Higher-magnification photomicrograph of the UVJ in an 18-week postconception human fetus (H&E,  $\times 200$ ). C) Photomicrograph of the UVJ in the same specimen demonstrating the ureteral lumen and its relationship to the surrounding muscular layer (Weigert stain,  $\times 200$ ). 1 - Ureteral muscular layer; 2 - Bladder wall; 3 - Urothelium

rived smooth muscle. It surrounds the distal muscularis and blends with the bladder detrusor, whereas the ureter at the UVJ contains urothelium, lamina propria, and muscularis (inner longitudinal, outer circular, and an additional outer longitudinal layer distally).

The intramural ureter within Waldeyer's sheath provides structural support to the antireflux mechanism and does not function as a true anatomical sphincter (26–28).

Waldeyer and colleagues in 1892 (24) were the first to describe the interureteral muscular junction, referred to as the "torus interureteralis," although the term "interureteral crest" later became more widely adopted. Some authors have described the trigone as a muscular formation resulting from the convergence of ureteral muscle fibers that descend in a fan-shaped pattern, with greater concentration at the lateral border (26). Others

suggest that most ureteral smooth muscle fibers blend contralaterally, forming an interureteral ridge, of which only a portion contributes to the prominence of the lateral border (27). A layer of smooth muscle derived from Waldeyer's sheath, located beneath the so-called superficial trigone, has been described as constituting the "deep trigone" (26, 29).

The concept of Waldeyer's sheath and the structure of the deep trigone were revised following a reassessment of the anatomy of the ureterovesical junction (28, 30, 31). More recently, the existence of an independent vesical muscular sphincter has been postulated, which is thought to traverse the internal urethral orifice in an elliptical manner (32, 33).

Detailed anatomical studies conducted by Tanagho and Pugh (26) confirmed, through dissections

**Figure 6 - Original drawing of Heinrich von Waldeyer (1836-1921).**



and serial histological sections, that this sheath constitutes a continuous mantle of fibromuscular tissue surrounding the juxtavesical and intravesical segments of the ureter. The authors demonstrated that it does not originate from the bladder musculature, as previously proposed, but rather represents an extension of the outer layers of the ureter (Figure-7).

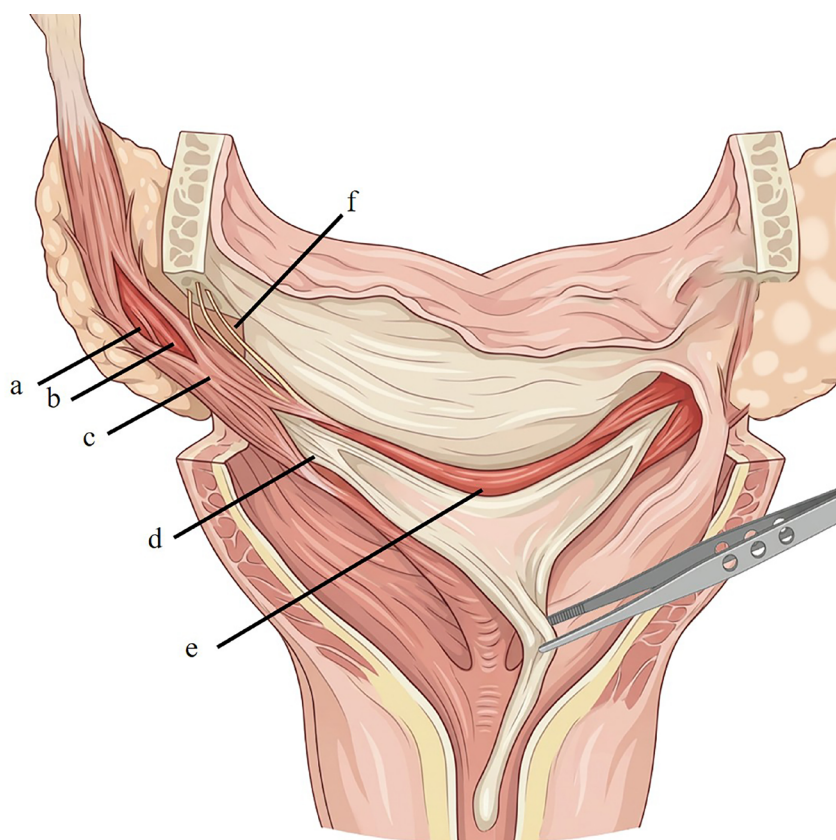
Although most anatomical studies recognize that Waldeyer's sheath continues into the trigone of the bladder, there is disagreement regarding the designation of the anatomical layer with which it integrates. In the study by Tanagho and Pugh (26), the sheath is described as forming the middle layer of the trigone, located between the superficial layer (formed by submucosal ureteral fibers) and the deep layer (composed of the detrusor muscle). More recent descriptions refer to this same structure as the deep layer, considering three distinct planes: submucosal (superficial), Waldeyer's sheath (deep), and detrusor (basal). This therefore represents a terminological variation rather than a structural or embryological difference. Rusu et al. (34) highlighted the compartmental character of the sheath in the regulation of ureterovesical continence and observed that similar

structures may be present along the proximal ureter, suggesting that this represents a common anatomical feature of the human ureter (35).

Functionally, Waldeyer's sheath contributes to the lengthening and stabilization of the intravesical ureter and, consequently, to the competence of the antireflux mechanism. The interaction between its fibers and the trigonal muscle complex facilitates proper anatomical positioning of the ureter and effective occlusion of the ureteral orifice during bladder filling and voiding. Tanagho and Pugh (26) described that the coordinated contraction of the superficial trigonal layer acts as an oblique sphincter-like mechanism, promoting collapse of the intravesical ureter by approximating its superior and inferior walls. Waldeyer's sheath reinforces this mechanism by stabilizing the ureter within the vesical hiatus and contributing to dynamic sealing of the orifice. These findings support the hypothesis that morphological or embryological alterations of this sheath—such as those occurring in central nervous system malformations or urogenital developmental disorders—may compromise the architecture and function of the bladder trigone, thereby predisposing to congenital urinary dysfunction.



**Figure 7 - Anatomical relationships of Waldeyer's sheath at the ureterovesical junction.**



a - Muscular bundle connecting Waldeyer's sheath to the ureter; b - Juxtavesical ureter; c - Waldeyer's sheath surrounding the intramural segment of the ureter; d - Submucosal segment; e - Middle ureterovesical trigonal layer — continuation of Waldeyer's sheath; f - Muscular bundles arising from the middle circular layer and joining Waldeyer's sheath within the ureteral canal.

Proper development of the trigone and ureterovesical junction is essential for maintaining continence and preventing vesicoureteral reflux. The configuration of the ureteral tunnel, its intramural extension, and adequate muscular support together provide a functional valve mechanism that permits unidirectional urine flow toward the bladder, thereby protecting the kidneys from retrograde pressure and ascending infection (36) (Figure-7).

The morphogenesis of these structures is critical for establishing normal urinary tract function. Disturbances in this embryological process may lead to structural alterations of the bladder and urethra, resulting in functional impairment (37), as demonstrated in cases of bladder exstrophy, in which urethral length plays a determining role

in achieving continence and, consequently, in planning reconstructive surgical interventions (38).

A summary of the differences between the ureterovesical junction and Waldeyer's sheath is presented in Table-1.

## CONCLUSIONS

The evolution in the understanding and management of the ureterovesical junction reflects the broader trajectory of urologic surgery—from anatomical observation to reconstructive refinement and minimally invasive precision. Although surgical techniques continue to evolve, the fundamental anatomical principles governing antireflux function remain constant.

**Table 1 - The table shows the differences between the ureterovesical junction and Waldeyer's sheath.**

| FEATURE                   | URETEROVESICAL JUNCTION              | WALDEYER'S SHEATH                           |
|---------------------------|--------------------------------------|---------------------------------------------|
| <b>Definition</b>         | Junction of ureter & bladder         | Fibromuscular covering of intramural ureter |
| <b>Embryologic origin</b> | Ureteric bud + trigone incorporation | Differentiated detrusor muscle              |
| <b>Main function</b>      | Prevent reflux, allow urine entry    | Structural support & valve mechanism        |
| <b>Clinical link</b>      | VUR, megaureter, ureterocele         | Anti-reflux failure if defective            |

## CONFLICT OF INTEREST

None declared.

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# Safety, Complications, and Procedural Efficiency of Neonatal Circumcision Devices: A Network Meta-Analysis

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## ABSTRACT

**Purpose:** This study aims to compare safety, complications, and procedural characteristics of commonly used circumcision devices in neonates and early infants.

**Methods:** We searched PubMed, EMBASE, Web of Science, and SCOPUS through January 2026 for randomized controlled trials comparing infant circumcision devices (Plastibell™, Mogen™, ShangRing™, AccuCirc™) in infants ≤3 months. The primary outcome was total adverse events; secondary outcomes included bleeding, infection, redundant skin, adhesions, parental satisfaction, and procedure time. A random-effects network meta-analysis estimated relative effects with 95% confidence intervals (CI), using Gomco™ or Mogen™ as reference devices. Analyses were performed in R.

**Results:** Ten trials including 3,984 infants from Africa, the Middle East, and the United States were analyzed. No device differed significantly from Gomco™ in total adverse events: Plastibell™ (risk ratios, [RR] 1.53, 95% CI 0.56–4.21), ShangRing™ (RR 2.70, 95% CI 0.31–23.66), Mogen™ (RR 3.83, 95% CI 0.97–15.17), and AccuCirc™ (RR 9.62, 95% CI 0.24–388.45). Plastibell™ was associated with a higher infection risk versus Gomco™ (RR 4.25, 95% CI 1.43–12.65). No significant differences were observed in bleeding, redundant skin, adhesions, or parental satisfaction. Mogen™ and ShangRing™ had shorter procedure times than Gomco™ (mean difference [MD] –3.29 minutes, 95% CI –4.82 to –1.76; MD –3.39 minutes, 95% CI –6.11 to –0.67).

**Conclusions:** Neonatal circumcision devices demonstrate generally comparable safety profiles, though Plastibell™ carries elevated infection risk. Mogen™ and ShangRing™ offer procedural efficiency advantages. Device selection should prioritize provider expertise, infection control capabilities, and programmatic efficiency requirements alongside safety considerations.

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## INTRODUCTION

Neonatal and early infant male circumcision is among the most frequently performed surgical procedures worldwide, with an estimated 30% of males circumcised globally (1). In many regions, including sub-Saharan Africa, the Middle East, and North America, circumcision is performed during the neonatal period or early infancy for cultural, religious, or medical reasons (2). Clinically, early circumcision has been associated with reduced risks of urinary tract infections during infancy and long-term protection against sexually transmitted infections, including human immunodeficiency virus (HIV) (3, 4).

Several devices are routinely used for neonatal circumcision, including the Gomco™ clamp, Plastibell™, Mogen™ clamp, ShangRing™, and AccuCirc™. These devices vary substantially in design and technique. For example, the Gomco™ and Mogen™ clamps require immediate foreskin excision, whereas Plastibell™ and ShangRing™ involve delayed tissue necrosis (5). Reported complication rates across randomized controlled trials (RCTs) range from less than 1% to more than 10%, depending on device type, operator experience, and outcome definitions (5-7). Procedure time also varies considerably, with mean durations reported as short as 3-5 minutes for clamp-based devices and longer for ring-based techniques (8).

Although numerous RCTs have compared individual circumcision devices, most studies are limited by small sample sizes and restricted head-to-head comparisons. The largest multicenter trial to date enrolled more than 1,300 infants and compared ShangRing™ with Mogen™, demonstrating comparable safety but differences in procedural characteristics and acceptability, including variations in operative time, need for device removal, post-procedural follow-up requirements, and caregiver and provider satisfaction (9).

Other trials have reported conflicting findings regarding bleeding, infection, and cosmetic outcomes, making it difficult to draw definitive conclusions (6, 7). Moreover, prior reviews have often pooled neonates with older children or adults, de-

spite important anatomical and physiological differences that may influence outcomes (10, 11).

Given the limited number of large head-to-head trials and the fragmented nature of the available evidence, a comprehensive comparative evaluation of circumcision devices remains lacking. Network meta-analysis (NMA) enables simultaneous comparison of multiple interventions by integrating direct and indirect evidence, allowing estimation of relative effects and ranking of competing devices even in the absence of head-to-head trials (12). Accordingly, we conducted a systematic review and NMA of randomized controlled trials comparing commonly used circumcision devices in neonates and infants within the first three months of life, a restriction that improves clinical homogeneity and relevance to early circumcision practice.

## MATERIALS AND METHODS

### Study design

This study was conducted as a systematic review and network meta-analysis comparing commonly used neonatal circumcision devices. The review was performed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Cochrane handbook guidelines (13, 14). The protocol was registered in PROSPERO (CRD420261305036).

### Literature search strategy

A comprehensive literature search was conducted in PubMed, EMBASE, Web of Science, and SCOPUS from database inception to January 2026. Terms included "circumcision" and device-related key words such as "circumcision device," "circular circumcision device," "disposable circumcision device," "in situ circumcision," and specific device names including Plastibell™, Shang Ring, PrePex, Tara KLamp, Ali's clamp, circular stapler, circumcision stapler, and compression device. Database-specific adaptations were applied for each platform. Reference lists of relevant articles were manually screened to identify additional eligible studies.

### Eligibility criteria

Studies were included if they met the following criteria: (1) RCTs; (2) enrolled neonates or infants within the first three months of life undergoing circumcision; (3) compared at least two circumcision devices of interest; and (4) reported one or more outcomes related to safety, complications, parental satisfaction, or procedural characteristics; and (5) were published in English. Studies were excluded if they involved adult populations, enrolled infants older than three months, used non-randomized designs, included control groups without device comparison, were published in languages other than English, or were conference abstracts without full-text data.

### Study selection

After removal of duplicate records, titles and abstracts were independently screened by two reviewers. Full texts of potentially eligible studies were assessed for inclusion. Disagreements were resolved through discussion or consultation with a third reviewer. Reasons for exclusion at the full-text stage were documented.

### Data extraction

Data were independently extracted by two reviewers using a standardized data collection form. Extracted information included study characteristics, participant characteristics (age, weight, gestational age, HIV exposure), device types, follow-up duration, and reported outcomes. When required, corresponding authors were contacted for missing or unclear data.

### Risk of bias assessment

Risk of bias was assessed independently by two reviewers using the Cochrane Risk of Bias 2.0 tool (15). Bias was evaluated across five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting. Each study was classified as having low risk, some concerns, or high risk of bias. Discrepancies were resolved by consensus.

### Data synthesis and statistical analysis

A random-effects network meta-analysis was performed to compare all devices simultaneously while preserving within-study randomization. Gomco™ or Mogen™ were used as the reference comparator depending on outcome availability. Effect estimates were presented as pooled risk ratios (RRs) or mean differences (MDs) with corresponding 95% confidence intervals (CIs). Ranking probabilities were summarized using P-scores to estimate the relative performance of each device. All statistical analyses were conducted using R programming software. Statistical heterogeneity was assessed using the  $I^2$  statistic and Cochran's Q test within designs. Inconsistency between direct and indirect evidence was evaluated using design-by-treatment interaction models when applicable.

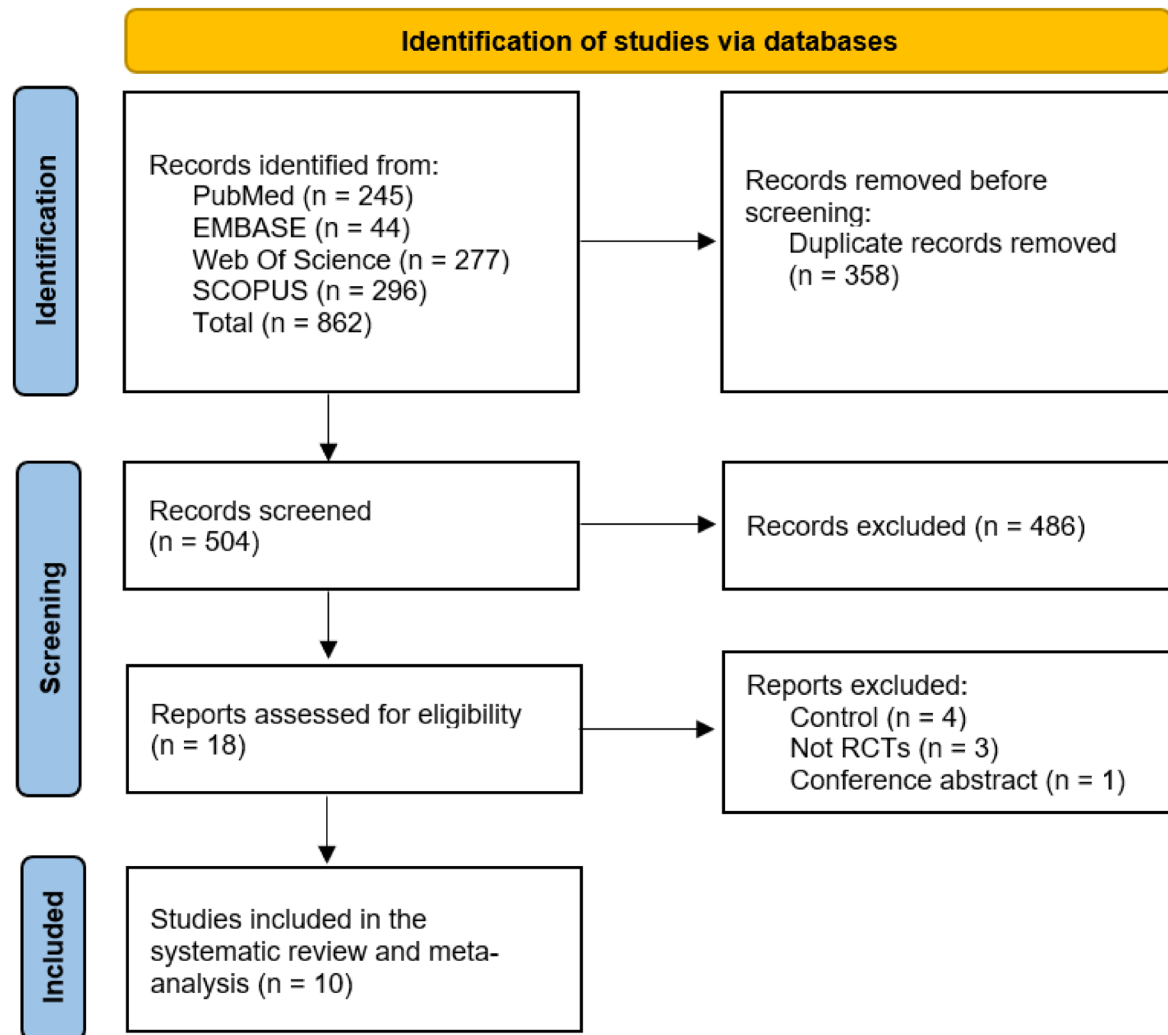
## RESULTS

A total of 862 records were identified from PubMed, EMBASE, Web of Science, and SCOPUS. After removing 358 duplicate records, 504 studies were screened, of which 486 were excluded. Eighteen reports were assessed for eligibility. Eight studies were excluded for predefined reasons: use of control groups ( $n = 4$ ), not randomized controlled trials ( $n = 3$ ), and conference abstracts ( $n = 1$ ). Ultimately, 10 studies were included in the meta-analysis (6-9, 16-21) (Figure-1).

### Baseline and summary of the included studies

The 10 included RCTs were conducted between 2002 and 2024 across Africa, the Middle East, and the United States. Sample sizes ranged from 59 infants to 1,378 participants, with the largest trial comparing ShangRing™ and Mogen™ devices (689 infants per group) (9). All procedures were performed in the neonatal period or early infancy, with mean ages generally between 3 and 28 days. Mean infant weights were consistently around 3.2–4.2 kg. Gestational age, when reported, indicated predominantly term infants (mean ~39–40 weeks). Several African studies included HIV-exposed infants, ranging from 16% to 41%. Devices evaluated included Gom-

Figure 1 - PRISMA Flow Diagram of Study Selection.



co™, Plastibell™, Mogen™, ShangRing™, and AccuCirc™. Follow-up durations varied from immediate assessment to 6 months. Outcomes commonly assessed safety, complications, pain, healing, cosmesis, and caregiver satisfaction, with comparable baseline characteristics across intervention groups (Table-1).

#### Quality assessment

The risk of bias assessment across the 10 included studies showed generally good methodological quality. Four studies demonstrated an overall low risk of bias, reflecting good randomization, outcome mea-

surement, and reporting (9, 19-21). Some concerns were identified in five studies, particularly in the randomization process and outcome measurement (6, 7, 16-18). One early study was judged to have a high overall risk of bias, mainly due to limitations in outcome measurement and reporting (8). Overall, the evidence base was considered moderate to high quality (Figures 2A and 2B).

#### Outcomes

##### Total adverse events

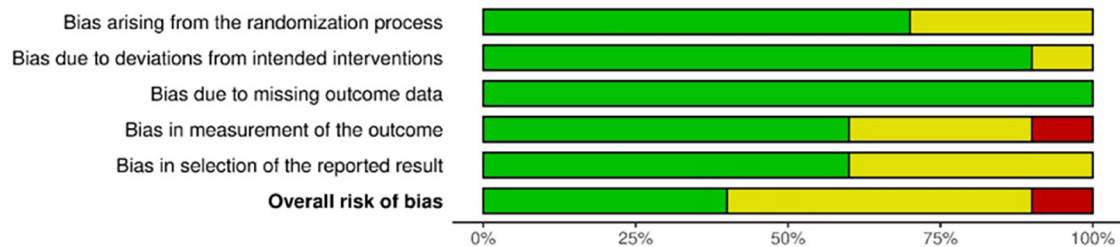
Using Gomco™ as the reference, no statistically significant differences were observed in total

**Table 1 - Baseline and Summary of the included studies.**

| ID                            | Design              | Country      | Registration         | Follow-up         | Primary outcomes              | Device     | Sample size (n) | Age at circumcision, days, Mean $\pm$ SD | Weight at circumcision, Kg, Mean $\pm$ SD | Infant exposure to HIV, % | gestational age in weeks Mean $\pm$ SD |
|-------------------------------|---------------------|--------------|----------------------|-------------------|-------------------------------|------------|-----------------|------------------------------------------|-------------------------------------------|---------------------------|----------------------------------------|
| <b>Alsowayan et al. 2024</b>  | RCT                 | Saudi Arabia | IRB-PCSS201901-042   | 1-3 weeks         | Parent/physician satisfaction | Gomco      | 98              | <3 months                                | Mean 4.19                                 | NR                        | NR                                     |
|                               |                     |              |                      |                   |                               | Plastibell | 92              |                                          |                                           |                           |                                        |
| <b>Ibiyeye et al. 2024</b>    | RCT                 | Nigeria      | NR                   | 7 d & 4 weeks     | Healing, cosmesis             | Gomco      | 50              | 14.08 $\pm$ 7.19                         | 3.71 $\pm$ 0.65                           | NR                        | 39.54 $\pm$ 1.17                       |
|                               |                     |              |                      |                   |                               | Plastibell | 50              | 15.17 $\pm$ 6.16                         | 3.71 $\pm$ 0.65                           |                           | 38.58 $\pm$ 1.22                       |
| <b>Basourakos et al. 2022</b> | Non-inferiority RCT | East Africa  | NCT03338699          | Until healing     | Safety                        | ShangRing  | 689             | 26 $\pm$ 23.8                            | 4.1 $\pm$ 0.89                            | NR                        | NR                                     |
|                               |                     |              |                      |                   |                               | Mogen      | 689             | 26.3 $\pm$ 22.3                          | 4.2 $\pm$ 1.04                            |                           |                                        |
| <b>Bawazir et al. 2019</b>    | RCT                 | Saudi Arabia | NR                   | 1 week & 6 months | Complications                 | Gomco      | 410             | Mean 19 days                             | NR                                        | NR                        | NR                                     |
|                               |                     |              |                      |                   |                               | Plastibell | 383             |                                          |                                           |                           |                                        |
| <b>El-Asmar et al. 2017</b>   | RCT                 | Egypt        | ACTRN12616000190404  | 1 & 4 weeks       | Pain, complications           | Gomco      | 50              | NR                                       | NR                                        | NR                        | NR                                     |
|                               |                     |              |                      |                   |                               | Plastibell | 50              |                                          |                                           |                           |                                        |
| <b>Mavhu et al. 2015</b>      | Non-inferiority RCT | Zimbabwe     | PACTR201301000465398 | 14 days           | Safety, acceptability         | AccuCirc   | 100             | 8 $\pm$ 8                                | 3.2 $\pm$ 0.38                            | 18 (18%)                  | 40 $\pm$ 0.83                          |
|                               |                     |              |                      |                   |                               | Mogen      | 50              | 8 $\pm$ 11.5                             | 3.2 $\pm$ 0.48                            | 8 (16%)                   | 40 $\pm$ 1                             |
| <b>Sinkey et al. 2015</b>     | RCT                 | USA          | NCT01726036          | Short-term        | Neonatal pain                 | Gomco      | 137             | NR                                       | 3.45 $\pm$ 5.15                           | NR                        | 39.44 $\pm$ 1.08                       |
|                               |                     |              |                      |                   |                               | Mogen      | 137             |                                          | 3.4 $\pm$ 4.18                            |                           | 39.29 $\pm$ 1.14                       |
| <b>Bowa et al. 2013</b>       | RCT                 | Zambia       | NR                   | 1 & 6 weeks       | Safety, adverse events        | Mogen      | 216             | 27.3 $\pm$ 5.97                          | 3.57 $\pm$ 0.6                            | 45 (20.8%)                | NR                                     |
|                               |                     |              |                      |                   |                               | Gomco      | 206             | 28.3 $\pm$ 6.7                           | 3.6 $\pm$ 0.6                             | 45 (20.8%)                |                                        |
|                               |                     |              |                      |                   |                               | Plastibell | 218             | 28.7 $\pm$ 7.5                           | 3.6 $\pm$ 0.6                             | 59 (27.1%)                |                                        |
| <b>Plank et al. 2013</b>      | RCT                 | Botswana     | NCT00971958          | 6 weeks, 4 months | Adverse events                | Mogen      | 153             | 5.7 $\pm$ 6.74                           | 3.2 $\pm$ 0.45                            | 62 (41.1%)                | 39.3 $\pm$ 2.45                        |
|                               |                     |              |                      |                   |                               | Plastibell | 147             | 3 $\pm$ 2.45                             | 3.3 $\pm$ 0.45                            | 51 (35.4%)                | 38.7 $\pm$ 0.75                        |
| <b>Tausch et al. 2002</b>     | RCT                 | USA          | NR                   | Immediate         | Pain & duration               | Mogen      | 30              | NR                                       | NR                                        | NR                        | NR                                     |
|                               |                     |              |                      |                   |                               | Plastibell | 29              |                                          |                                           |                           |                                        |

RCT, randomized controlled trial; NR, not reported; d, days; SD, standard deviation; kg, kilograms; HIV, human immunodeficiency virus.

Figure 2 - (A) Risk of bias graph and (B) Risk of bias summary.

**(A) Risk of bias graph****(B) Risk of bias summary**

|       |                        | Risk of bias domains |    |    |    |    |         |
|-------|------------------------|----------------------|----|----|----|----|---------|
|       |                        | D1                   | D2 | D3 | D4 | D5 | Overall |
| Study | Alsowayan et al. 2024  | +                    | +  | +  | -  | +  | -       |
|       | Basourakos et al. 2022 | +                    | +  | +  | +  | +  | +       |
|       | Bawazir et al. 2019    | -                    | +  | +  | +  | -  | -       |
|       | Bowa et al. 2013       | -                    | +  | +  | +  | -  | -       |
|       | El-Asmar et al. 2017   | +                    | +  | +  | -  | -  | -       |
|       | Ibiyeye et al. 2024    | +                    | +  | +  | -  | +  | -       |
|       | Mavhu et al. 2015      | +                    | +  | +  | +  | +  | +       |
|       | Plank et al. 2013      | +                    | +  | +  | +  | +  | +       |
|       | Sinkey et al. 2015     | +                    | +  | +  | +  | +  | +       |
|       | Taeusch et al. 2002    | -                    | -  | +  | X  | -  | X       |

Domains:  
D1: Bias arising from the randomization process.  
D2: Bias due to deviations from intended intervention.  
D3: Bias due to missing outcome data.  
D4: Bias in measurement of the outcome.  
D5: Bias in selection of the reported result.

Judgement  

X

 High  

-

 Some concerns  

+

 Low

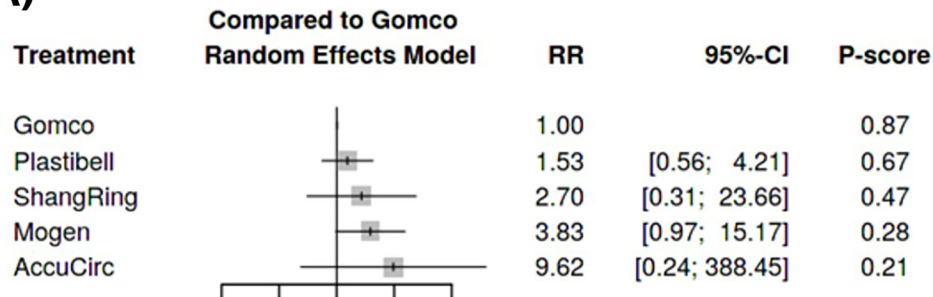
adverse events across devices, as follows: Plastibell™ (RR 1.53, 95% CI 0.56–4.21), ShangRing™ (RR 2.70, 95% CI 0.31–23.66), Mogen™ (RR 3.83, 95% CI 0.97–15.17), and AccuCirc™ (RR 9.62, 95% CI 0.24–388.45). Head-to-head comparisons among AccuCirc™, Mo-

gen™, Plastibell™, and ShangRing™ similarly showed no significant differences. Substantial heterogeneity was present ( $I^2 = 78.5\%$ ), mainly due to inconsistency between direct and indirect evidence ( $Q = 18.6$ ,  $p < 0.001$ ) (Figures 3A, 3B and 3C).

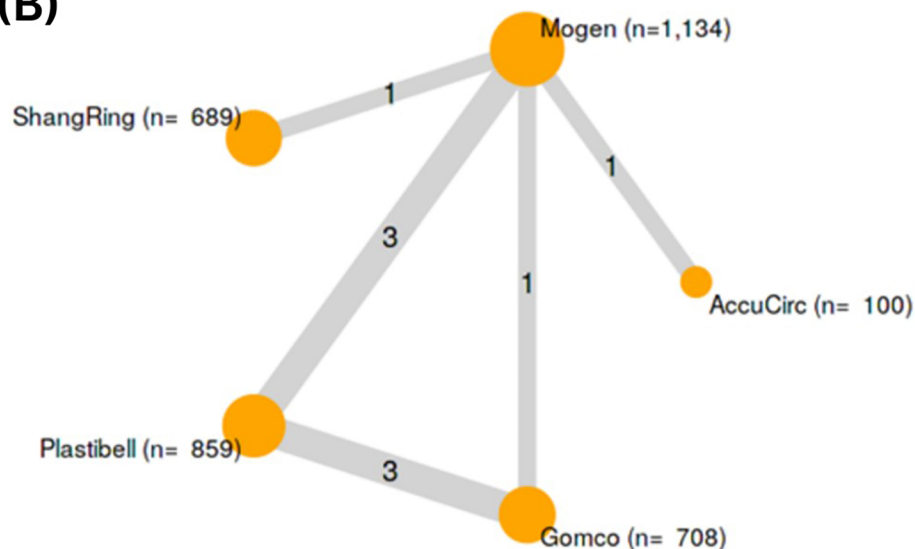


Figure 3 - Total Adverse Events, (A) Network Meta-analysis, (B) Network graph, and (C) Net league

(A)



(B)



(C)

| AccuCirc            | Gomco             |  |  |  | Mogen             |  | Plastibell        |  | ShangRing |  |
|---------------------|-------------------|--|--|--|-------------------|--|-------------------|--|-----------|--|
| 9.62 [0.24; 388.45] | 0.26 [0.07; 1.03] |  |  |  | 2.50 [0.76; 8.23] |  | 0.57 [0.07; 4.45] |  |           |  |
| 2.51 [0.08; 77.75]  | 0.65 [0.24; 1.79] |  |  |  |                   |  |                   |  |           |  |
| 6.28 [0.17; 237.50] |                   |  |  |  |                   |  |                   |  |           |  |
| 3.56 [0.08; 162.61] | 0.37 [0.04; 3.25] |  |  |  | 1.42 [0.26; 7.60] |  |                   |  |           |  |

**Bleeding risk**

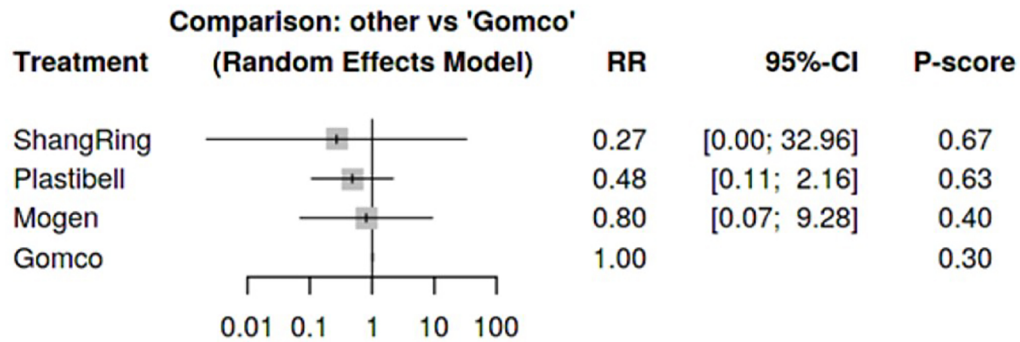
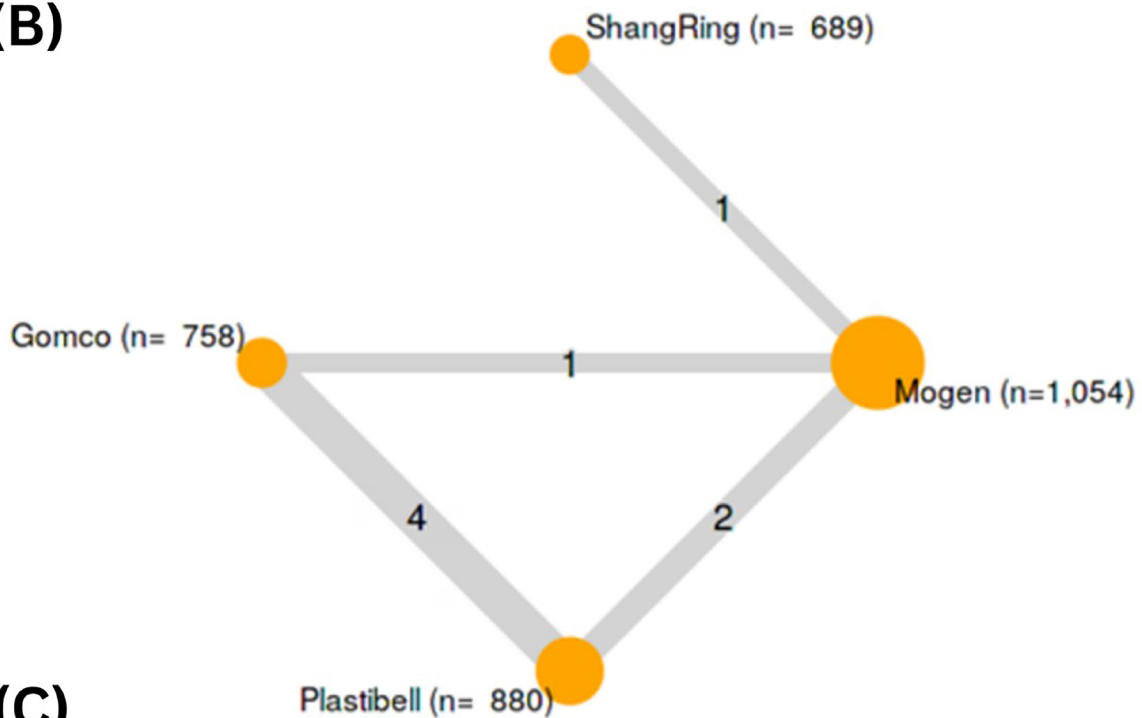
Similarly, compared with Gomco™, no significant differences were found in the risk of bleeding across devices. ShangRing™ showed a risk ratio of 0.27 (95% CI 0.00–32.96), Plastibell™ a risk ratio of 0.48 (95% CI 0.11–2.16), and Mogen™ a risk ratio of 0.80 (95% CI 0.07–9.28). Head-to-head comparisons among ShangRing™, Plastibell™, and Mogen™

similarly demonstrated no significant differences in bleeding risk. High heterogeneity was present ( $I^2 = 77.6\%$ ) (Figures 4A, 4B, and 4C).

**Infection risk**

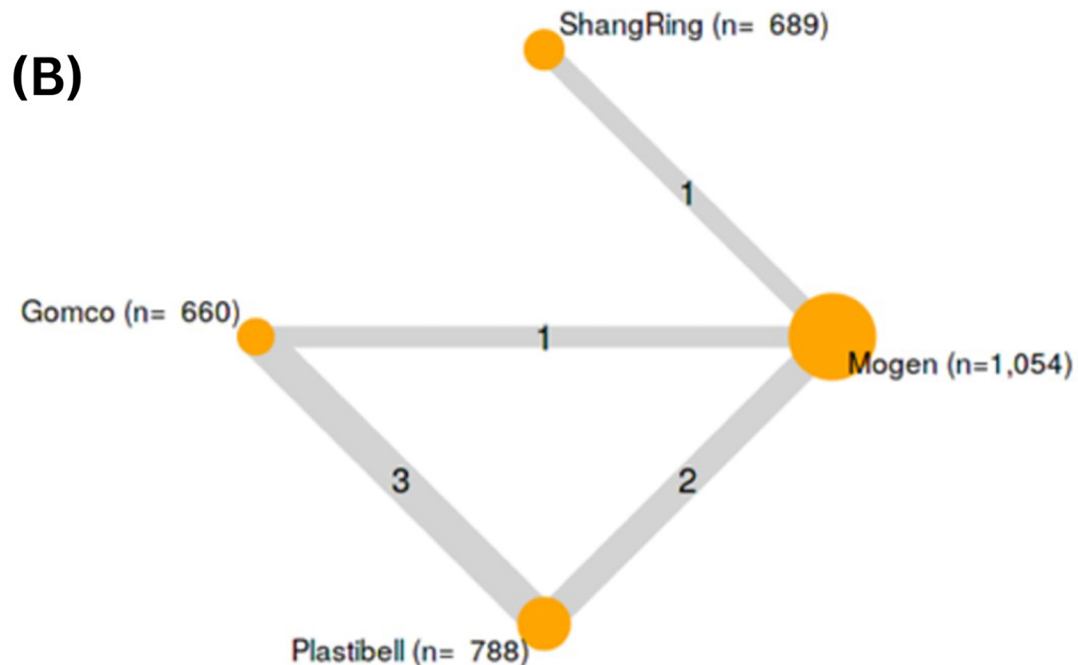
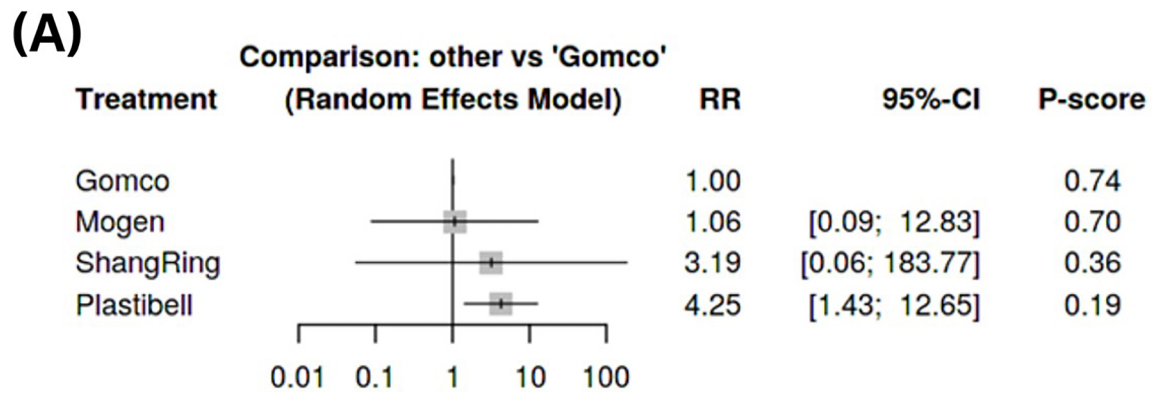
Compared with Gomco™, no statistically significant difference in infection risk was observed for Mogen™ (RR 1.06, 95% CI 0.09–12.83) or ShangRing™

Figure 4 - Bleeding Risk, (A) Network Meta-analysis, (B) Network graph, and (C) Net league

**(A)****(B)****(C)**

| Gomco |                | Mogen |                | Plastibell |                | ShangRing |
|-------|----------------|-------|----------------|------------|----------------|-----------|
| 1.25  | [0.11; 14.42]  |       |                |            |                |           |
| 2.08  | [0.46; 9.37]   | 1.67  | [0.17; 16.91]  |            |                |           |
| 3.74  | [0.03; 460.99] | 3.00  | [0.05; 189.40] | 1.79       | [0.02; 206.86] |           |

Figure 5 - Infection Risk, (A) Network Meta-analysis, (B) Network graph, and (C) Net league



**(C)**

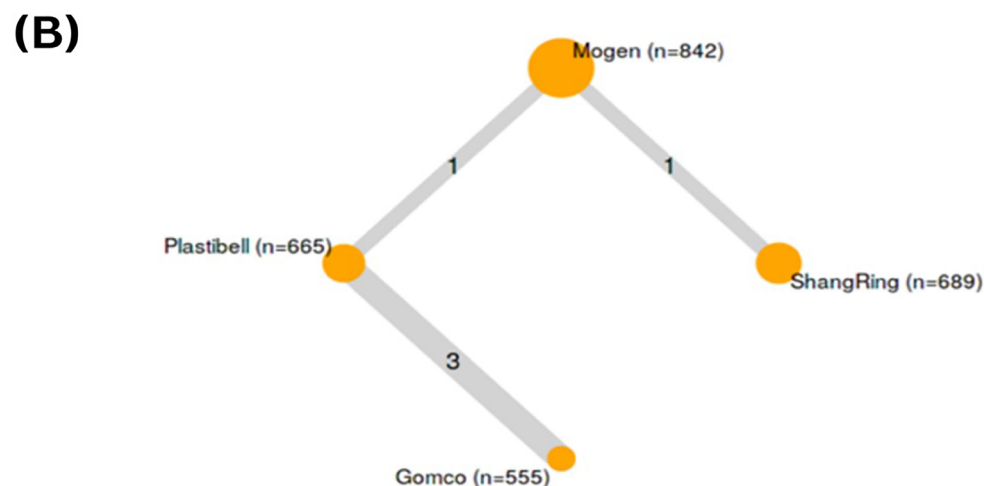
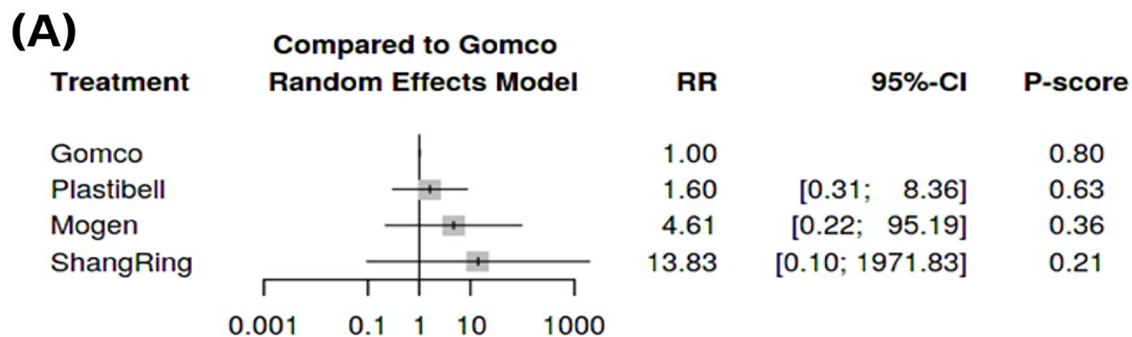
|                          |                   |                    |                  |
|--------------------------|-------------------|--------------------|------------------|
| <b>Gomco</b>             |                   |                    |                  |
| 0.94 [0.08; 11.38]       | <b>Mogen</b>      |                    |                  |
| <b>0.24 [0.08; 0.70]</b> | 0.25 [0.02; 2.60] | <b>Plastibell</b>  |                  |
| 0.31 [0.01; 18.11]       | 0.33 [0.01; 8.17] | 1.33 [0.03; 70.24] | <b>ShangRing</b> |

(RR 3.19, 95% CI 0.06–183.77), whereas Plastibell™ was associated with a significantly higher risk of infection (RR 4.25, 95% CI 1.43–12.65). No significant differences were observed in head-to-head comparisons. Heterogeneity was negligible, with no evidence of within-design variability or inconsistency between direct and

indirect results ( $I^2 = 0\%$ ) (Figures 5A, 5B and 5C).

No statistically significant differences were observed between devices in terms of redundant skin. No major heterogeneity was detected within study designs ( $Q = 5.5$ ,  $p = 0.064$ ), while overall heterogeneity was moderate ( $I^2 = 63.6\%$ ) (Figures 6A, 6B and 6C).

**Figure 6 - Residual (Redundant) Skin, (A) Network Meta-analysis, (B) Network graph, and (C) Net league**



**(C)**

|                    |                    |                    |                  |
|--------------------|--------------------|--------------------|------------------|
| <b>Gomco</b>       |                    |                    |                  |
| 0.22 [0.01; 4.48]  | <b>Mogen</b>       |                    |                  |
| 0.63 [0.12; 3.27]  | 2.88 [0.23; 36.39] | <b>Plastibell</b>  |                  |
| 0.07 [0.00; 10.31] | 0.33 [0.01; 16.94] | 0.12 [0.00; 12.41] | <b>ShangRing</b> |

### Adhesions

For adhesions, Mogen™ was used as the reference (RR = 1.00; P-score = 0.16). Lower risks were estimated for Plastibell™ (RR 0.28, 95% CI 0.08–1.00) and ShangRing™ (RR 0.50, 95% CI 0.05–5.50), with no statistically significant differences observed. Heterogeneity could not be formally assessed because only two studies were included in the analysis (Figures 7A, 7B, and 7C).

### Parental satisfaction rate

Compared with Gomco™, estimated parental satisfaction was comparable for Plastibell™ (RR 0.35, 95% CI 0.05–2.67; P-score 0.73), AccuCirc™ (RR 0.99, 95% CI 0.02–54.98), ShangRing™ (RR 1.00, 95% CI 0.02–55.28), and Mogen™ (RR 1.00, 95% CI 0.06–17.14). However, substantial heterogeneity was observed ( $I^2 = 97.2\%$ ), because of significant within-design variability (Figures 8A, 8B and 8C).

**Figure 7 - Adhesions, (A) Network Meta-analysis, (B) Network graph, and (C) Net league**

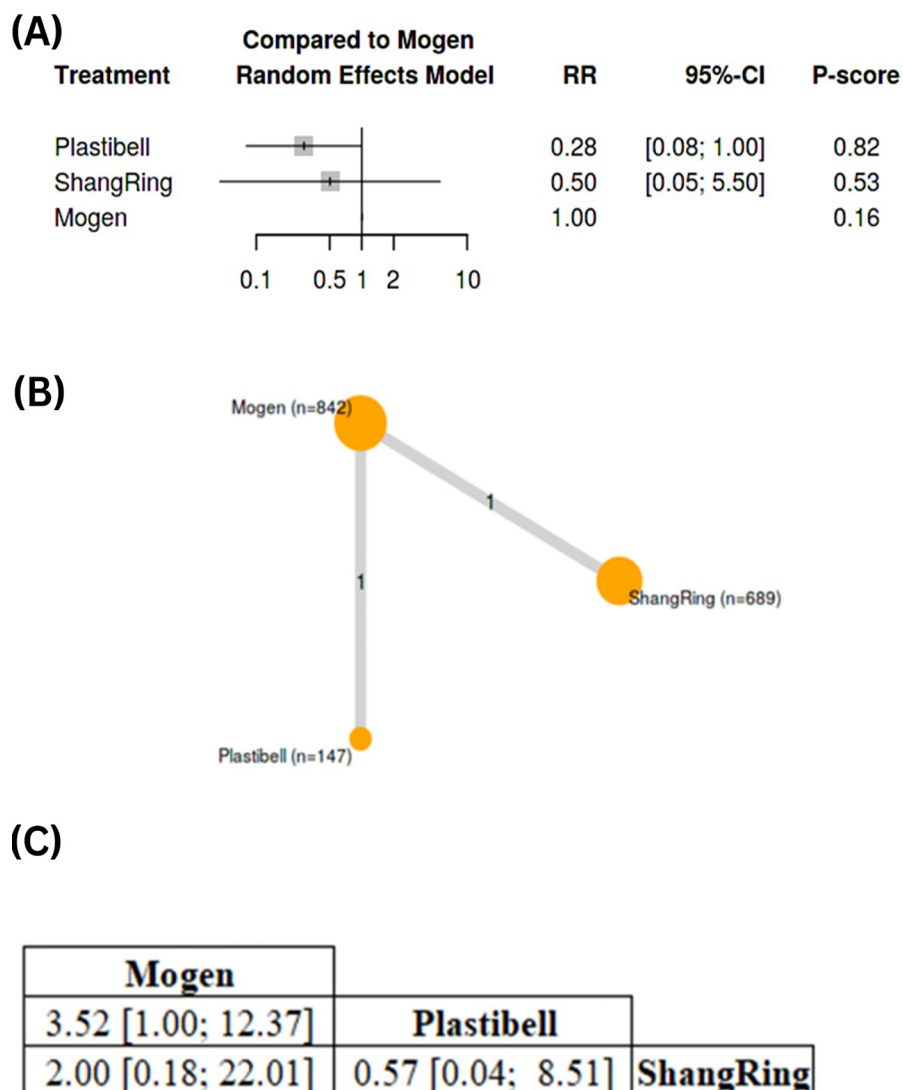
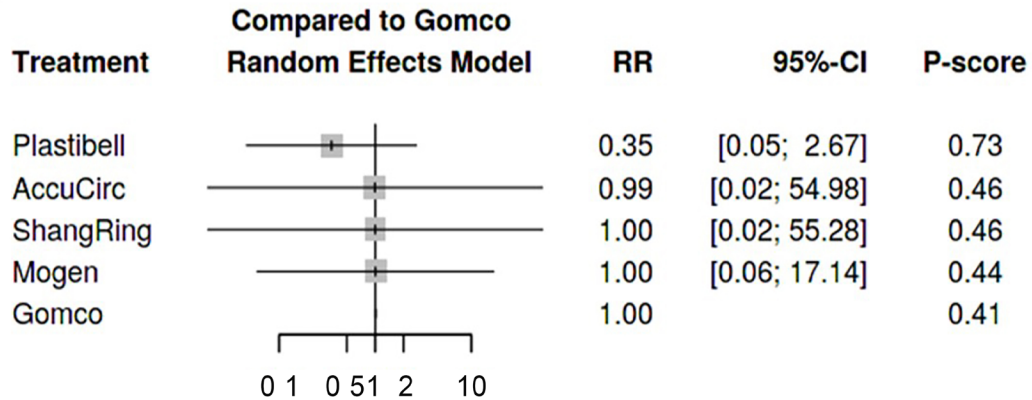
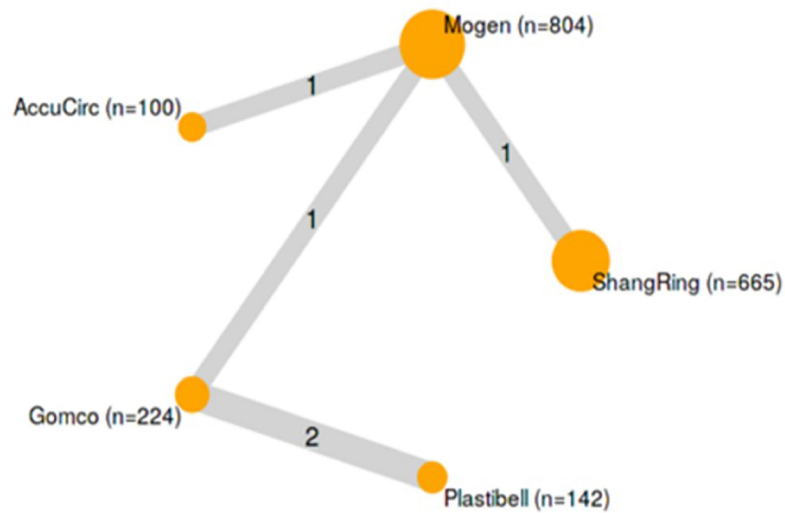


Figure 8 - Parental Satisfaction Rate, (A) Network Meta-analysis, (B) Network graph, and (C) Net league

(A)



(B)



(C)

| AccuCirc            |                    |                    |                    |           |  |
|---------------------|--------------------|--------------------|--------------------|-----------|--|
| 0.99 [0.02; 54.98]  |                    | Gomco              |                    |           |  |
| 0.99 [0.06; 16.92]  | 1.00 [0.06; 17.06] | Mogen              |                    |           |  |
| 2.85 [0.03; 256.46] | 2.87 [0.37; 21.95] | 2.87 [0.09; 94.53] | Plastibell         |           |  |
| 0.99 [0.02; 55.10]  | 1.00 [0.02; 55.53] | 1.00 [0.06; 17.17] | 0.35 [0.00; 31.49] | ShangRing |  |

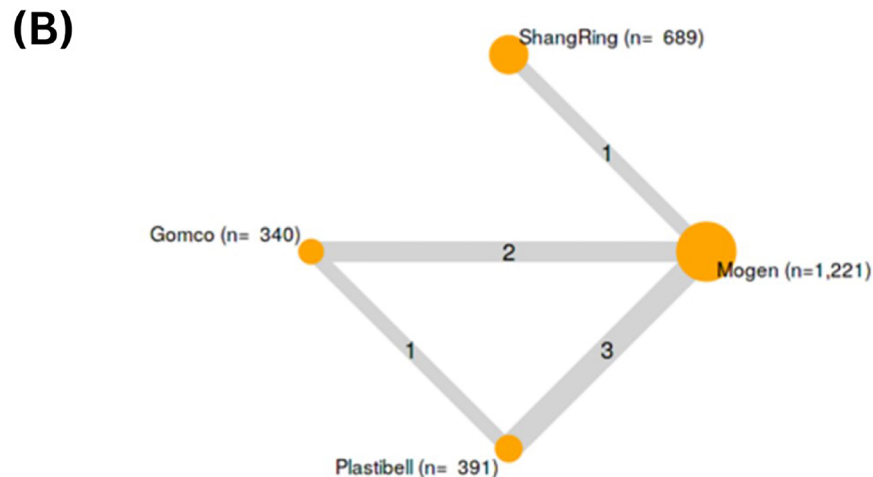
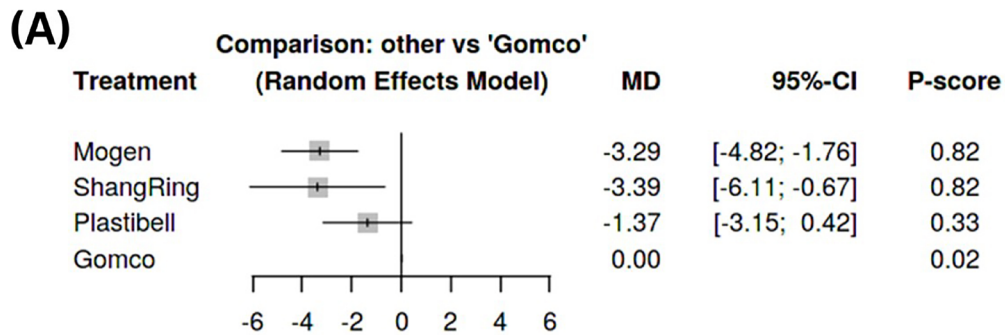


**Procedure Time (minutes)**

Compared to Gomco™, both Mogen™ (MD -3.29 minutes, 95% CI -4.82 to -1.76; P-score 0.82) and ShangRing™ (MD -3.39 minutes, 95% CI -6.11 to -0.67; P-score 0.82) were associated with shorter procedure times. Plastibell™ did not show time reduction (MD -1.37 minutes, 95% CI -3.15 to 0.42). Direct

comparison between Mogen™ and Plastibell™ favored Mogen™, indicating a shorter procedure time (MD -1.92, 95% CI -3.33 to -0.52). Heterogeneity was observed within study designs ( $Q = 10.6$ ,  $p = 0.001$ ), with no inconsistency between direct and indirect evidence (Figures 9A, 9B and 9C).

**Figure 9 - Procedure Time, (A) Network Meta-analysis, (B) Network graph, and (C) Net league**



**(C)**

| Gomco              | Mogen                | Plastibell         | ShangRing |
|--------------------|----------------------|--------------------|-----------|
| 3.29 [ 1.76; 4.82] | -1.92 [-3.33; -0.52] | 2.02 [-0.63; 4.68] |           |
| 1.37 [-0.42; 3.15] | 0.10 [-2.15; 2.35]   |                    |           |
| 3.39 [ 0.67; 6.11] |                      |                    |           |

## DISCUSSION

This network meta-analysis synthesized evidence from 10 RCTs involving neonates and infants within the first three months of life to compare commonly used circumcision devices. Our findings refine current assumptions about device safety and performance.

The most important finding was the absence of significant differences in total adverse events across most devices. This overall safety equivalence is reassuring for clinicians and parents facing device selection decisions. However, further analysis of specific complications revealed important distinctions. Plastibell™ demonstrated a notable elevated infection risk compared to Gomco™, a finding that warrants clinical attention despite the device's widespread use. The mechanism behind this increased infection risk likely relates to the Plastibell™'s design principle of delayed tissue necrosis, where the plastic ring remains in place for several days post-procedure (22). This extended period, during which the Plastibell™ ring typically remains in place for 5–10 days (mean  $\approx$ 8.7 days in infants under three months) (23), creates a potential site for bacterial colonization beneath the device, particularly if hygiene protocols are not maintained or if the ring does not detach as expected.

In contrast, bleeding complications showed no significant differences across devices, suggesting that when properly applied by trained providers, all devices provide adequate hemostasis. The lack of differences in redundant skin and adhesions further supports that device choice may be less critical than operator skill and experience for these specific outcomes (24). Perhaps most relevant for clinical workflow, both Mogen™ and ShangRing™ demonstrated significantly shorter procedure times compared to Gomco™, approximately 3 minutes faster on average. For busy clinical practices or resource-limited settings conducting high-volume circumcision programs, this efficiency gain could translate into substantial time savings. The mechanism is straightforward: both Mogen™ and ShangRing™ require fewer procedural steps and simpler application tech-

niques than the more complex Gomco™ clamp assembly (21).

Our findings both align with and extend previous systematic syntheses while highlighting important distinctions. Meta-analyses comparing device-assisted with conventional circumcision techniques have consistently reported shorter operative times and reduced bleeding with device-based approaches. For example, Kafagi et al. (2025) demonstrated improved procedural efficiency with device-assisted techniques, findings that are consistent with our results on operative duration (11). However, their inclusion of older children limits direct comparability with our exclusively neonatal population.

Similarly, Güler et al. (2022) reported that ring devices were associated with shorter surgical duration and higher satisfaction compared with classic open methods (25). Notably, they identified an increased hemorrhage risk with Plastibell™ relative to open procedures. In our analysis, Plastibell™ also demonstrated an elevated complication profile, although this manifested primarily as increased infection risk rather than bleeding, suggesting device-specific patterns of adverse events in early infancy.

Broader evaluations of circumcision safety further contextualize our findings. Shabanzadeh et al. (2021) reported an overall complication rate of 3.84% across all ages, with higher risks observed in therapeutic procedures (26). Consistent with established evidence, Weiss et al. (2010) demonstrated substantially lower complication rates in neonates compared with older children (median 1.5% vs 6%) (27). By restricting our analysis to neonatal nontherapeutic circumcision, we observed generally lower complication rates, reinforcing the safety advantage of early intervention.

Importantly, while prior meta-analyses such as Huo et al. (2017) concluded that disposable circumcision devices and conventional methods have comparable overall safety profiles (10), these studies relied primarily on pairwise comparisons. In contrast, our network meta-analysis provides device-specific relative effect estimates and hierarchical rankings, allowing simultaneous comparison of multiple commonly used

devices and offering more granular evidence to inform clinical decision-making.

Our findings have several important implications for clinical practice and public health programming. First, the overall safety equivalence across most devices empowers clinicians to select instruments based on their training, comfort level, and procedural context rather than safety concerns alone. An exception is the higher infection risk associated with the Plastibell™ device, which warrants careful consideration, particularly in settings with limited follow-up capacity or where caregiver education on device hygiene may be inadequate.

Second, shorter procedure times with Mogen™ and ShangRing™ devices hold particular relevance for resource-constrained settings implementing large-scale early infant male circumcision programs for HIV prevention in sub-Saharan Africa. Third, time savings of 3-4 minutes per procedure could enable substantially increased daily case volumes without compromising quality. However, in circumcision programs for HIV prevention our parental satisfaction data showed no significant differences between devices, possibly reflecting the multifactorial nature of satisfaction.

Finally, the high heterogeneity observed in several outcomes suggests that some differences between devices may be influenced by variability in study design, outcome definitions, provider expertise, and follow-up duration rather than true device-related effects. This variability, along with wide confidence intervals, reduces the certainty of pooled estimates and limits the reliability and consistency of effect direction. Therefore, findings should be interpreted with caution, as standardization of surgical technique, provider training, and postoperative care may be as important as device selection in optimizing outcomes.

This network meta-analysis represents the most comprehensive simultaneous comparison of neonatal circumcision devices to date, employing a rigorous methodology including systematic literature search, independent dual review, and validated risk-of-bias assessment. By restricting our analysis to the first three months of life, we achieved greater clinical homogeneity than previous reviews that pooled neo-

nates with older children or adults. The network approach enabled both direct and indirect comparisons, generating relative effect estimates even for device pairs rarely compared head-to-head in primary trials.

However, several limitations warrant acknowledgment. First, substantial statistical heterogeneity in some outcomes suggests unmeasured variability across studies in patient populations, surgical techniques, or outcome definitions. Second, the small number of trials for certain device comparisons (particularly AccuCirc™) limited precision for some estimates, reflected in wide confidence intervals. Third, follow-up duration varied considerably across studies, potentially affecting late complication detection. Finally, all included studies were conducted in hospital or clinic settings; generalizability to traditional or community-based circumcision programs remains uncertain.

This network meta-analysis demonstrates that commonly used circumcision devices for neonates and early infants offer generally comparable safety profiles, with the notable exception of increased infection risk with Plastibell™. Mogen™ and ShangRing™ provide procedural efficiency advantages through significantly shorter operating times, making them particularly attractive for high-volume settings. Device selection should be guided by provider expertise, procedural context, infection control capabilities, and efficiency requirements rather than fears of safety concerns.

We recommend that circumcision programs emphasize comprehensive provider training, standardized technique, and strong infection prevention protocols regardless of device choice. Future research should prioritize large-scale pragmatic trials with extended follow-up to capture late complications, economic analyses comparing device costs and efficiency, and implementation studies examining optimal training and quality assurance strategies. Particular attention should be directed toward understanding and mitigating the elevated infection risk associated with Plastibell™, potentially through enhanced caregiver education and closer follow-up during the critical period before ring detachment.

## CONFLICT OF INTEREST

None declared.

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# Multicentre Validation of the 2019 Briganti Nomogram: One Threshold Does Not Fit All

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## ABSTRACT

**Purpose:** The 2019 Briganti nomogram is widely used to guide the indication for pelvic lymph node dissection (LND) at the time of radical prostatectomy in patients with localized prostate cancer. Although previously validated, its generalizability across distinct clinical settings remains uncertain.

**Materials and methods:** We conducted a multicentre external validation of the nomogram in 481 patients from three French academic institutions (Centre A n=198, Centre B n=183 and Centre C n=100). Discrimination, calibration, and clinical utility were assessed. Spared LNDs and missed lymph node invasions (LNIs) were evaluated across risk thresholds.

**Results:** The overall area under the receiver operating characteristics curve (AUC) was 0.733 but varied across centres (0.580-0.768). Calibration was acceptable overall but showed systematic overestimation in low-prevalence centres. At the 7% recommended threshold, the proportion of spared LNDs ranged from 51% to 76%, while missed LNIs ranged from 0% to 8.9%. Decision curve analysis revealed that the optimal threshold differed between centres.

**Conclusions:** These results underscore the need for local validation and population-specific threshold adjustment before clinical implementation. Fixed thresholds may lead to under- or overtreatment depending on institutional case mix. Nomogram-based decision-making should be individualized based on local performance and patient-centred risk tolerance.

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## INTRODUCTION

In contemporary urologic oncology, nomograms have become essential tools to support individualized clinical decision-making (1-3). By integrating multiple clinical, biological, and imaging variables, these models provide patient-specific risk estimates that often outperform traditional risk stratification systems. Their use has been associated with improved risk discrimination, better patient counselling, and more rational use of invasive procedures (4, 5). However, their performance is highly dependent on the population in which they are applied, and concerns remain regarding their transportability across different healthcare settings, particularly when derived from highly selected cohorts or single institutions.

In patients with localized prostate cancer (PCa), such nomograms have become integral to preoperative decision-making, particularly for evaluating the indication for pelvic lymph node dissection (LND) at the time of radical prostatectomy. The 2019 Briganti nomogram, developed by Gandaglia et al. (6), is one of the most widely adopted tools for predicting the risk of lymph node invasion (LNI), incorporating prostate-specific antigen (PSA), magnetic resonance imaging (MRI) findings, and results from both targeted and systematic biopsies. The authors proposed a 7% risk threshold above which an extended LND should be performed (6).

Although the 2019 Briganti nomogram underwent external validation shortly after its publication (7), its generalizability across diverse clinical settings remains incompletely characterized. We hypothesized that the nomogram's performance may vary depending on the population to which it is applied, thus requiring centre-specific validation. Furthermore, the optimal trade-off between the potential benefits and harms of LND likely depends on cohort-specific disease characteristics and may not align with the originally proposed 7% threshold. In the present study, we externally evaluated the 2019 Briganti nomogram in a multi-institutional cohort of patients diagnosed with PCa via MRI-targeted and systematic biopsies and investigated the optimal risk threshold for guiding the decision to perform extended LND.

## MATERIALS AND METHODS

After obtaining institutional review board (IRB) approval at each participating centre and for the overall cohort (IRB number: CRI-DATA DATA240274), we retrospectively identified 481 patients with clinically localized PCa who underwent robotic radical prostatectomy and extended pelvic lymph node dissection according to a standardized template including the external iliac, obturator, and hypogastric nodes (8). Patients were enrolled between October 2020 and December 2024 at three French academic institutions. All individuals were diagnosed using a combination of multiparametric magnetic resonance imaging (mpMRI)-targeted and concomitant systematic prostate biopsies. Magnetic resonance imaging was performed using either 1.5-T or 3.0-T scanners, following the European Society of Urogenital Radiology (ESUR) guidelines (9). The imaging protocol included T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences. Lesions were scored according to the Prostate Imaging-Reporting and Data System (PI-RADS) version 2.1 (10) by uro-radiologists with an experience in prostate MRI (>500 cases) at each centre. Targeted biopsies were conducted using elastic fusion with the KOELIS® system (KOELIS, La Tronche, France) by experienced urologists (>50 procedures a year for at least 5 years), with a minimum of two targeted cores sampled per index lesion. Systematic biopsies included a minimum of 6 to 12 cores outside the MRI index lesion. All prostatectomy specimens were evaluated by dedicated uropathologists at each centre following standardized histopathological protocols, in accordance with the 2019 International Society of Urological Pathology (ISUP) consensus (11). Pathological staging and grading were reported using the TNM system and ISUP grade group (11, 12), ensuring consistency across institutions. Patients were excluded if data on MRI, biopsy findings, or final pathology were incomplete.

The predicted probability of LNI for each patient was calculated using the logistic regression formula published in the original development study of the 2019 Briganti nomogram (6). The linear predic-

tor (LP) was computed using the original coefficients (see supplementary Table-1). The predicted probability was then obtained by applying the logistic transformation:  $P_{LNI} = \frac{1}{1+e^{-LP}}$ . Discrimination was evaluated using the area under the receiver operating characteristics (ROC) curve (AUC), and 95% confidence intervals (95% CI) were estimated via bootstrapping. Calibration was assessed using calibration plots, and clinical utility was assessed through decision curve analysis (DCA) across thresholds from 2% to 15%. Additionally, we calculated spared LNDs and missed LNIs at each threshold from 2% to 10%. The number of spared LNDs and missed LNIs was calculated by applying each risk threshold to the predicted probabilities: patients with predicted risks below the threshold were considered as candidates to omit LND (spared LNDs), and among these, those who had pathologically confirmed LNI were counted as missed LNIs. All statistical analyses were performed using R Studio Version 4.4.2 2024-10-31 (R Foundation for Statistical Computing, Vienna, Austria) employing the "pROC", "boot", "CalibrationCurves", and "dcurves" packages. This external validation study followed the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) recommendations (13).

## RESULTS

Population characteristics varied across centres (Table-1). Median PSA ranged from 7.14 to 9.4 ng/mL, and the proportion of extra-capsular extension and seminal vesicle invasion ranged from 9% to 15% and from 2% to 6% respectively. Prostate imaging reporting and data system (PIRADS) 5 lesions and International Society of Urological Pathology (ISUP) grade group 5 were more frequent in Centre A. The prevalence of LNI ranged from 2% (Centre C) to 14% (Centre A). Patients characteristics from the original "development" and "validation" cohorts can be found in Supplementary Table-2.

Discrimination analysis showed variability in the nomogram's performance. The AUC values were 0.77 (95% CI 0.67-0.85) in Centre A, 0.73 (95% CI

0.43-0.91) in Centre B, and 0.58 (95% CI 0.37-0.86) in Centre C, with an overall AUC of 0.73 (95% CI 0.64-0.82). These were markedly lower than the 0.86 (95% CI not available) reported in the original development study (6) or the 0.79 (range 0.77-0.81) in the validation study (7). Calibration analysis showed reasonable alignment between predicted and observed risks overall, but miscalibration were obvious in Centre B and C, characterized by systematic overestimation of the predicted risk (Figure-1).

The number of spared LNDs and missed LNIs at different thresholds are summarized in Table-2. At the original 7% threshold, spared LNDs ranged from 51% (Centre A) to 56% (Centre C) and 76% (Centre B), while missed LNIs ranged from 0% (Centre C) to 2.9% (Centre B) and 8.9% (Centre A). Decision curve analyses (DCA) (Figure-2) revealed different optimal thresholds for each centre; the 7% threshold did not consistently yield the maximum net benefit.

## DISCUSSION

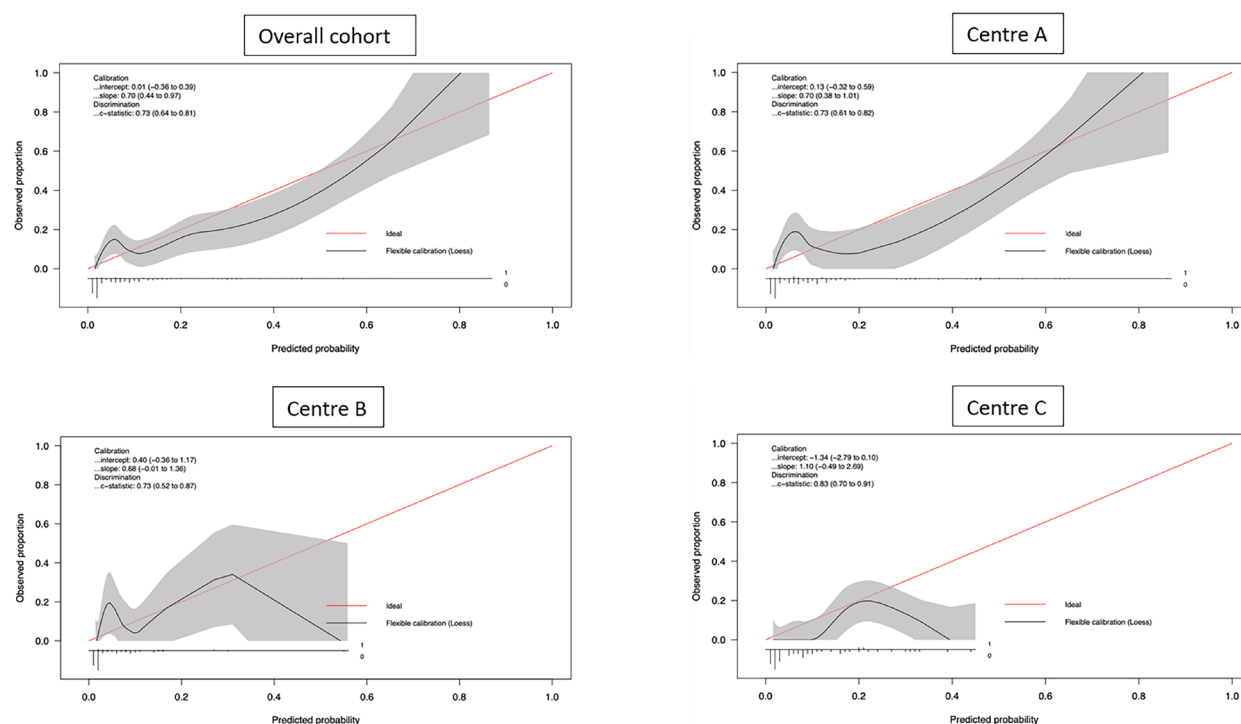
Our findings confirm the variable performance of the 2019 Briganti nomogram when applied across distinct clinical settings. While the overall discriminatory ability remained acceptable (AUC 0.73), significant heterogeneity was observed between centres, with AUC values ranging from 0.58 to 0.77. Calibration analysis further revealed systematic overestimation of risk in two of the three cohorts, and DCA demonstrated that the originally proposed 7% threshold did not consistently yield optimal net benefit. These results provide robust evidence that the nomogram, although previously externally validated, does not perform uniformly across populations and should not be applied in a one-size-fits-all manner.

First, the variability in nomogram performance highlights the inherent limitations of applying predictive tools developed in one setting to external populations. The original 2019 Briganti model demonstrated strong discrimination (AUC 0.86) in the development cohort (6) and a slightly reduced but still robust AUC (0.79) in its external validation (7). In contrast, our results show a broader range and, in

**Table 1 - Descriptives characteristic of the population for the whole population and for the three centres.**

|                                                                   | Overall cohort<br>(n=481) | Centre A<br>(n=198) | Centre B<br>(n=183) | Centre C<br>(n=100) |
|-------------------------------------------------------------------|---------------------------|---------------------|---------------------|---------------------|
| Age at surgery (yr), median (IQR)                                 | 68 (62-73)                | 68 (63-72)          | 65 (61-75)          | 67 (61-70)          |
| Preoperative PSA (ng/mL), median (IQR)                            | 8.6 (5.93-12.7)           | 9.4 (6.57-14.8)     | 7.14 (5.57-10.4)    | 8.65 (5.53-17)      |
| Clinical stage at DRE, n (%)                                      |                           |                     |                     |                     |
| cT1                                                               | 274 (57)                  | 91 (46)             | 113 (61.5)          | 70 (70)             |
| cT2                                                               | 201 (42)                  | 102 (52)            | 69 (38)             | 30 (30)             |
| cT3                                                               | 6 (1)                     | 5 (2)               | 1 (0.5)             | 0 (0)               |
| PI-RADS score of index lesion, n (%)                              |                           |                     |                     |                     |
| No lesion                                                         | 20 (4)                    | 3 (2)               | 3 (2)               | 14 (14)             |
| 3                                                                 | 27 (6)                    | 4 (2)               | 12 (6)              | 11 (11)             |
| 4                                                                 | 234 (48)                  | 90 (46)             | 96 (52)             | 48 (48)             |
| 5                                                                 | 200 (42)                  | 101 (50)            | 72 (40)             | 27 (27)             |
| Maximum lesion diameter of index lesion at MRI (mm), median (IQR) | 14 (10-20)                | 14.5 (11-20)        | 12 (10-17)          | 15 (10-20)          |
| ECE at MRI, n (%)                                                 | 69 (14)                   | 30 (15)             | 30 (16)             | 9 (9)               |
| SVI at MRI, n (%)                                                 | 17 (4)                    | 12 (6)              | 3 (2)               | 2 (2)               |
| ISUP grade group on targeted biopsy, n (%)                        |                           |                     |                     |                     |
| Negative                                                          | 51 (11)                   | 17 (9)              | 30 (16)             | 4 (4)               |
| 1                                                                 | 93 (19)                   | 16 (8)              | 66 (36)             | 11 (11)             |
| 2                                                                 | 166 (35)                  | 74 (37)             | 51 (28)             | 41 (41)             |
| 3                                                                 | 77 (16)                   | 40 (20)             | 17 (10)             | 20 (20)             |
| 4                                                                 | 60 (12)                   | 20 (10)             | 19 (10)             | 21 (21)             |
| 5                                                                 | 34 (7)                    | 31 (16)             | 0 (0)               | 3 (3)               |
| Number of cores taken at targeted biopsy, median (IQR)            | 3 (2-4)                   | 3 (2-4)             | 2 (2-3)             | 4 (3-6)             |
| Number of positive cores at targeted biopsy, median (IQR)         | 2 (1-3)                   | 2 (1-3)             | 2 (1-2)             | 4 (2-5)             |
| ISUP grade group on systematic biopsy, n (%)                      |                           |                     |                     |                     |
| Negative                                                          | 23 (5)                    | 12 (6)              | 5 (3)               | 6 (6)               |
| 1                                                                 | 36 (7)                    | 6 (3)               | 22 (12)             | 8 (8)               |
| 2                                                                 | 224 (47)                  | 87 (44)             | 81 (44)             | 56 (56)             |
| 3                                                                 | 131 (27)                  | 67 (34)             | 40 (22)             | 24 (24)             |
| 4                                                                 | 41 (9)                    | 11 (6)              | 28 (15)             | 2 (2)               |
| 5                                                                 | 26 (5)                    | 15 (7)              | 7 (4)               | 4 (4)               |
| Number of cores taken at systematic biopsy, median (IQR)          | 12 (12-12)                | 12 (6-12)           | 12 (12-12)          | 12 (10-15)          |
| Number of positive cores at systematic biopsy, median (IQR)       | 4 (2-6)                   | 4 (2-6)             | 4 (3-7)             | 3 (2-6)             |
| ISUP grade group (overall), n (%)                                 |                           |                     |                     |                     |
| 1                                                                 | 12 (2)                    | 1 (0.5)             | 7 (4)               | 4 (4)               |
| 2                                                                 | 204 (42)                  | 85 (43)             | 62 (34)             | 57 (7)              |
| 3                                                                 | 156 (33)                  | 75 (38)             | 49 (27)             | 32 (32)             |
| 4                                                                 | 76 (16)                   | 15 (7.5)            | 58 (31)             | 3 (3)               |
| 5                                                                 | 33 (7)                    | 22 (11)             | 7 (4)               | 4 (4)               |
| ISUP grade group at final pathology, n (%)                        |                           |                     |                     |                     |
| 1                                                                 | 32 (7)                    | 1 (0.5)             | 30 (16)             | 1 (1)               |
| 2                                                                 | 241 (50)                  | 79 (40)             | 98 (54)             | 64 (64)             |
| 3                                                                 | 151 (31)                  | 85 (43)             | 36 (20)             | 30 (30)             |
| 4                                                                 | 19 (4)                    | 9 (4.5)             | 8 (4)               | 2 (2)               |
| 5                                                                 | 38 (8)                    | 24 (12)             | 11 (6)              | 3 (3)               |
| ECE at final pathology, n (%)                                     | 190 (40)                  | 95 (48)             | 54 (30)             | 41 (41)             |
| SVI at final pathology, n (%)                                     | 52 (11)                   | 32 (16)             | 14 (8)              | 6 (6)               |
| Positive surgical margin, n (%)                                   | 165 (34)                  | 67 (34)             | 70 (38)             | 28 (28)             |
| Number of lymph nodes removed, median (IQR)                       | 12 (9-15)                 | 15 (12-18)          | 16 (10-20)          | 10 (8-12)           |
| Lymph node invasion at final pathology, n (%)                     | 38 (8)                    | 28 (14)             | 8 (4)               | 2 (2)               |

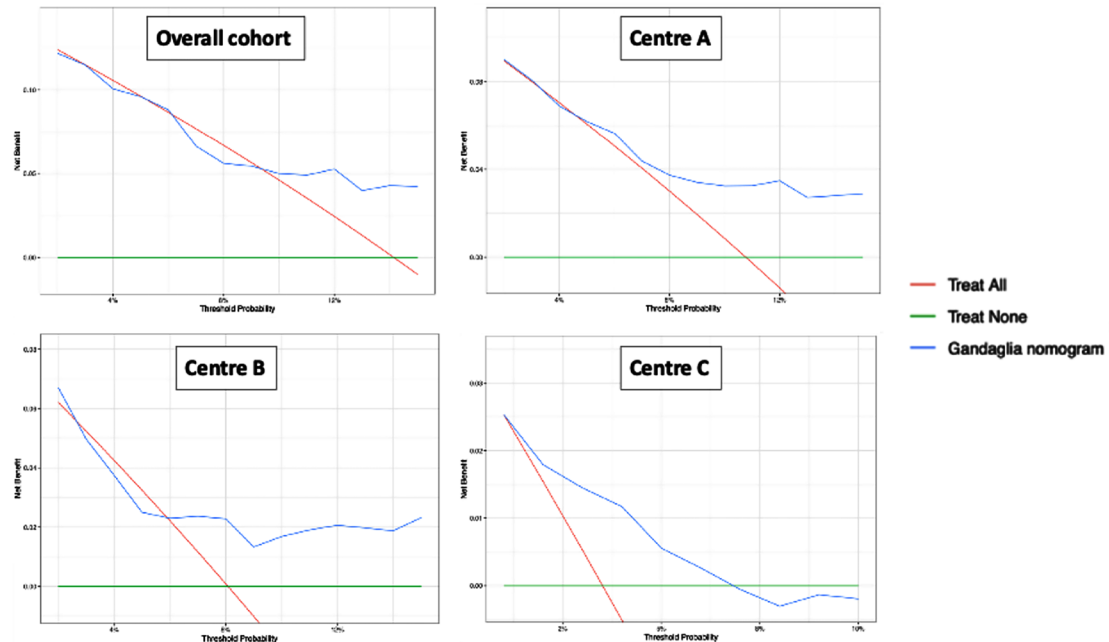
Yr = Year; IQR = Inter-Quartile Range; DRE = Digital Rectal Examination; PI-RADS = Prostate Imaging - Reporting and Data System; MRI = Magnetic Resonance Imaging; ECE = Extra-Capsular Extension; SVI = Seminal Vesicle Invasion; ISUP = International Society of Urological Pathology.

**Figure 1 - Calibration plots of predicted (ie, expected) versus observed probabilities of the populations.****Table 2 - Detailed threshold analysis. In blue is highlighted the proposed 7% threshold by Gandaglia et al. in their original study.**

|            | Whole cohort<br>(n=481) |               | Centre A<br>(n=198) |               | Centre B<br>(n=183) |               | Centre C<br>(n=100) |               | 2019<br>Briganti* |               |
|------------|-------------------------|---------------|---------------------|---------------|---------------------|---------------|---------------------|---------------|-------------------|---------------|
|            | Spared<br>LND           | Missed<br>LNI | Spared<br>LND       | Missed<br>LNI | Spared<br>LND       | Missed<br>LNI | Spared<br>LND       | Missed<br>LNI | Spared<br>LND     | Missed<br>LNI |
| <b>2%</b>  | 102 (21)                | 1 (1)         | 29 (15)             | 1 (3.4)       | 57 (31)             | 0 (0)         | 16 (16)             | 0 (0)         | 13 (3.2)          | 1 (7.7)       |
| <b>3%</b>  | 214 (44)                | 4 (1.9)       | 66 (33)             | 2 (3)         | 109 (60)            | 2 (1.8)       | 39 (39)             | 0 (0)         | 164 (38)          | 2 (1.2)       |
| <b>4%</b>  | 241 (50)                | 7 (2.9)       | 76 (38)             | 4 (5.3)       | 119 (65)            | 3 (2.5)       | 46 (46)             | 0 (0)         | 200 (47)          | 3 (1.5)       |
| <b>5%</b>  | 249 (52)                | 8 (3.2)       | 79 (40)             | 4 (5.1)       | 123 (67)            | 4 (3.3)       | 47 (47)             | 0 (0)         | 217 (51)          | 4 (1.8)       |
| <b>6%</b>  | 267 (56)                | 9 (3.4)       | 88 (44)             | 5 (5.7)       | 128 (70)            | 4 (3.1)       | 51 (51)             | 0 (0)         | 231 (54)          | 4 (1.7)       |
| <b>7%</b>  | 296 (62)                | 13 (4.4)      | 101 (51)            | 9 (8.9)       | 139 (76)            | 4 (2.9)       | 56 (56)             | 0 (0)         | 244 (57)          | 4 (1.6)       |
| <b>8%</b>  | 316 (66)                | 15 (4.7)      | 113 (57)            | 11 (9.7)      | 145 (79)            | 4 (2.8)       | 58 (58)             | 0 (0)         | 256 (60)          | 5 (2)         |
| <b>9%</b>  | 334 (70)                | 16 (4.8)      | 118 (60)            | 11 (9.3)      | 153 (84)            | 5 (3.3)       | 63 (63)             | 0 (0)         | 266 (62)          | 6 (2.3)       |
| <b>10%</b> | 353 (73)                | 17 (4.8)      | 127 (64)            | 12 (9.4)      | 159 (87)            | 5 (3.1)       | 67 (67)             | 0 (0)         | 283 (66)          | 7 (2.5)       |

\*Based on the original development study (Gandaglia et al. Eur Urol. 2019) (6). Data were not available for the external validation dataset (Gandaglia et al. Eur Urol. 2020).

**Figure 2 - Decision-curve analysis assessing the net benefit associated with the use of the 2019 Briganti model for the detection of lymph node invasion at extended pelvic lymph node dissection depending on the cohort.**



some centres, suboptimal performance. These findings underscore the need for interpreting predictive performance metrics within the context of the population to which they are applied, particularly in light of differences in disease prevalence, risk distribution, and case mix (14).

Second, differences in patients and diseases' characteristics between centres likely contributed to the observed heterogeneity. For instance, Centre A exhibited a higher prevalence of aggressive disease features such as PI-RADS 5 lesions and ISUP grade group 5, as well as a higher overall rate of LNI (14%) than Centres B and C. Conversely, Centre C had a very low LNI prevalence (2%), which likely limited the nomogram's discrimination and calibration in that setting. One could think that differences in LND templates would explain these results, but the median number of lymph nodes removed did not differ substantially between centres, supporting the homogeneity of the surgical template and suggesting that differences in nomogram performance were unlikely to be explained by variations in lymphadenectomy extent. These discrepancies may

also reflect subtle variations in MRI interpretation, biopsy technique, or pathology review, even though all participating institutions followed standardized protocols. Importantly, the 2019 Briganti nomogram does not account for such inter-centre variability, which may undermine its generalizability. Hence, our data reinforce the need for local validation prior to clinical implementation of predictive models. Even when a model is robustly developed and externally validated, its utility in clinical decision-making depends on its performance within the target population. Discrimination, calibration, and decision-analytic utility should all be reassessed locally.

Third, our study provides concrete evidence that using a fixed decision threshold such as the 7% cutoff proposed by the original 2019 Briganti nomogram may lead to unintended consequences depending on the clinical context. For example, in Centre A, applying the 7% threshold would have spared 51% of patients from undergoing LND but at the cost of missing 8.9% of node-positive cases. In contrast, in Centre B, the same threshold would have spared 76% of LNDs while missing only 2.9%

of LNIs, and in Centre C, it would have spared 56% of LNDs without missing any LNIs. These data illustrate the different trade-offs resulting from applying a uniform threshold across heterogeneous populations. Beyond the statistical measures of model performance, clinical decision-making ultimately depends on how much risk an individual urologist/patient is willing to accept to avoid harm. There may not be a single "correct" threshold, but rather a continuum of acceptable strategies informed by population data, clinical judgment and shared decision making with the patient. This highlights the importance of site-specific threshold selection based on both statistical evidence and real-world clinical considerations.

Taken together, these findings support the recommendation that each centre should validate the performance of nomograms within their own clinical environment. Where appropriate, thresholds should be adapted based on local data and applied within a shared decision-making framework. Nevertheless, the 2019 Briganti nomogram is of utmost importance and remains among the most accurate and extensively validated tools currently available for preoperative prediction of LNI in patients assessed with MRI-targeted and systematic biopsies (15, 16). Importantly, the field of preoperative risk stratification is evolving rapidly. Recent developments, including nomograms incorporating PSMA-PET imaging, show encouraging improvements in predictive accuracy (17). Notably, novel models developed by the same group have demonstrated enhanced diagnostic accuracy in patients staged with PSMA-PET/CT prior to surgery (18, 19).

Hence, our findings have direct implications for clinical practice. Rather than relying on fixed thresholds derived from external cohorts, clinicians should adopt a more dynamic approach integrating local data, institutional outcomes, and patient preferences. The use of decision curve analysis and centre-specific calibration may help refine the indication for lymph node dissection and reduce both overtreatment and undertreatment. Ultimately, embedding predictive models within a framework of

shared decision-making and continuous local validation may represent a more sustainable strategy for precision surgery in prostate cancer.

These data should also be interpreted within the context of a rapidly evolving surgical ecosystem. The role of extended lymph node dissection itself remains debated, with emerging concepts of surgical de-escalation aiming to minimize morbidity without compromising oncological outcomes (20). However, recent high-level evidence has challenged this paradigm, suggesting a potential benefit of extended lymph node dissection on long-term oncological outcomes, including distant metastasis-free survival (21). In parallel, the increasing use of PSMA-PET imaging is reshaping preoperative staging and may lead to stage migration, potentially altering the performance of traditional nomograms developed in pre-PSMA eras (22). Together, these evolutions further support the need for continuous re-evaluation and adaptation of predictive tools in line with contemporary practice.

Despite its appealing findings, our study has some limitations. Its retrospective design may have introduced selection or information bias. Despite efforts to standardize imaging, biopsy, and pathological assessment across centres, inter-observer variability may have influenced the results. The relatively small sample size in Centre C, along with its low LNI prevalence, may limit the robustness of findings in that specific setting. Nonetheless, the multicentre nature of this study, the consistency of the methodological approach, and the inclusion of calibration and clinical utility analyses strengthen relevance of our conclusions.

Beyond the present findings, improving the robustness and generalizability of predictive models will require access to large, heterogeneous, and well-annotated datasets. Many existing nomograms have been developed from relatively small cohorts originating from high-volume academic centres, which may introduce institutional biases related to patient selection and clinical practice patterns. Expanding multicentre and international data collection initiatives is therefore critical to enhance



calibration and external validity. In this context, the emergence of artificial intelligence (AI) and automated data capture systems in healthcare may play a pivotal role. AI-enabled platforms, particularly those integrated into digitally connected surgical environments, have the potential to systematically capture high-resolution clinical and intraoperative data at scale, facilitating large epidemiological analyses and the development of more robust and generalizable predictive models (23).

## CONCLUSIONS

In conclusion, while the Briganti nomogram remains the most validated tool available for LNI prediction in the era of MRI-targeted biopsies, its performance varies between centres. Our multicentre study is a call for urologist to locally validate and personalize their threshold selection. As new predictive algorithms (particularly those integrating PSMA-PET) emerge, future decision-making will likely become even more tailored, precise, and patient-centred. The integration of AI-driven data ecosystems and large-scale real-world datasets may further enhance the development and continuous recalibration of predictive models, paving the way toward more adaptive and generalizable decision-support tools.

## ADVANCING PRACTICE

This study highlights the importance of validating the 2019 Briganti nomogram within each clinical setting. Our results support individualized threshold selection for lymph node dissection, based on local performance and patient population characteristics. Fixed thresholds may lead to inconsistent or suboptimal treatment decisions, reinforcing the need for precision-guided surgical planning.

## CONFLICT OF INTEREST

None declared.

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## APPENDIX

**Supplementary Table 1 - Regression coefficients predicting lymph node involvement (LNI) from the 2019 Briganti nomogram as described by Gandaglia et al. Eur Urol 2019.**

|                                                                                      | Value   |
|--------------------------------------------------------------------------------------|---------|
| Intercept                                                                            | -4.5974 |
| Preoperative PSA                                                                     | 0.0416  |
| Extracapsular extension at MRI                                                       | 1.2214  |
| Seminal vesicle invasion at MRI                                                      | 1.4672  |
| Maximum lesion diameter at MRI                                                       | 0.0311  |
| Biopsy Gleason grade group 3 at targeted biopsy                                      | 1.2032  |
| Biopsy Gleason grade group $\geq 4$ at targeted biopsy                               | 1.8063  |
| Percentage of cores with clinically significant PCa at concomitant systematic biopsy | 0.0119  |

PSA = Prostate Specific Antigen; MRI = Magnetic Resonance Imaging; PCa = Prostate Cancer

**Supplementary Table 2 - Descriptives characteristic of the population for the development and validation datasets of the 2019-Briganti nomogram. Yr: Year; IQR: Inter-Quartile Range; DRE: Digital Rectal Examination; PI-RADS: Prostate Imaging - Reporting and Data System; MRI: Magnetic Resonance Imaging; ECE: Extra-Capsular Extension; SVI: Seminal Vesicle Invasion; ISUP: International Society of Urological Pathology.**

|                                                                          | 2019 Briganti       |             |                               |
|--------------------------------------------------------------------------|---------------------|-------------|-------------------------------|
|                                                                          | Development dataset |             | Validation dataset<br>(n=487) |
|                                                                          | pN0 (n=433)         | pN1 (n=62)  |                               |
| <b>Age at surgery (yr), median (IQR)</b>                                 | 65 (60-70)          | 64 (60-71)  | 65 (60-69)                    |
| <b>Preoperative PSA (ng/mL), median (IQR)</b>                            | 7.2 (5.1-11)        | 11 (6.7-21) | 7.6 (5.5-10.8)                |
| <b>Clinical stage at DRE, n (%)</b>                                      |                     |             | -                             |
| cT1                                                                      | 335 (77)            | 30 (48)     |                               |
| cT2                                                                      | 96 (22)             | 21 (34)     |                               |
| cT3                                                                      | 4 (1)               | 11 (17)     |                               |
| <b>PI-RADS score of index lesion, n (%)</b>                              |                     |             |                               |
| No lesion                                                                | 0 (0)               | 0 (0)       | 0 (0)                         |
| 3                                                                        | 121 (28)            | 4 (6)       | 27 (5.5)                      |
| 4                                                                        | 235 (54)            | 26 (42)     | 268 (56)                      |
| 5                                                                        | 79 (18)             | 32 (52)     | 185 (39)                      |
| <b>Maximum lesion diameter of index lesion at MRI (mm), median (IQR)</b> | 10 (9-14)           | 15 (10-18)  | 11 (8-16)                     |
| <b>ECE at MRI, n (%)</b>                                                 | 49 (12)             | 19 (31)     | 79 (16)                       |
| <b>SVI at MRI, n (%)</b>                                                 | 13 (3)              | 14 (22)     | 20 (4.1)                      |
| <b>ISUP grade group on targeted biopsy, n (%)</b>                        |                     |             |                               |
| Negative                                                                 | 0 (0)               | 0 (0)       | 0 (0)                         |
| 1                                                                        | 72 (17)             | 1 (2)       | 72 (14)                       |
| 2                                                                        | 225 (52)            | 15 (24)     | 221 (45)                      |
| 3                                                                        | 72 (17)             | 16 (26)     | 124 (25)                      |
| 4                                                                        | 46 (11)             | 17 (27)     | 52 (11)                       |
| 5                                                                        | 20 (5)              | 13 (21)     | 18 (3.7)                      |
| <b>Number of cores taken at targeted biopsy, median (IQR)</b>            | 3 (2-4)             | 3 (2-4)     | -                             |
| <b>Number of positive cores at targeted biopsy, median (IQR)</b>         | 2 (1-3)             | 2 (2-3)     | -                             |
| <b>ISUP grade group on systematic biopsy, n (%)</b>                      |                     |             |                               |
| Negative                                                                 | 80 (18)             | 4 (7)       | 49 (10)                       |
| 1                                                                        | 100 (23)            | 6 (10)      | 70 (14)                       |
| 2                                                                        | 171 (40)            | 14 (23)     | 234 (48)                      |
| 3                                                                        | 44 (10)             | 15 (24)     | 69 (14)                       |
| 4                                                                        | 25 (6)              | 9 (15)      | 47 (10)                       |
| 5                                                                        | 15 (4)              | 14 (23)     | 18 (3.7)                      |

|                                                                    |             |              |          |
|--------------------------------------------------------------------|-------------|--------------|----------|
| <b>Number of cores taken at systematic biopsy, median (IQR)</b>    | 12 (10-15)  | 12 (10-16)   | -        |
| <b>Number of positive cores at systematic biopsy, median (IQR)</b> | 12 (0-37) * | 42 (17-76) * | -        |
| <b>ISUP grade group (overall), n (%)</b>                           |             |              | -        |
| 1                                                                  | 55 (13)     | 1 (2)        |          |
| 2                                                                  | 236 (54)    | 15 (24)      |          |
| 3                                                                  | 78 (18)     | 16 (26)      |          |
| 4                                                                  | 45 (10)     | 15 (24)      |          |
| 5                                                                  | 21 (5)      | 15 (24)      |          |
| <b>ISUP grade group at final pathology, n (%)</b>                  |             |              | -        |
| 1                                                                  | 15 (3.5)    | 0 (0)        |          |
| 2                                                                  | 218 (50)    | 3 (4.8)      |          |
| 3                                                                  | 147 (34)    | 25 (40)      |          |
| 4                                                                  | 22 (5.1)    | 4 (6.5)      |          |
| 5                                                                  | 30 (6.9)    | 30 (48)      |          |
| <b>ECE at final pathology, n (%)</b>                               | 180 (41)    | 20 (32)      | 160 (33) |
| <b>SVI at final pathology, n (%)</b>                               | 40 (9.2)    | 39 (63)      | 61 (13)  |
| <b>Positive surgical margin, n (%)</b>                             | 103 (24)    | 40 (48)      | -        |
| <b>Lymph node invasion at final pathology, n (%)</b>               | 0 (0)       | 100 (100)    | 38 (7.8) |

\*Median cores with clinically significant prostate cancer on systematic biopsy, % (IQR)





# Patient-reported Outcomes of Transperineal Reanastomosis for Recurrent or Obliterative Post-prostatectomy Vesicourethral Anastomotic Stenosis

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## ABSTRACT

**Purpose:** Post-prostatectomy vesicourethral anastomotic stenosis (VUAS) affects up to 5% of patients. A subset of cases remains refractory to endoscopic treatment, significantly impacting quality of life in the long-term. This study presents 15-year follow-up data on patients undergoing open reanastomosis for refractory or obliterative VUAS.

**Patients and Methods:** We included patients who underwent transperineal vesicourethral reanastomosis from 2009–2023. The procedure was often staged, with artificial urinary sphincter (AUS) implantation three months later. Co-primary endpoints included re-treatment-free survival (RFS) and patient-reported outcome measures (PROMs). RFS was analyzed with Kaplan-Meier estimators, and PROMs were evaluated per scoring manuals. Additionally, we conducted a scoping review of all studies reporting outcomes following complex VUAS reconstruction.

**Results:** Among 46 patients with VUAS, prior endoscopic interventions included dilation (17%), incision (61%), and resection (80%). Median time from prostatectomy to reanastomosis was 23 months (IQR 16–42). At a median follow-up of 80 months (IQR 41–149), RFS rates were 91% at two years and 88% at five years. 30 patients (65%) required staged AUS implantation for stress urinary incontinence. PROMs, assessed in 28 patients (61%), indicated restored voiding function, absence of fecal incontinence, high treatment satisfaction, and low decision regret. Limitations include the absence of preoperative PROMs for baseline comparisons. The scoping review revealed varying success rates ranging from 60% to 92% and a significant underuse of validated PROMs.

**Conclusions:** Transperineal reanastomosis offers an effective and lasting solution for treating recurrent or obliterative VUAS, with encouraging long-term results and favorable patient-reported outcomes, underscoring its critical role in salvage posterior urethral reconstruction after prostatectomy.

## ARTICLE INFO

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## INTRODUCTION

Despite the long-standing use of prostatectomy and radiotherapy as primary treatments for prostate cancer, these modalities continue to be associated with functional complications such as urethral stricture and vesicourethral anastomotic stenosis (VUAS) (1-3). VUAS occurs in up to 5% of patients following prostatectomy (1, 2) and is typically managed with endoscopic interventions, which generally offer acceptable short-term outcomes (4, 5). However, repeated procedures are strongly associated with an increased risk of treatment failure (6, 7). Transperineal reanastomosis serves as a salvage option for patients with refractory VUAS, particularly those with complete obliteration or those who have failed prior endoscopic management (4, 8). In up to 10% of patients, endoscopic approaches ultimately prove ineffective, making complex reconstruction necessary (9, 10). As prostate cancer therapies continue to improve and contribute to prolonged survival, the management of long-term functional complications becomes increasingly important to preserve quality of life in these patients. However, for this challenging subset of patients suffering from VUAS, the existing evidence is limited. Although quality of life is emphasized in both the European Association of Urology (EAU) guidelines for prostate cancer and urethral stricture disease (11, 12), with the latter explicitly recommending the use of patient-reported outcome measures (PROMs), most published studies are small, retrospective, and single-center in design, with short follow-up periods and minimal integration of PROMs. As a result, little is known about the long-term functional course after surgical revision, including the need for artificial urinary sphincter (AUS) implantation to manage persistent urinary incontinence. In line with current guidelines on urethral stricture disease (4, 8), which recommend reconstruction for refractory VUAS, the present study aims to fill these gaps. We describe our step-by-step technique for transperineal reanastomosis, report the longest follow-up to date for this approach, and provide a comprehen-

sive assessment that integrates both objective outcomes and PROMs. Finally, we set our findings in the context of the existing literature by performing a scoping review on reconstruction for VUAS.

## PATIENTS AND METHODS

### Study Population and Data Extraction

This retrospective observational study was approved by the Ethics Committee of the Medical Council of Hamburg (IRB No. PV4123) and conducted in accordance with the Hamburg Hospital Act (§12.1 HmbKHG). We identified all men who underwent transperineal reanastomosis between January 2009 and December 2023. A comprehensive digital chart review was performed to collect data on demographics, etiological factors, prior VUAS treatments, previous prostate cancer therapies, prostatectomy approach, and surgical characteristics. Cross-sectional follow-up was conducted via telephone interviews and a web-based survey to gather additional outcomes.

### Study Endpoints

Study endpoints were defined as both objective and subjective outcomes. Objective outcomes included functional success, defined as retreatment-free survival (RFS) (13), with retreatment specified as any postoperative intervention for recurrent VUAS confirmed by imaging. An additional objective measure was explantation-free survival following AUS implantation. The short term (<30 days) postoperative major complication burden was also evaluated using the Clavien-Dindo classification (>grade IIIa).

Subjective outcomes were assessed through a range of validated PROMs. These included the six-item lower urinary tract symptoms (LUTS) score from the Urethral Stricture Surgery (USS) PROM (14), and the Wexner fecal incontinence score (15). Treatment satisfaction and decisional regret were further evaluated using the International Consultation on Incontinence Questionnaire-Satisfaction (ICIQ-S) (16), and the Decision Regret Scale (DRS) (17), respectively. All PROMs used in this study have undergone rigorous validation to ensure reliable representation of

patient-centered outcomes. These linear scoring systems allow for comprehensive evaluation of voiding symptoms, fecal continence, as well as treatment satisfaction and decisional regret following the surgical intervention.

### Perioperative Management and Surgical Procedure

Patients underwent preoperative evaluations according to our institutional protocol. This involved a detailed medical history, physical examination, urinalysis, uroflowmetry, and a combined retrograde urethrography with voiding cystourethrography, if possible. Transperineal reanastomosis is the standard salvage procedure at our institution for patients with recurrent VUAS refractory to endoscopic management or with long, obliterative stenoses unsuitable for endoscopic treatment. In accordance with our institutional practice, up to three endoscopic interventions are typically performed prior to offering open surgical reconstruction (5). In patients with a history of pelvic radiotherapy, this approach is generally avoided due to unfavorable local tissue conditions and the associated increased risk of complications and recurrence (18). In such cases, open reconstruction is considered only in highly selected, well-informed patients who explicitly wish to pursue this option despite thorough counseling and after discussion of alternative strategies, including urinary diversion procedures such as a Mitrofanoff stoma or suprapubic diversion. The surgical procedure was conducted by two surgeons with extensive expertise in the field (RD, MF) as previously described (19, 20), follows the transperineal approach to the posterior urethra as described by Young (21), and is depicted step-by-step in Figure-1.

If stress urinary incontinence was present following transperineal reanastomosis, AUS implantation was performed three months postoperatively. For AUS implantation, the AMS 800™ system by Boston Scientific was used. A double-cuff configuration was placed at a location sufficiently distant from the anastomosis to maximize the urethral surface encompassed by the cuffs and thereby reducing the pressure exerted by a single cuff on a smaller urethral segment.

### Statistical Analyses

Clinical baseline characteristics were analyzed through descriptive analyses. Continuous variables are presented as medians with interquartile ranges (IQRs), while categorical variables are reported as frequencies and proportions. Median follow-up time was calculated using reverse Kaplan-Meier estimates. Kaplan-Meier curves were generated to illustrate retreatment-free survival as well as AUS explantation-free survival.

PROMs were assessed according to their respective scoring manuals. Voiding symptoms were measured using the LUTS score from the USS PROM, which ranges from 0 to 24 and includes six questions. Fecal incontinence was assessed using the Wexner fecal incontinence score, ranging from 0 to 20 and consisting of five questions. Higher scores on indicate a greater symptom burden.

Treatment satisfaction was measured with the ICIQ-S outcome score, scored from 0 to 24 across six questions addressing satisfaction with surgical outcomes, alongside a separate overall satisfaction item scored from 0 to 10. Decisional regret was assessed using a five-question questionnaire with a total score range of 0 to 100. Higher scores on the ICIQ-S indicate greater treatment satisfaction, respectively, while higher scores on the DRS indicate greater regret.

PROM scores were summarized as medians with IQRs and their distributions were visualized using violin plots.

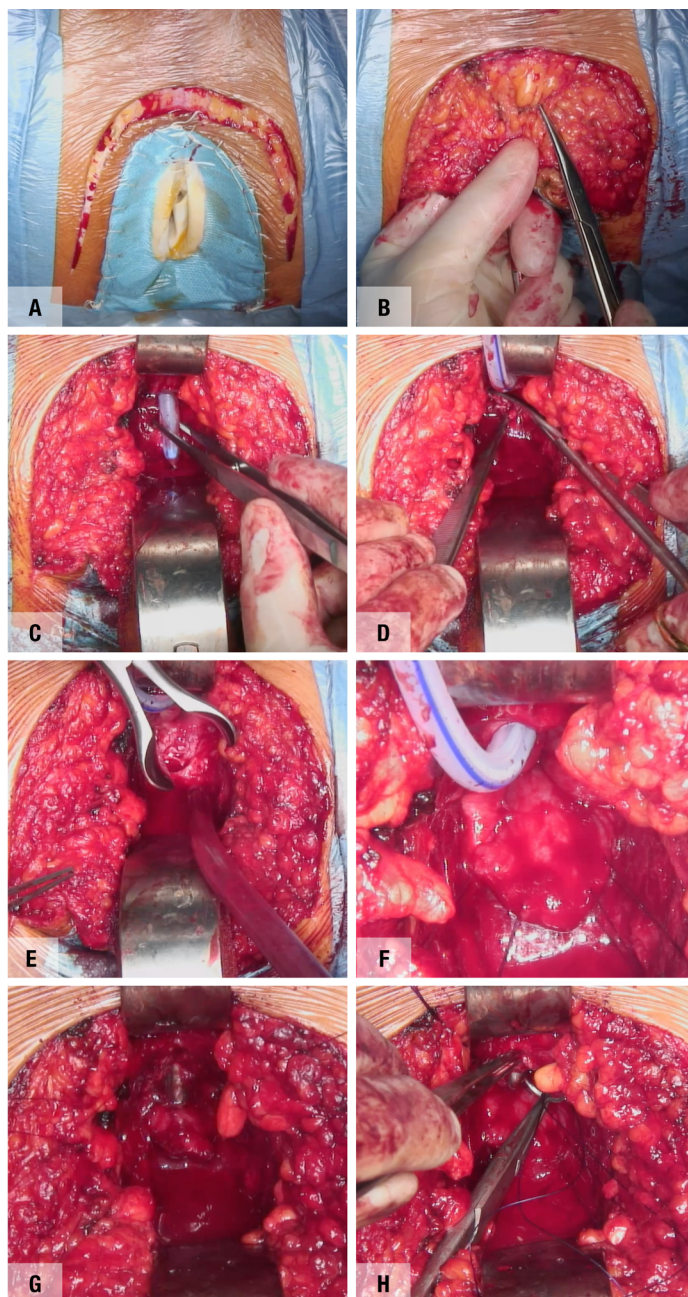
All statistical analyses were performed using Stata® (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC).

Assistance in improving the English language and style was provided by ChatGPT (GPT-5, OpenAI). The tool was used exclusively for linguistic editing. No content, data interpretation, or conclusions were generated by artificial intelligence.

### Scoping Review on Outcomes After Salvage Surgical VUAS Treatment

In order to provide a broader context for our findings, a comprehensive literature review was con-

**Figure 1 - Key surgical steps of transperineal vesicourethral reanastomosis. The patient is placed in an exaggerated lithotomy position, and a half-moon perineal incision is made (1A). Dissection of the urethra is performed under digital rectal guidance (1B). After exposure of the anastomotic site and identification of the stenosis (1C), the scar tissue is meticulously excised (1D-E). The urethra and bladder are then extensively mobilized to enable a tension-free reanastomosis (1F). Eight sutures are preplaced circumferentially around the anastomotic site. The three dorsal sutures at the 11-, 12-, and 1-o'clock lithotomy positions are tied first, followed by insertion of the Foley catheter into the bladder and completion of the remaining five sutures (1G-H). The procedure concludes with leakage testing, placement of a perineal Jackson-Pratt drain, and layered closure of the wound.**



ducted in August November 30, 2024. This review involved searching the databases of PubMed with the objective of identifying studies that reported on outcomes following complex VUAS reconstruction. The search strategy employed the terms "vesicourethral anastomosis stenosis" OR "urethrovesical anastomosis stenosis" OR "prostatectomy anastomosis stenosis" OR "prostatectomy anastomotic stricture" OR "bladder neck contracture" AND "repair" OR "reconstruction" OR "revision" OR "urethroplasty". Our analysis encompassed all original articles that reported on outcomes following open, laparoscopic, or robotic VUAS repair. Additionally, we meticulously screened the reference lists of pertinent articles to identify any additional studies meeting our criteria.

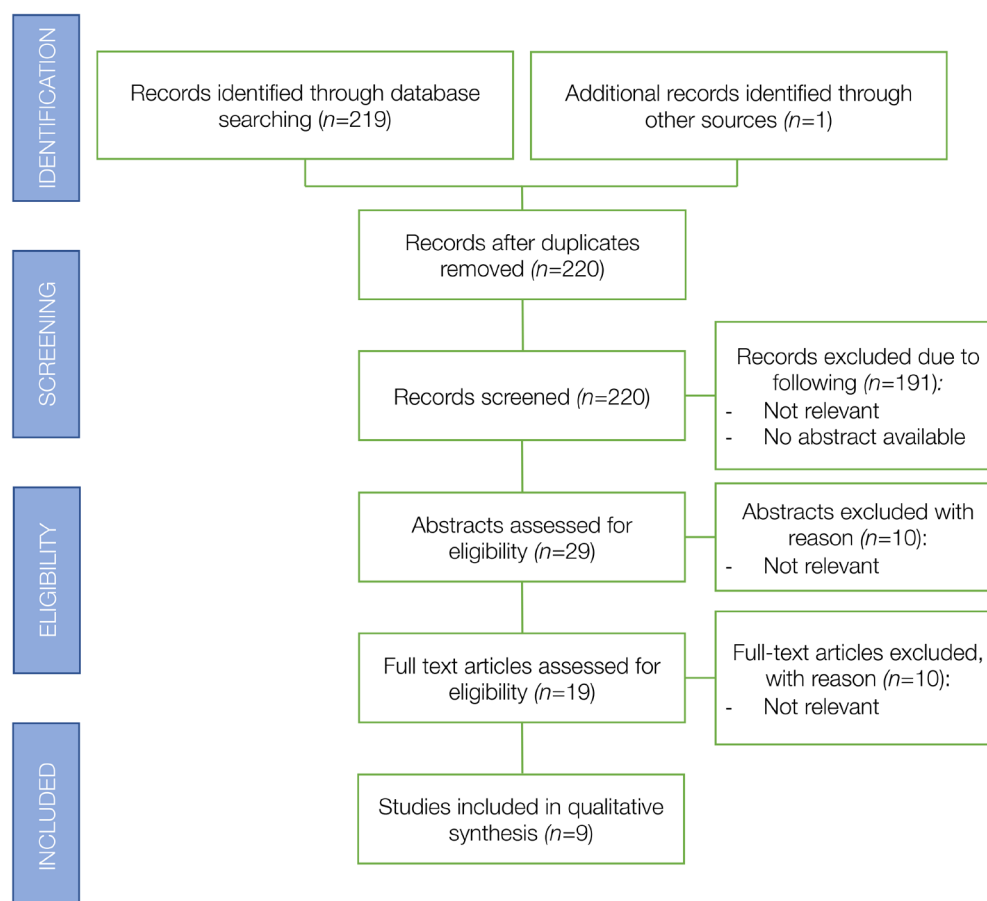
Only series with at least 10 patients were considered. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was created to elucidate our search strategy (Figure-2). The selected studies were tabulated, providing information on authors, publication year, cohort size, surgical approach, length of follow-up, success rate and definition, and the specific (validated) questionnaires used.

## RESULTS

### Clinical Baseline Characteristics

A total of 46 transperineal vesicourethral reanastomoses were performed at our institution be-

**Figure 2 - Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram illustrating the article selection process for the scoping review on outcomes after vesicourethral reanastomosis.**





tween January 2009 and December 2023. The baseline characteristics of the study cohort are summarized in Table-1. The participants had a median age of 69 years (IQR 65–72) and a median body mass index (BMI) of 28 kg/m<sup>2</sup> (IQR 26–32). The most prevalent preexisting medical conditions were hypertension (57%) and coronary artery disease (22%).

The majority of patients (85%) had undergone open radical prostatectomy, with the remainder having undergone robot-assisted radical prostatectomy. Nearly

all patients (96%) had received prior endoscopic interventions for VUAS with a median of 3 (IQR 2–5) per patient. Two patients (4.3%) did not undergo prior endoscopic treatment, as they presented with long, highly obliterative VUAS not amenable to endoscopic management. The most commonly performed procedures included transurethral resection (80%), transurethral incision (61%), and endoscopic dilation (17%).

The median time from prostatectomy to first VUAS intervention was seven months (IQR 4–31) and

**Table 1 - Clinical baseline characteristics in 46 men undergoing transperineal excision and primary reanastomosis for recurrent or obliterative vesicourethral anastomotic stenosis between January 2009 and December 2023 at a tertiary reconstructive referral center.**

| Baseline and surgical characteristics                       |              |
|-------------------------------------------------------------|--------------|
| Patients, n (%)                                             | 46 (100)     |
| Age at surgery (yr), median (IQR)                           | 69 (65–72)   |
| BMI, median (IQR)                                           | 28 (26–32)   |
| Comorbidities, n (%)                                        |              |
| Diabetes                                                    | 7 (15)       |
| Hypertension                                                | 26 (57)      |
| Coronary artery disease                                     | 10 (22)      |
| COPD                                                        | 2 (4.4)      |
| Prior pelvic radiotherapy                                   | 1 (2.2)      |
| Prostatectomy approach, n (%)                               |              |
| Open                                                        | 39 (85)      |
| Robotic                                                     | 7 (15)       |
| Previous VUAS treatments, n (%)                             |              |
| Any prior endoscopic intervention                           | 44 (96)      |
| Endoscopic dilation                                         | 8 (17)       |
| Transurethral incision                                      | 28 (61)      |
| Transurethral resection                                     | 37 (80)      |
| Number of previous endoscopic interventions, median (IQR)   | 3 (2–5)      |
| Previous TURP, n (%)                                        | 1 (2.2)      |
| Time from prostatectomy to reanastomosis (mo), median (IQR) | 23 (16–42)   |
| Operative time (min), median (IQR)                          | 115 (99–132) |

BMI = body mass index; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; TURP = transurethral resection of the prostate; VUAS = vesicourethral anastomotic stenosis.



the median time from radical prostatectomy to transperineal reanastomosis was 23 months (IQR 16–42), median operative time was 115 minutes (IQR 99–132). There were no major short term postoperative complications > grade IIIa according to the Clavien-Dindo classification.

### Retreatment-free Survival and Staged AUS Implantation

At a median follow-up of 80 months (IQR 41–149), six patients (13%) required retreatment, resulting in RFS rates of 91% at two years and 88% at five years (Figure-3A). Of these, five patients underwent additional endoscopic interventions (transurethral resection or incision), while one patient required bladder neck closure followed by suprapubic catheter diversion.

Additionally, 30 patients (65%) received staged artificial urinary sphincter (AUS) implantation to address stress urinary incontinence. Of the 16 patients without AUS implantation at last follow-up, one (6.3%) had died, four were lost to follow-up (25%), four had low-capacity bladders (25%), two had significant detrusor overactivity (13%), one experienced recurrent VUAS (6.3%), and four (25%) were scheduled for AUS implantation that had not yet been performed. At a median follow-up of 97 months (IQR 32–158), seven AUS explantations (23%) were necessary. The reasons for explantation included five cases of urethral erosion, one case of relative urethral stenosis, and one case with an unknown cause managed at an external hospital. This corresponds to estimated AUS explantation-free survival rates of 97% at two years and 86% at five years (Figure-3B).

### PROMs

PROMs were assessed at a median of 78 months (IQR 41–138) following surgery in 28 patients, representing 61% of the cohort. It is noteworthy that five patients (11%) had passed away during the follow-up period.

The distribution of all evaluated PROMs is illustrated in Figure-4. The median (IQR) scores for

each PROM were as follows: the USS PROM six-item LUTS score (reference range: 0–24) was 2.5 (1–5.5), reflecting a low burden of voiding symptoms; the Wexner fecal incontinence score (reference range: 0–20) was 1 (0–3), indicating minimal fecal incontinence; the ICIQ-S outcome score (reference range: 0–24) was 21.5 (18.5–23), suggesting high satisfaction with surgical outcomes; the ICIQ-S satisfaction with surgery item (reference range: 0–10) was 9 (7.5–10), further highlighting positive treatment satisfaction; and the DRS (reference range: 0–100) was 0 (0–20), demonstrating low levels of regret associated with the treatment decision.

### Scoping Review on Outcomes After Salvage Surgical VUAS Treatment

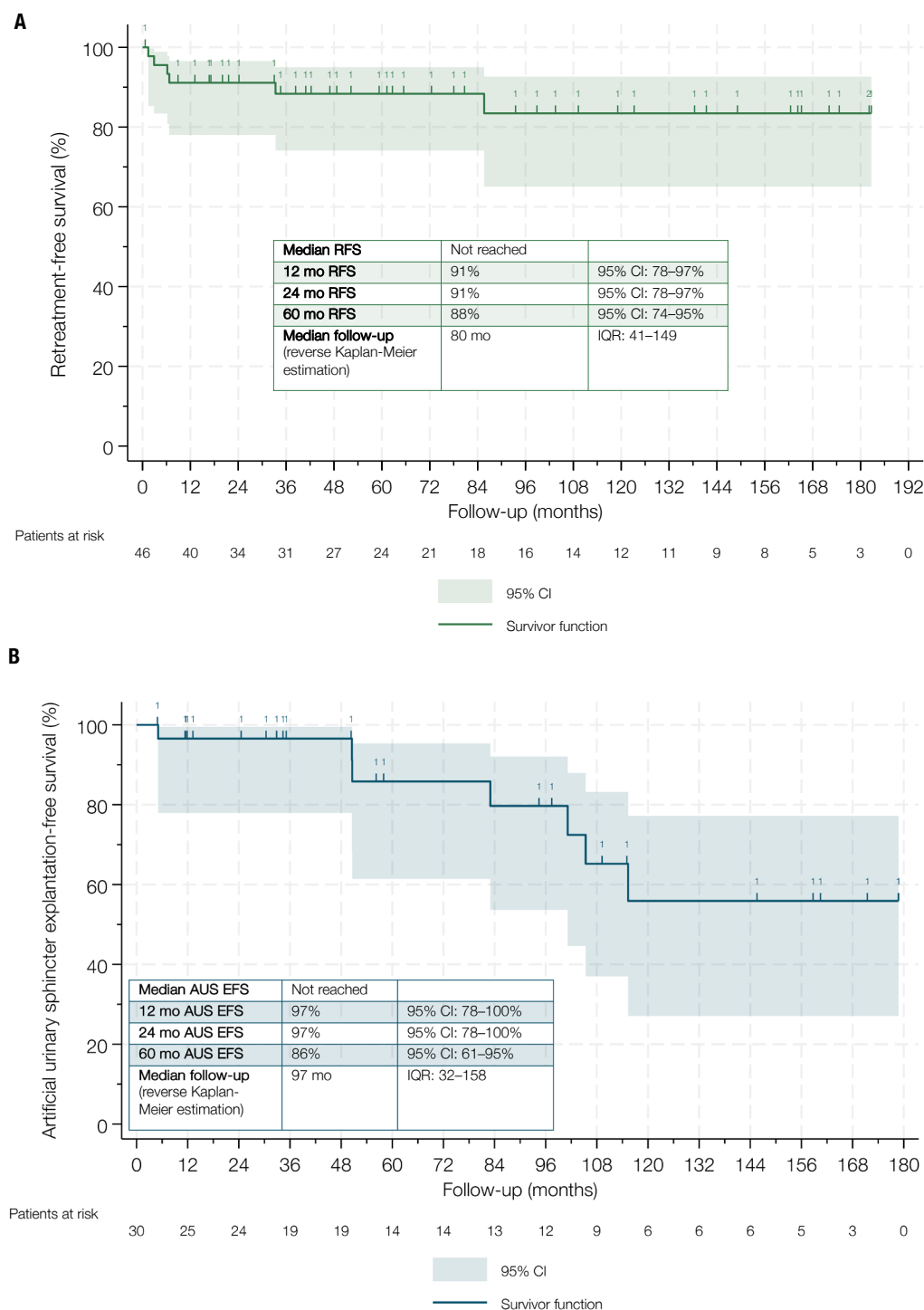
Following the selection process, nine articles comprising 189 patients that met our inclusion criteria were identified (20, 22–29). The reported success rates, predominantly defined as reintervention-free survival, ranged from 60% to 92%, with median/mean follow-up durations varying between 10 and 76 months (Table-2).

Apart from our earlier preliminary series on transperineal reanastomosis (20), only one study incorporated validated PROMs in their analysis, including the International Prostate Symptom Score (I-PSS) with the QOL item, and the Global Response Assessment to evaluate patient satisfaction (22). However, differences in follow-up durations, endpoint definitions, and cohort heterogeneity limit the comparability of these outcomes across studies.

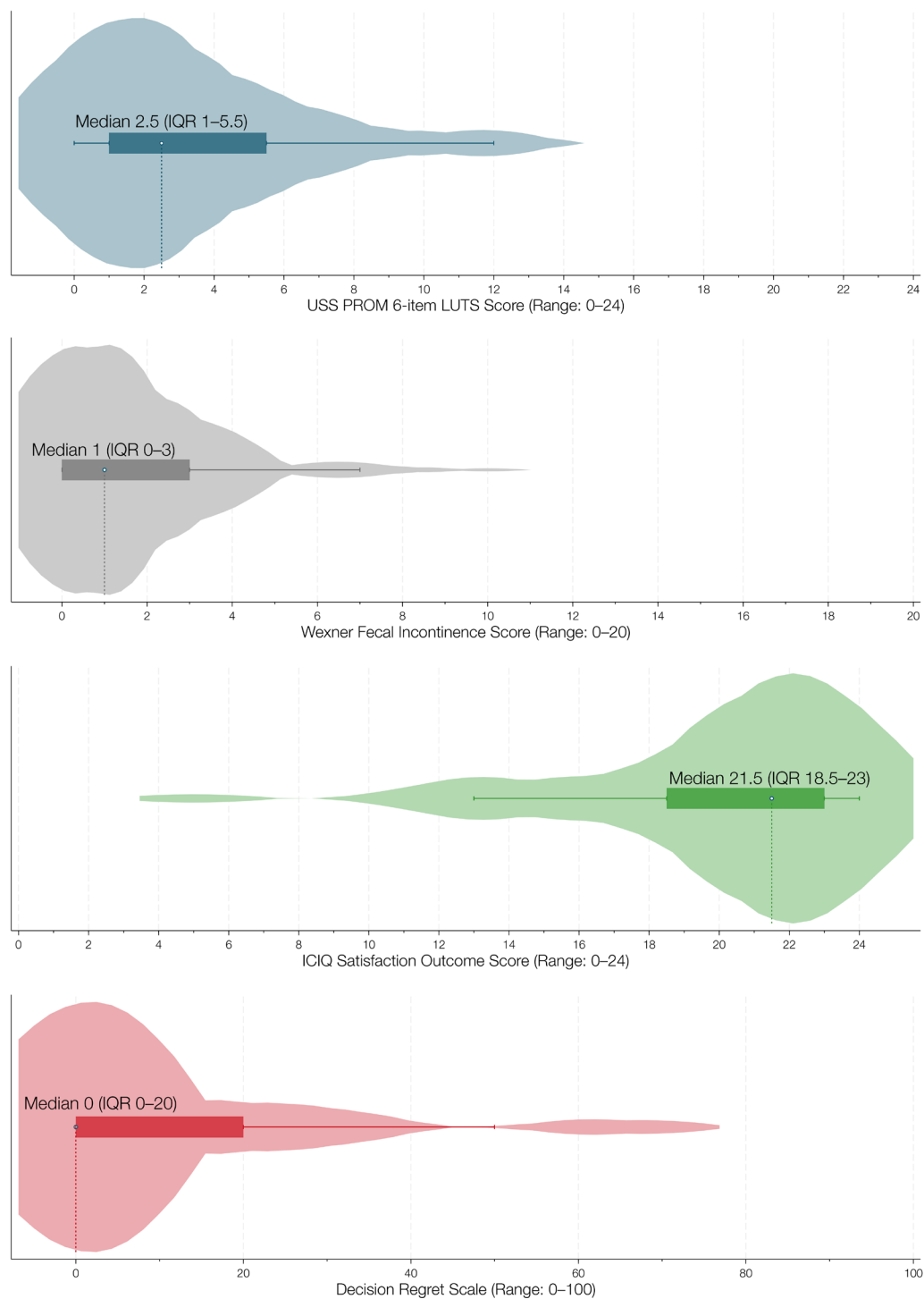
## DISCUSSION

Refractory VUAS is a challenging condition that significantly affects quality of life in prostate cancer survivors and often necessitates complex surgical reconstruction to avoid urinary diversion or long-term suprapubic catheterization. This series presents the largest single-center cohort with the longest follow-up to date for the treatment of complex post-prostatectomy VUAS following failed endoscopic management or complete stenotic obliteration. By

**Figure 3 - Kaplan-Meier curves depicting (A) retreatment-free survival in 46 patients undergoing transperineal reanastomosis for recurrent or obliterative vesicourethral anastomotic stenosis and (B) explantation-free survival in 30 patients undergoing AUS implantation following transperineal reanastomosis. AUS, artificial urinary sphincter; CI, confidence interval; EFS, explantation-free survival; IQR, interquartile range; RFS, retreatment-free survival.**



**Figure 4 - Violin plots illustrating the distribution of scores for validated patient-reported outcome measures in 28 of 46 patients undergoing transperineal vesicourethral reanastomosis.**



ICIQ = International Consultation on Incontinence Questionnaire; IQR = interquartile range; USS PROM = Urethral Stricture Surgery Patient-Reported Outcome Measure.

**Table 2 - Publications on outcomes after complex VUAS reconstruction as identified by a scoping literature review on November 30, 2024.**

| First author           | Year of publication | No. of patients | Surgical approach                                                                                               | Median/Mean follow-up (mo) | Success rate (%)* | PROMs                                          |
|------------------------|---------------------|-----------------|-----------------------------------------------------------------------------------------------------------------|----------------------------|-------------------|------------------------------------------------|
| Pfalzgraf et al. (28)  | 2012                | 20              | Open retropubic reanastomosis                                                                                   | 59                         | 60                | NR                                             |
| Simonato et al. (29)   | 2012                | 11              | Open Solovov-Badenoch 'pull-through urethroplasty'                                                              | 65                         | 91                | NR                                             |
| Nikolavsky et al. (27) | 2014                | 12              | Open abdominal reanastomosis (7), open transperineal reanastomosis (3), open abdominoperineal reanastomosis (2) | 76                         | 92                | NR                                             |
| Schuetfort et al. (20) | 2017                | 23              | Open transperineal reanastomosis                                                                                | 45                         | 87                | I-PSS and QOL item, ICIQ-UI SF, EQ-5D-3L       |
| Giúdice et al. (26)    | 2019                | 20              | Open transperineal reanastomosis (10), open transabdominal reanastomosis (10)                                   | 10                         | 70                | NR                                             |
| Şimşek et al. (25)     | 2021                | 16              | Open transperineal reanastomosis (12), robotic perineoscopic reanastomosis (4)                                  | 13                         | 81                | NR                                             |
| Bearrick et al. (24)   | 2022                | 10              | Open primary scar excision and re-anastomosis (5), YV plasty (3), downward rotational bladder advancement (2)   | 24                         | 90                | NR                                             |
| Shakir (23)            | 2022                | 32              | Robotic retropubic reanastomosis                                                                                | 12                         | 75                | NR                                             |
| Sterling et al. (22)   | 2024                | 45              | Open dorsal onlay buccal mucosal graft urethroplasty                                                            | 21                         | 84                | I-PSS and QOL item, Global Response Assessment |

\* Defined as reintervention-free survival; referred to as patency in Nikolavsky et al. (2014) and Giúdice et al. (2019). ICIQ-UI SF = International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; I-PSS = International Prostate Symptom Score

employing a predominantly staged approach—transperineal vesicourethral reanastomosis followed by AUS implantation—we achieved effective restoration of voiding function, high patient satisfaction, and negligible decision regret.

Our retreatment-free survival rates align with the >80% success reported in two-thirds of the existing literature on complex VUAS reconstruction. Two

factors likely contributed to this success: complete excision of scar tissue, which restores an uncompromised surgical field for optimal reconstruction (28), and the absence of prior pelvic radiation in nearly all patients, as radiotherapy negatively impacts surgical outcomes. For VUAS involving the urinary sphincter, a transperineal approach is often preferred, as it provides optimal anatomical exposure of critical

structures. In contrast, transabdominal or robot-assisted approaches may be more suitable when the VUAS extends toward the bladder with minimal or no sphincter involvement (30). The choice of surgical approach should be guided by the location and extent of the VUAS, both of which are influenced by the degree of membranous urethra preservation during prostatectomy and the number of prior endoscopic interventions. Moreover, variations in vesicourethral anastomosis technique may further impact scarring into the membranous urethra, as different approaches appear to carry varying risks for VUAS development (1). In our department, up to three prior endoscopic treatments are typically performed. As a result, VUAS in our cohort often exhibit significant scar tissue and frequently extend into the membranous urethra, precluding sphincter preservation in many cases and limiting the feasibility of a transabdominal approach, as a transperineal incision becomes necessary due to the distal extension of the stenosis. To improve patient selection in the future, a classification system for VUAS based on anatomical location and prior treatments would be highly valuable.

The AUS explantation-free survival rate in our cohort is slightly higher than those reported in a recent large French cohort (31). This difference may be partly explained by the lower incidence of prior pelvic radiotherapy in our cohort, as radiotherapy is known to increase reintervention rates. While no systematic review has reported reintervention-free survival for AUS implantations, a recent systematic review highlighted the significant concern of reinterventions following AUS implantation by reporting pooled reoperation rates of 22% in the short term (6–36 months) and 36% in the long term (>36 months), with a mean follow-up of 19 months (32).

According to our scoping review, our series is the first to assess patient-centered outcomes for anastomotic repair of refractory VUAS. Several validated PROMs were utilized, covering key functional domains such as voiding and fecal continence, as well as broader outcome measures, including treatment satisfaction and decision regret. Notably, the postoperative LUTS symptom burden observed in

our cohort is comparable to that reported for patients undergoing anterior urethroplasty in the pivotal USS PROM study (14). Our excellent results in fecal continence, as measured by the Wexner incontinence score, which has been shown to be associated with quality of life, were anticipated but remain significant, as pelvic surgeries and transperineal approaches can impact fecal continence (33).

Arguably of greater impact than PROMs for functional outcomes are overall patient satisfaction and decision regret—aspects that have been largely unexplored in the context of refractory VUAS. This is especially crucial when multiple treatment alternatives are available, requiring patients to make informed choices among them. The relatively novel and validated ICIQ-S effectively captures a broad range of critical perioperative aspects by aggregating patient feedback into a comprehensive overall score (16). It evaluates not only the surgical outcome through questions like “How would you rate the outcome of your surgery?” but also explores the patient’s emotional well-being post-surgery, their ability to resume normal life, and their willingness to undergo the procedure again or recommend it to others. In combination with the DRS, which evaluates decision regret following a patient’s choice through five questions addressing whether the decision was deemed “right,” “regretted,” “worth repeating,” “harmful,” or “wise,” these two PROMs provide a comprehensive overview of how patients assess their treatment. Despite the demanding nature of a staged procedure requiring two invasive surgeries, treatment satisfaction in our cohort remains high, with minimal decision regret, highlighting the fundamental rationale for this therapeutic approach.

Our study has several limitations. Its retrospective design precluded assessment of urinary continence after prostatectomy but before the first endoscopic intervention, which would have allowed evaluation of changes in stress urinary incontinence over the course of endoscopic therapies and transperineal reanastomosis. The relatively small sample size limited the use of multivariable regression analyses. Additional limitations include the cross-section-

al nature of follow-up, the absence of preoperative PROMs for baseline comparisons, and potential recall bias. Although the PROM response rate of 61% is comparable to similar long-term retrospective studies, the possibility of response bias should be acknowledged. Nevertheless, we believe this series makes a significant contribution to the literature by demonstrating highly satisfactory outcomes for open transperineal vesicourethral reanastomosis in a patient cohort facing a complex refractory post prostatectomy late complication with likely long-term survival, highlighting that definitive urinary diversion or long-term suprapubic catheterization should not be considered the ultimate solutions for these patients.

## CONCLUSIONS

Open transperineal reanastomosis is a valuable and durable option for managing recurrent or obliterative post-prostatectomy VUAS refractory to endoscopic therapy, demonstrating favorable long-term outcomes and positive patient-reported experiences. This largest series to date underscores the procedure's critical role in salvage posterior urethral reconstruction for long-term prostate cancer survivors.

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Jakob Klemm and Katharina Oberneder contributed equally as first author.

## CONFLICT OF INTEREST

Margit Fisch and Roland Dahlem have served as consultants for Boston Scientific.

### The other authors

None declared

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# Tubeless Retroperitoneal Robot-assisted Partial Nephrectomy: An Innovative Approach to Treat Early Renal Tumor

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## ABSTRACT

**Purpose:** Retroperitoneal robot-assisted partial nephrectomy (RRPN) has achieved widespread acceptance worldwide. However, the complications and discomfort associated with tubes cannot be overlooked. Consequently, we have initiated Tubeless RRPN (TLRRPN). This approach eliminates the need for tracheal intubation, central venous catheterization, urinary catheters, or abdominal drainage.

**Materials and Methods:** From 2024-07 to 2025-06, a total of 78 patients underwent RRPN at our center. Following a 1:1 propensity scores matching process, we compared 14 patients who underwent TLRRPN with 14 matched patients receiving Traditional RRPN (TRRPN). Anesthetic management and surgical procedures were systematically detailed, and perioperative outcomes were comprehensively assessed.

**Results:** All 28 patients underwent successful R0 tumor resection, with no conversions or major complications reported in either group. Patients who received TLRRPN resumed oral intake and ambulation significantly earlier (1.03 hours vs. 22.20 hours and 1.03 hours vs. 30.55 hours,  $p < 0.001$ ), experienced a shorter postoperative hospital stay (26.00 hours vs. 91.43 hours,  $p < 0.001$ ), and incurred lower overall costs. No anesthesia- or surgery-related complications were observed, and postoperative pain was significantly reduced in the TLRRPN group compared to the TRRPN group.

**Conclusions:** TLRRPN is a safe, efficient, innovative, cost-effective, and selective surgical procedure. This operation fundamentally reduces the adverse effects associated with tubes in patients and significantly facilitates rapid recovery.

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## INTRODUCTION

In recent decades, robot-assisted partial nephrectomy (RPN) has become increasingly favored due to its advantages of reduced postoperative pain, shorter hospitalization, and faster return to daily activities, while maintaining oncologic outcomes comparable to open partial nephrectomy (OPN) (1-3). The retroperitoneal RPN (RRPN) offers additional benefits by minimizing disturbance to intraperitoneal organs (4-7). Despite these advances, perioperative management often still involves substantial use of sedatives, muscle relaxants, and other pharmacological agents, which may impede postoperative recovery. Moreover, the routine use of tracheal intubation, urinary catheters, drainage tubes, and central venous access can contribute to increased patient discomfort and delayed rehabilitation (8-19). With ongoing progress toward precision surgery and enhanced recovery protocols, a critical question arises: Can RRPN be re-engineered to resemble the minimally invasive, rapid-recovery experience of painless gastroscopy? To explore this concept, our center developed a novel technique—tubeless retroperitoneal robot-assisted partial nephrectomy (TLRRPN)—aimed at eliminating unnecessary perioperative tubing and thereby promoting a truly minimally invasive surgical experience with enhanced postoperative recovery.

TLRRPN—a minimally invasive surgical approach that eliminates the need for tracheal intubation, central venous catheterization, urinary catheterization, and surgical drainage tubes—fundamentally avoids the complications associated with these invasive devices to promote postoperative recovery in patients with early-stage renal tumors.

## MATERIALS AND METHODS

### Surgeon and patient selection

Robot-assisted renal surgery has been routinely performed at our center since 2016. All procedures in this study were conducted by a single high-volume surgeon with experience in over 700 robot-assisted nephrectomies. This study has been

approved by the institutional review board (IRB) and the ethical committee of Sun Yat-sen University Cancer Center, the IRB number is SL-XJS2025-012. We retrospectively analyzed 78 patients who underwent RRPN between July 2024 and June 2025 (Supplementary Table). Following a 1:1 propensity score matching (PSM), 28 patients were selected and divided into two groups: the TLRRPN ( $n = 14$ ) and traditional RRPN (TRRPN) groups ( $n = 14$ ) (Figure-1).

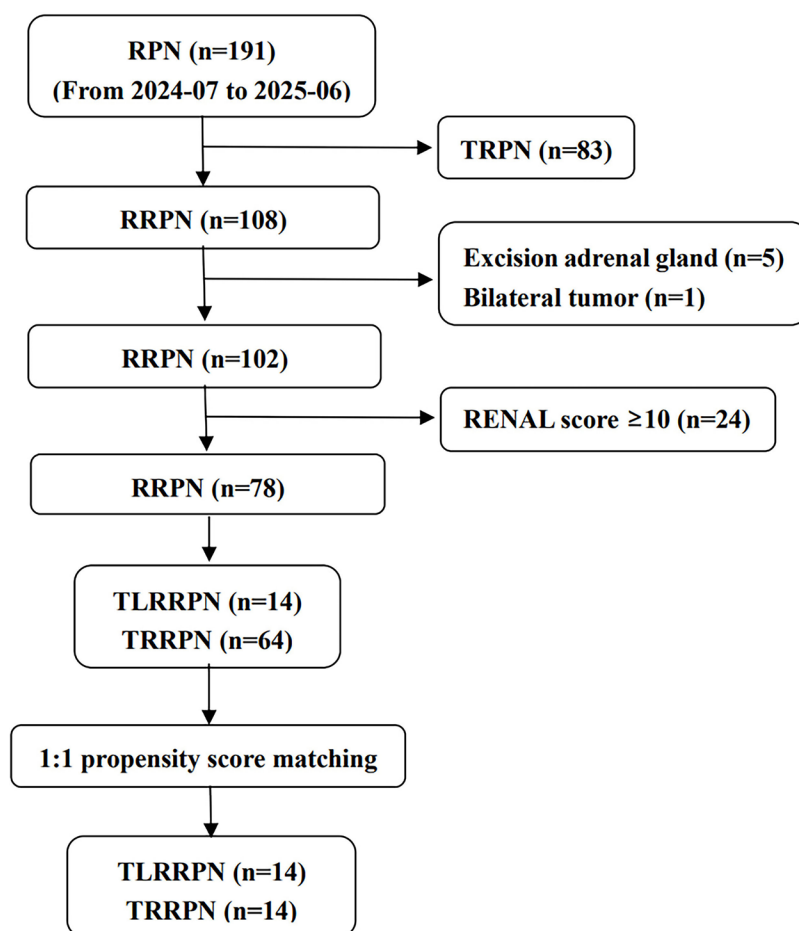
We have frequently conducted TRRPN surgeries in the past. With the enhancement of our proficiency, we initiated TLRRPN in April 2025. We assessed all patients eligible for TLRRPN based on specific criteria: estimated overall operative time  $\leq 90$  minutes, American Society of Anesthesiologists (ASA) score  $\leq 3$ , RENAL score  $\leq 9$ , absence of cardiopulmonary dysfunction, no history of lower urinary tract obstruction, no significant coagulopathy, and no evidence of gastroesophageal reflux or extrarenal invasion/metastasis. Exclusion criteria were bilateral tumors, concomitant organ resections, and RENAL score  $\geq 10$  (Figure-1). Baseline characteristics (age, sex, body mass index [BMI], tumor details, and RENAL and ASA scores) and perioperative outcomes were collected. Postoperative recovery time was calculated from the moment of anesthesia awakening.

Follow-up was conducted via telephone interview and review of medical records in accordance with standard clinical guidelines. Patient symptoms were evaluated within 24 hours postoperatively, and complications were evaluated up to 6 months after surgery. The final follow-up was completed on January 1, 2026.

### Preoperative preparation

All patients underwent standardized preoperative evaluation, including contrast-enhanced computed tomography (CT). The surgical site was marked one day before the operation. Bowel preparation was not performed. Patients were instructed to fast from 22:00 on the night prior to surgery. Two units of packed red blood cells were cross-matched and reserved in case intraoperative transfusion was required.

**Figure 1 - Flow chart of patient inclusion.** RPN, robot-assisted partial nephrectomy; TRPN, transperitoneal robot-assisted partial nephrectomy; RRPN, retroperitoneal robot-assisted partial nephrectomy; RENAL, R (radius), E (exophytic/endophytic), N (nearness), A (anterior), L (location); TLRRPN, tubeless retroperitoneal robot-assisted partial nephrectomy; TRRPN, traditional retroperitoneal robot-assisted partial nephrectomy.



### Anesthetic management

Standard intraoperative monitoring included electrocardiography (ECG), pulse oximetry (SpO<sub>2</sub>), non-invasive blood pressure (NIBP), End-Tidal Carbon Dioxide (ETCO<sub>2</sub>), and Narcotrend depth of anesthesia monitoring.

In the TRRPN group, patients underwent central venous and radial arterial cannulation. General anesthesia was induced and maintained with ciprofol, sufentanil, and rocuronium, targeting a Narcotrend index of 45-60. Ventilation was managed using a single-lumen endotracheal tube under intermittent positive pressure ventilation with 50% inspired oxy-

gen, tidal volume of 6-8 mL/kg, respiratory rate of 12-15 breaths/min, and oxygen flow of 2 L/min.

In the TLRRPN group, ultrasound-guided epidural catheterization (T9/10 or T10/11) was performed following establishment of a 20G peripheral venous line. Epidural analgesia was achieved using 0.5% ropivacaine (sensory block T4-T12). Sedation was maintained with intravenous ciprofol to achieve a Narcotrend index of 40-60, while patients maintained spontaneous respiration (15-30 breaths/min) with facemask oxygen at 6 L/min, SpO<sub>2</sub> >95%, ETCO<sub>2</sub> <80 mmHg, and tidal volume ≥5 mL/kg.



### Camera point location

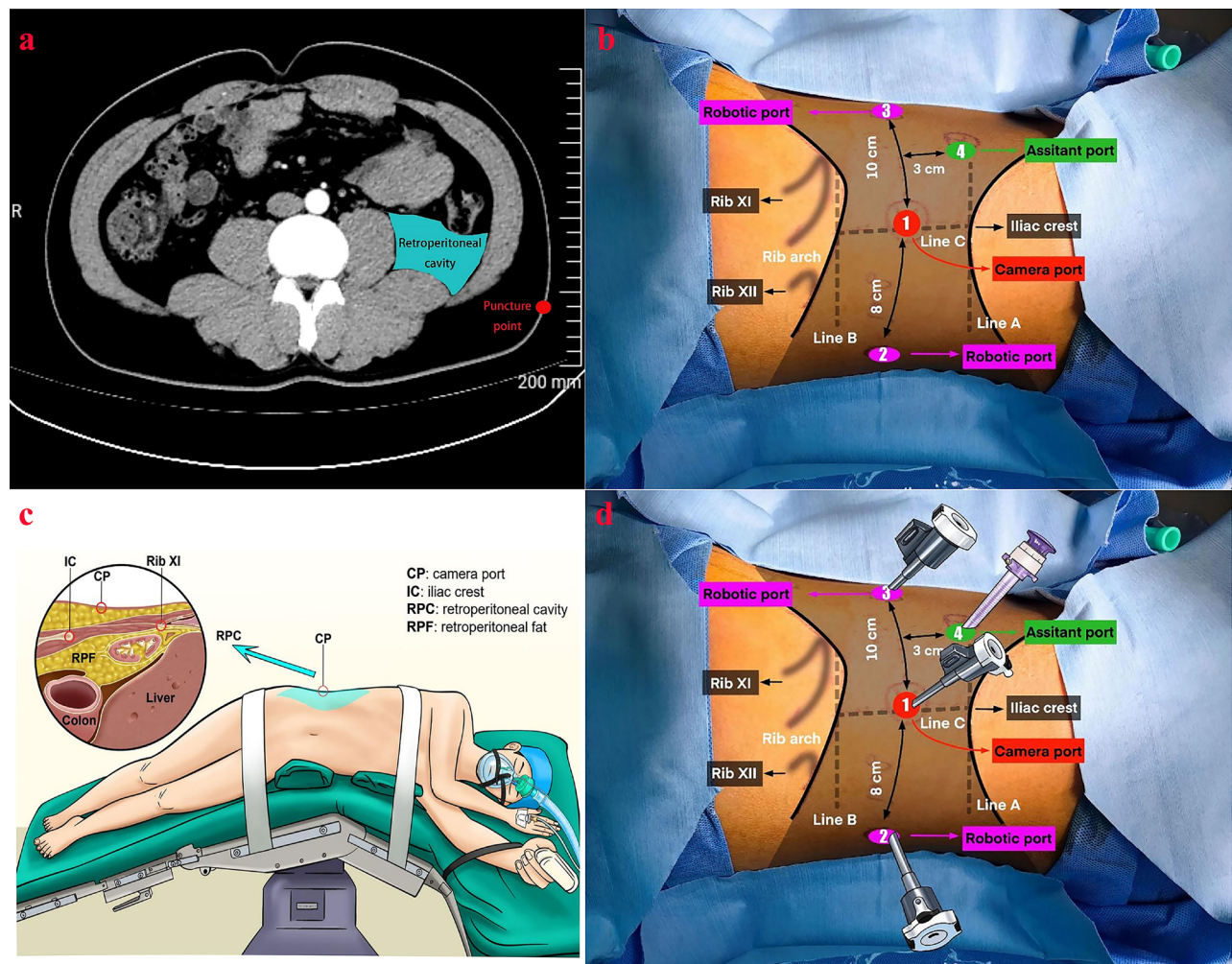
Preoperative CT was used to evaluate volume of the retroperitoneal cavity and determine the ideal camera puncture site by measuring the thickness of subcutaneous fat and muscle (Figure-2a). Initially, the highest point of the iliac crest was marked to create a sagittal reference axis (Line A). Next, the costal margin between the 11th and 12th ribs was identified to draw a second sagittal axis (Line B). From the highest point on the iliac crest, a perpendicular line (Line C) was drawn to intersect line AB. The midpoint of line C was designated as the camera port puncture site (Figure-2b).

### Patient positioning and surgical procedure

Following anesthesia induction, urinary catheterization was omitted in the TLRRPN group and routinely applied in the TRRP group. All patients were placed in a lateral decubitus position with the tumor side up. The coronal plane was maintained perpendicular to the operating table. Both arms were positioned forward, and the table was flexed to enlarge the retroperitoneal space between the iliac crest and costal margin (Figure-2c).

A 1.2 cm vertical incision was made at the midpoint of Line C. The depth of puncture was manually controlled, guided by subcutaneous and muscle

**Figure 2 - Procedures. 2a) Retroperitoneal cavity and puncture point; 2b) Trocars location; 2c) Patient position; 2d), Port placement.**





thickness measurements from preoperative CT. Once a “breakthrough” sensation indicated entry into the posterior abdominal cavity, the surgeon inserted an index finger and gently rotated 180° along the abdominal wall to develop a retroperitoneal space between the posterior renal fascia and transversalis fascia (see video). During this maneuver, tactile confirmation of the smooth transversalis fascia, the 12th rib, and the psoas muscle body was required.

The first 8 mm robotic port was placed 8 cm posterior to the camera port in the same sagittal plane. The second 8 mm port was inserted 10-12 cm anterior to the first. A 12 mm assistant port was positioned 3-5 cm below the midpoint between the camera and anterior robotic ports. All ports were inserted bluntly under tactile guidance with the index finger placed through the camera incision to ensure safe passage into the retroperitoneal space (Figure-2d and see video). Following these highly simplified steps, the surgeon can complete the trocar placement within one minute.

The da Vinci Xi System™ was docked dorsally. Bipolar forceps were positioned in the left robotic arm and monopolar curved scissors in the right, with pneumoperitoneum maintained at 12 mmHg. After incising the lateral fascia, the perirenal fat was exposed, enlarging the working cavity. Retroperitoneal fat was cleared as required. Using the psoas muscle as a reference, we identified the perirenal fat and traced the renal artery pulsation to locate the renal hilum, after which standard RPN procedures were performed (see video). The specimen was extracted via the camera port with meticulous hemostasis.

In TLRRPN cases, no drainage tube was placed. However, if intraoperative suturing is deemed unsatisfactory, placement of an abdominal drainage tube is permitted. In contrast, a drainage tube was routinely inserted in the TRRPN group.

### Postoperative management

Hemoglobin levels were monitored via complete blood counts immediately after surgery, at 9 hours, and on postoperative day 1. Absence of a significant decline suggested a low risk of active bleed-

ing. TLRRPN patients were encouraged to resume oral intake and ambulation within 1 hour postoperatively. No routine intravenous fluids or antibiotics were used, and only minimal oral analgesics were provided as needed. In contrast, TRRPN patients received patient-controlled analgesia, intravenous hydration until return of gastrointestinal function, and progressive mobilization. The urinary catheter, central venous catheter, and drainage tube were removed sequentially before discharge. Postoperative complications were graded using the Clavien-Dindo system, and pain intensity was assessed using the Visual Analog Scale (VAS).

### Statistical Analysis

PSM using logistic regression was applied to minimize confounding and balance baseline variables (age, sex, BMI, and RENAL score). A 1:1 nearest-neighbor match was performed with a caliper of 0.05 on the logit scale.

Continuous variables were compared using two-tailed Student's t-tests, while categorical variables were analyzed using chi-square or Fisher's exact tests, as appropriate. A two-sided p-value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (Version 27.0; IBM Corp, Armonk, NY, USA).

### RESULTS

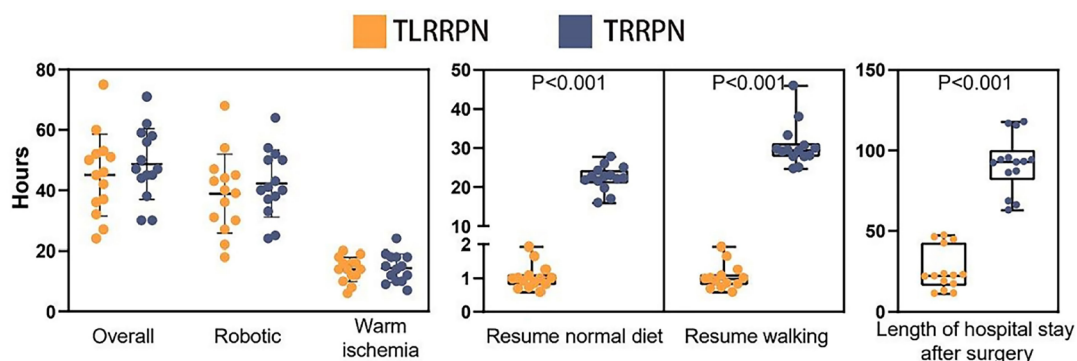
Twenty-eight patients were included in the final analysis (TLRRPN, n = 14; TRRPN, n = 14), with a median follow-up of 303 days (range: 195-540 days). The median age was  $48.86 \pm 13.39$  years, the median BMI was  $24.97 \pm 3.76$  kg/m<sup>2</sup>, and the median RENAL score was  $7.64 \pm 1.44$ . Baseline characteristics did not differ significantly between groups (Table-1). There were no anesthesia- or surgery-related deaths, no conversions to open surgery, and all patients achieved R0 resection. Overall operative time, robotic operating time, warm ischemia time, and estimated blood loss were comparable between the TLRRPN and TRRPN groups (Figure-3 and Table-2).

**Table 1 - Baseline preoperative characters of study after 1:1 propensity score match.**

| Characteristic                                      | Total (n=28) | TLRRPN (n=14) | TRRPN (n=14) | P value |
|-----------------------------------------------------|--------------|---------------|--------------|---------|
| <b>Median Age</b>                                   | 48.86±13.39  | 48.57±12.43   | 49.14±14.75  | 0.913   |
| <b>Gender</b>                                       |              |               |              |         |
| Male                                                | 24 (85.7%)   | 12 (85.7%)    | 12 (85.7%)   | 1.000   |
| Female                                              | 4 (14.3%)    | 2 (14.3%)     | 2 (14.3%)    |         |
| <b>BMI(Kg/m<sup>2</sup>)</b>                        | 24.97±3.76   | 25.24±3.68    | 24.71±3.97   | 0.716   |
| <b>18.5-23.9</b>                                    | 13 (46.4%)   | 7 (50.0%)     | 6 (42.9%)    | 0.705   |
| ≥24                                                 | 15 (53.6%)   | 7 (50.0%)     | 8 (57.1%)    |         |
| <b>Tumor laterality</b>                             |              |               |              |         |
| Left                                                | 14 (50.0%)   | 6 (42.9%)     | 8 (57.1%)    | 0.450   |
| Right                                               | 14 (50.0%)   | 8 (57.1%)     | 6 (42.9%)    |         |
| <b>Tumor positions</b>                              |              |               |              |         |
| Anterior                                            | 17 (60.7%)   | 10 (71.4%)    | 7 (50.0%)    | 0.246   |
| Posterior                                           | 11 (29.3%)   | 4 (28.6%)     | 7 (50.0%)    |         |
| <b>Tumor size (cm)</b>                              | 3.02±0.68    | 3.04±0.61     | 3.00±0.76    | 0.893   |
| <b>RENAL score</b>                                  | 7.64±1.44    | 7.64±1.49     | 7.64±1.44    | 1.000   |
| <b>ASA status class</b>                             |              |               |              |         |
| I                                                   | 23 (82.1%)   | 11 (78.6%)    | 12 (85.7%)   | 1.000   |
| II                                                  | 5 (17.9%)    | 3 (21.4%)     | 2 (14.3%)    |         |
| <b>Abdominal surgery history</b>                    |              |               |              |         |
| No                                                  | 25 (89.3%)   | 13 (92.9%)    | 12 (85.7%)   | 1.000   |
| Yes                                                 | 3 (10.7%)    | 1 (7.1%)      | 2 (14.3%)    |         |
| <b>Preoperative eGFR (mL/min/1.73m<sup>2</sup>)</b> | 101.58±31.80 | 107.61±36.44  | 95.56±26.36  | 0.326   |

Qualitative Variables are given as number (%); Quantitative Variables are given as median ± SD.

TLRRPN = tubeless robot-assisted partial nephrectomy; TRRPN = traditional retroperitoneal robot-assisted partial nephrectomy; BMI = body mass index; RENAL = R (radius), E (exophytic/ endophytic), N (nearness), A (anterior), L (location); ASA = American Society of Anesthesiologist; eGFR = estimated glomerular filtration rate.

**Figure 3 - Intraoperative and postoperative outcomes. TLRRPN, tubeless retroperitoneal robot-assisted partial nephrectomy; TRRPN, traditional retroperitoneal robot-assisted partial nephrectomy.**

**Table 2 - Comparison of perioperative outcomes between TLRRPN and TRRPN.**

| Characteristic                                          | Total (n=28)        | TLRRPN (n=14)        | TRRPN (n=14)        | P value        |
|---------------------------------------------------------|---------------------|----------------------|---------------------|----------------|
| <b>Overall operative time (min)</b>                     | 46.86±12.58         | 45.00±13.55          | 48.71±11.73         | 0.445          |
| <b>Robotic operative time (min)</b>                     | 40.54±12.04         | 38.86±13.11          | 42.21±11.09         | 0.471          |
| <b>Trocar placement and robot docking time (min)</b>    | 3.39±0.49           | 3.36±0.49            | 3.43±0.51           | 0.712          |
| <b>Opening and closing abdomen time (min)</b>           | 2.93±0.60           | 2.79±0.42            | 3.07±0.73           | 0.217          |
| <b>Estimated blood loss (ml)</b>                        | 26.96±13.69         | 29.29±14.39          | 24.64±13.07         | 0.380          |
| <b>Warm ischemia time (min)</b>                         | 14.14±4.30          | 13.93±4.04           | 14.36±4.70          | 0.798          |
| <b>Transfusion required</b>                             | None                | None                 | None                | 1.000          |
| <b>Conversion to open</b>                               | None                | None                 | None                | 1.000          |
| <b>Conversion to radical nephrectomy</b>                | None                | None                 | None                | 1.000          |
| <b>Peritoneal rupture</b>                               | None                | None                 | None                | 1.000          |
| <b>Time to begin walking after surgery (h)</b>          | 15.79±15.51         | 1.03±0.36            | 30.55±5.50          | <0.001         |
| <b>Time to resume normal diet after surgery (h)</b>     | 11.61±11.00         | 1.03±0.36            | 22.20±3.18          | <0.001         |
| <b>Length of hospital stay after surgery (h)</b>        | 58.72±36.61         | 26.00±13.11          | 91.43±17.52         | <0.001         |
| <b>1d postoperative eGFR (ml/min/1.73m<sup>2</sup>)</b> | 93.11±26.90         | 97.34±32.78          | 88.87±19.74         | 0.415          |
| <b>Pathology</b>                                        |                     |                      |                     | 0.677          |
| Clear cell                                              | 20 (71.4%)          | 9 (64.3%)            | 11 (78.6%)          |                |
| Chromophobe                                             | 3 (10.7%)           | 2 (14.3%)            | 1 (7.1%)            |                |
| SDHRCC                                                  | 1 (3.6%)            | 1 (7.1%)             | 0 (0.0%)            |                |
| Benign                                                  | 4 (14.3%)           | 2 (14.3%)            | 2 (14.3%)           |                |
| <b>Pathological stage</b>                               |                     |                      |                     | 0.593          |
| T1a                                                     | 23 (82.1%)          | 12 (85.7%)           | 11 (78.6%)          |                |
| T3a                                                     | 1 (3.6%)            | 0 (0.0%)             | 1 (7.1%)            |                |
| Benign                                                  | 4 (14.3%)           | 2 (14.3%)            | 2 (14.3%)           |                |
| <b>Positive surgical margin</b>                         | All negative        | All negative         | All negative        | 1.000          |
| <b>Hospitality cost (thousands CNY)</b>                 | 63.93±6.48          | 58.14±1.56           | 69.71±3.56          | <0.001         |
| <b>Postoperative symptoms and complications</b>         | <b>Total (n=28)</b> | <b>TLRRPN (n=14)</b> | <b>TRRPN (n=14)</b> | <b>P value</b> |
| <b>Anesthesia-related symptoms</b>                      |                     |                      |                     |                |
| Dizziness                                               | 14 (50.0 %)         | 0 (0.0%)             | 14 (100%)           | <0.001         |
| Nausea and vomiting                                     | 12 (42.8 %)         | 0 (0.0%)             | 12 (85.7%)          | <0.001         |
| Hoarseness                                              | 1 (3.5%)            | 0 (0.0%)             | 1 (7.1%)            | 0.500          |
| Cough                                                   | 14 (50%)            | 0 (0.0%)             | 14 (100%)           | <0.001         |
| Hemoptysis                                              | 1 (3.5%)            | 0 (0.0%)             | 1 (7.1%)            | 0.500          |
| Sore throat                                             | 6 (21.4%)           | 0 (0.0%)             | 6 (42.8%)           | 0.008          |
| <b>Other symptoms</b>                                   |                     |                      |                     |                |
| Fever                                                   | 2 (7.1%)            | 0 (0.0%)             | 2 (14.2%)           | 0.481          |
| Drainage tube associated pain                           | 9 (32.1%)           | 0 (0.0%)             | 9 (64.2%)           | <0.001         |
| Urethral discomfort                                     | 13 (46.4%)          | 0 (0.0%)             | 13 (92.8%)          | <0.001         |
| <b>Clavien-Dindo Complication</b>                       |                     |                      |                     |                |
| Clavien I                                               | 6 (21.4%)           | 0 (0.0%)             | 6 (42.8%)           | 0.008          |
| <b>VAS pain score</b>                                   | 3.18±1.15           | 2.14±0.36            | 4.21±0.57           | <0.001         |

Note: Qualitative Variables are given as number (%); Quantitative Variables are given as median ± SD.

Abbreviation: TLRRPN, tubeless robot-assisted partial nephrectomy; TRRPN, traditional retroperitoneal robot-assisted partial nephrectomy; eGFR, estimated glomerular filtration rate; SDHRCC, succinate dehydrogenase renal cell cancer; CNY, Chinese Yuan; VAS, visual analog scale.

Postoperative recovery was markedly faster in the TLRRPN group. Time to oral intake ( $1.03 \pm 0.36$  hours vs.  $22.20 \pm 3.18$  hours,  $p < 0.001$ ) and time to ambulation ( $1.03 \pm 0.36$  hours vs.  $30.55 \pm 5.50$  hours,  $p < 0.001$ ) were markedly shorter in the TLRRPN group. Median postoperative length of stay was notably reduced ( $26.00 \pm 13.11$  hours vs.  $91.43 \pm 17.52$  hours;  $p < 0.001$ ), as were hospitalization costs (58,500 CNY vs. 69,000 CNY;  $p < 0.001$ ) (Figure 3 and Table-2). The tumor margins for all patients were negative. Pathological analysis showed that 82.1% (23/28) of tumors were pT1a, while 1 TRRPN patient had pT3a disease and is under close follow-up without recurrence (Table-2).

In the TLRRPN group, no anesthesia- or surgery-related symptoms were reported (Table-2). In contrast, the TRRPN group reported dizziness in 14 patients ( $p < 0.001$ ), nausea/vomiting in 12 patients ( $p < 0.001$ ), hoarseness in 1 patient, productive cough in 14 patients ( $p < 0.001$ ), hemoptysis in 1 patient, and sore throat in 6 patients ( $p = 0.008$ ). Furthermore, 2 patients from the TRRPN group developed postoperative fever, 9 reported drain-associated pain ( $p < 0.001$ ), and 13 experienced urethral discomfort ( $p < 0.001$ ). According to the Clavien-Dindo classification system, 6 patients within the TRRPN group experienced Grade I complications ( $p = 0.008$ ). Pain scores assessed using the VAS were significantly lower in the TLRRPN group ( $2.14 \pm 0.36$  vs.  $4.21 \pm 0.57$ ;  $p < 0.001$ ) (Table-2).

## DISCUSSION

The progression from OPN to RRPN represents the continuous pursuit of greater surgical precision, reduced trauma, and enhanced perioperative recovery (1-4, 20, 21). In addition to oncological efficacy, contemporary practice increasingly emphasizes patient-centered care, including individualized treatment and improved perioperative experience. Tubeless pulmonary surgery has demonstrated safety, feasibility, and rapid recovery, and has therefore gained widespread adoption globally (22-24). Anatomically, the retroperitoneal cavity is isolated from

intraperitoneal organs, allowing CO<sub>2</sub> insufflation to be contained without significant diaphragmatic or respiratory compromise (25-27). This enables maintenance of spontaneous ventilation using TLRRPN and avoids the need for tracheal intubation, muscle relaxants, and excessive sedatives. Moreover, by eliminating bowel manipulation, the physiological stress of surgery is reduced. Robotic precision contributes to minimal tissue injury, accurate suturing, and reliable hemostasis, obviating the need for retroperitoneal drainage. Within this controlled operative environment, all procedures were successfully completed within 90 minutes, without urinary catheterization. Fluid requirements remained low, and central venous access was unnecessary.

This study presents preliminary findings of TLRRPN, an innovative technique that avoids tracheal intubation, central venous access, urinary catheterization, and abdominal drainage. Our findings demonstrate clear advantages over TRRPN. Compared to TRRPN, patients undergoing TLRRPN were able to resume oral intake and ambulation within 1 hour postoperatively, effectively reducing tube-related discomfort and accelerating functional recovery. The perioperative experience closely resembled that of painless gastroscopy, enabling discharge within 24 hours. Furthermore, this approach significantly reduced overall hospitalization costs.

From the patient's perspective, TLRRPN significantly alleviates discomfort and reduces the risk of complications. Avoiding tracheal intubation, muscle relaxants, and excessive sedatives minimizes postoperative symptoms, such as sore throat, cough, dizziness, and sputum retention. Similarly, omission of central venous and urinary catheters reduces the incidence of infection, thrombosis, and lower urinary tract irritation, while the absence of a drain leads to less postoperative pain. Notably, the simplified anesthetic regimen also helps preserve gastrointestinal function, enabling rapid resumption of oral intake and early ambulation.

From the surgeon's standpoint, TLRRPN focuses on atraumatic peritoneal handling to prevent intraoperative escalation. Adopting a three-arm ro-

botic configuration enhances maneuverability in the retroperitoneal space while significantly reducing the risk of peritoneal injury compared to conventional four-arm systems. Tumor exposure is optimized by targeted incision of the lateral conal fascia and selective insufflation, allowing focused dissection without extensive mobilization. Resection and renorrhaphy follow standard RPN protocols, and any peritoneal breach is promptly closed with clips to maintain operative integrity. In our clinical practice, a pneumoperitoneum pressure of 12 mmHg is sufficient to maintain the surgical space. If peritoneal rupture is detected intraoperatively, it compromises the surgical space and allows pneumoperitoneum to enter the abdominal cavity, impairing diaphragmatic respiration. Prompt repair is therefore essential. Abdominal gas can be evacuated with an aspirator, and the defect may be closed using clips or barbed sutures.

Anesthesiologists are integral to the safe and effective implementation of TLRRPN. Preoperative preparation involves placing an epidural catheter and securing peripheral venous access. Throughout the procedure, continuous monitoring of hemodynamic and respiratory parameters is essential. With the robotic tower positioned posteriorly, adequate anterior workspace remains for anesthesiologists to manage the airway and ventilation.

In patients at increased risk of collecting system rupture or postoperative hematuria, selective postoperative urinary catheterization may be warranted. If required, intraoperative conversion to a traditional airway or vascular access is feasible: ultrasound-guided central venous catheterization in the lateral position can usually be accomplished within 3 to 5 minutes, and video laryngoscope-assisted tracheal intubation requires a similar time frame. Therefore, TLRRPN can be safely and rapidly converted to TRRPN when necessary.

Owing to the robot's high-precision suturing capability, the risk of postoperative bleeding following early-stage renal tumor surgery is exceedingly low. Consequently, we routinely omit placement of an abdominal drainage tube during the procedure. Ronney Abaza et al. have demonstrated the safety and

feasibility of omitting routine abdominal drainage following partial nephrectomy for early-stage renal tumors (28). Nevertheless, selective use of an abdominal drainage tube remains an option. Specifically, we might place a drain in cases involving deeply located tumors, large surgical wounds, substantial perirenal fat, or anticipated significant postoperative fluid accumulation, as judged intraoperatively.

TLRRPN necessitates a highly experienced surgical team to ensure both patient safety and procedural success. Although TLRRPN presents considerable technical challenges, we carefully selected patients with localized, early-stage renal tumors and rigorously standardized each step of the highly simplified, reproducible surgical protocol. Adherence to this protocol enabled successful completion of TLRRPN in our cohort; we hope that this approach will herald a new, tubeless era in the management of renal tumors.

This article presents the first reported description of a tubeless surgical approach for the management of early-stage renal tumors. It further validates both the safety of tubeless surgery under pneumoperitoneum and its feasibility for routine clinical implementation. By minimizing or eliminating the use of tubes, this technique fundamentally mitigates tube-related complications and patient discomfort. Patients may resume normal activities and oral intake as early as one hour postoperatively. However, this surgical strategy is highly selective and is not indicated for patients with complex renal tumor.

Despite the promising results, our study has several limitations. From April 2025 to the present, we have successfully performed over 90 cases of TLRRPN; however, only 14 cases have achieved adequate follow-up duration. As such, our assessment primarily reflects feasibility and perioperative safety, while long-term oncologic outcomes remain to be determined. The sample size is relatively small, and the procedure is currently applicable only to carefully selected patients with early-stage renal tumors (RENAL score  $\leq 9$ ) and expected operative times under 90 minutes. Successful implementation also necessitates an experienced surgical, anesthetic, and nurs-

ing team, thereby confining its use to high-volume centers. Finally, data were collected retrospectively, and the small sample size may introduce potential selection bias. Therefore, larger prospective clinical studies are needed to validate the long-term safety, oncologic efficacy, and broader applicability of this novel approach.

## CONCLUSIONS

TLRRPN is a safe and effective surgical option for carefully selected patients with early-stage renal tumors. By minimizing perioperative invasiveness, it improves patient comfort, accelerates recovery, and reduces overall hospitalization costs. This technique represents a promising step toward more refined, patient-centered minimally invasive surgery.

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## CONFLICT OF INTEREST

None declared.

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## APPENDIX

**Supplementary Table. Preoperative characters of study before 1:1 propensity score match.**

| Characteristic                                      | Total (n=78) | TLRRPN (n=14) | TRRPN (n=64) | P value |
|-----------------------------------------------------|--------------|---------------|--------------|---------|
| <b>Median Age</b>                                   | 51.86±1.66   | 48.57±12.43   | 52.58±15.14  | 0.359   |
| <b>Gender</b>                                       |              |               |              | 0.211   |
| Male                                                | 55 (70.5%)   | 12 (85.7%)    | 43 (67.2%)   |         |
| Female                                              | 23 (29.5%)   | 2 (14.3%)     | 21 (32.8%)   |         |
| <b>BMI(Kg/m<sup>2</sup>)</b>                        | 24.2±0.3     | 25.2±3.6      | 24.0±3.4     | 0.231   |
| 18.5-23.9                                           | 38 (48.7%)   | 7 (50.0%)     | 31 (48.4%)   | 1.000   |
| ≥24                                                 | 40 (51.3%)   | 7 (50.0%)     | 33 (51.6%)   |         |
| <b>Tumor laterality</b>                             |              |               |              | 0.486   |
| Left                                                | 40 (51.3%)   | 6 (42.9%)     | 34 (53.1%)   |         |
| Right                                               | 38 (48.7%)   | 8 (57.1%)     | 30 (46.9%)   |         |
| <b>Tumor positions</b>                              |              |               |              | 0.015   |
| Anterior                                            | 33 (42.3%)   | 10 (71.4%)    | 23 (35.9%)   |         |
| Posterior                                           | 45 (57.7%)   | 4 (28.6%)     | 41 (64.1%)   |         |
| <b>Tumor size (cm)</b>                              | 3.10±0.96    | 3.04±0.61     | 3.11±0.90    | 0.775   |
| <b>RENAL score</b>                                  | 7.60±0.17    | 7.64±1.49     | 7.59±1.50    | 0.912   |
| <b>ASA status class</b>                             |              |               |              | 0.554   |
| I                                                   | 52 (66.7%)   | 11 (78.6%)    | 41 (64.0%)   |         |
| II                                                  | 24 (32.1%)   | 3 (21.4%)     | 22 (34.4%)   |         |
| III                                                 | 1 (1.2%)     | 0 (0.0%)      | 1 (1.6%)     |         |
| <b>Abdominal surgery history</b>                    |              |               |              | 0.678   |
| No                                                  | 67 (85.9%)   | 13 (92.9%)    | 54 (84.4%)   |         |
| Yes                                                 | 11 (14.1%)   | 1 (7.1%)      | 10 (15.6%)   |         |
| <b>Preoperative eGFR (mL/min/1.73m<sup>2</sup>)</b> | 96.17±3.92   | 107.61±36.44  | 93.67±34.02  | 0.174   |

Qualitative Variables are given as number (%); Quantitative Variables are given as median ± SD.

TLRRPN, tubeless robot-assisted partial nephrectomy; TRRPN, traditional retroperitoneal robot-assisted partial nephrectomy; BMI, body mass index; RENAL, R (radius), E (exophytic/ endophytic), N (nearness), A (anterior), L (location); ASA, American Society of Anesthesiologist; eGFR, estimated glomerular filtration rate.



# Redefining Surgical Collaboration: The First Structured Transcontinental Robotic Telementoring Experience Between Africa and South America

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## COMMENT

Robotic surgery has progressively transformed minimally invasive surgery by expanding technical precision, ergonomics, and visualization (1). More recently, telementoring and telesurgery-enabled platforms have emerged as potential strategies to mitigate geographic disparities in access to specialized surgical expertise (2–4). In this context, the landmark transcontinental robotic surgery performed between Orlando (United States) and Luanda (Angola) demonstrated the technical feasibility and clinical safety of long-distance surgical collaboration and served as a foundational proof of concept for the current telesurgery scenario worldwide (5). Similarly, the present study was designed to expand the scope of telesurgery-enabled care and to evaluate whether a similar, ethically structured model could be translated to other regions of the globe, particularly within the American continent. In this study we report expert insights from the first transcontinental telesurgery study performed in Brazil, using a structured telementoring framework during robot-assisted radical prostatectomy.

In this experience, the patient and operative team were located in Brazil, while the remote surgeon was physically based in Angola. To specifically evaluate feasibility and safety, the procedure was performed by an experienced local robotic urology team at Hospital Mãe de Deus (Porto Alegre, Brazil), with the remote surgeon at Hospital Cardeal Dom Alexandre do Nascimento (Luanda, Angola) participating exclusively in a telementoring role. The interaction consisted of real-time intraoperative guidance, technical discussion, and exchange of surgical strategies. Full procedural responsibility, including initiation, execution of critical steps, and completion of the surgery, remained entirely with the local operating surgeon, thereby preserving local surgical autonomy while safely integrating international expertise into the operative workflow.

The study was conducted under full ethical and regulatory oversight, with approval by the Comitê de Ética em Pesquisa (CEP) of Hospital Mãe de Deus and formal registration on Plataforma Brasil under the Universal Trial Number (UTN): U1111-1331-3810. All procedures were performed in accordance with the Declaration of Helsinki and national regulations governing research involving human subjects. The explicit inclusion of institutional review, national registration, and

transparent documentation was central to ensuring regulatory legitimacy and reproducibility.

A transcontinental connection was established between Luanda and Porto Alegre through a multi-segment public fiber-optic network, comprising a submarine fiber route from Luanda to Fortaleza (Brazil), followed by a terrestrial fiber from Fortaleza to Porto Alegre. The estimated end-to-end fiber distance was approximately 9,000 km. Biomedical and network engineers were present at both endpoints throughout the procedure, continuously monitoring latency, jitter, frame loss, and overall link stability, allowing real-time quality assessment and immediate response to any connectivity degradation during the telementoring phase.

A crucial component of this project was the use of a dedicated, procedure-specific informed consent for Telesurgery, developed based on prior FDA-approved experience between Orlando and Luanda (5). This consent addressed the role of the remote surgeon, cybersecurity safeguards, predefined connectivity thresholds (including latency and jitter limits), intraoperative contingency protocols, data protection measures, and the patient's right to withdraw consent at any time. The separation of telesurgery consent from standard surgical consent represents a relevant ethical advance in telesurgery-enabled care. Both teams followed a predefined contingency protocol, which was explicitly discussed with the patient as part of the consent process (6, 7).

During the Telesurgery, surgeons at both ends of the connection engaged in real-time discussion of surgical techniques and exchanged robotic console control at predefined key steps of the procedure. The local surgeon in Porto Alegre maintained full control and ultimate responsibility throughout the operation. At selected moments, the remote surgeon temporarily assumed console control to demonstrate technical variations and highlight relevant anatomical landmarks. **Supplementary Video 1** illustrates the key operative steps and the knowledge exchange that occurred among both teams during the procedure. This illustrates the potential of Telesurgery for surgical education and telementoring, while minimizing complications.

The case involved a 62-year-old male patient diagnosed with acinar prostate adenocarcinoma, ISUP Grade Group 2 (Gleason score 3+4=7), with a preoperative PSA of

6.47 ng/mL and normal Digital rectal exam (DRE). A robot-assisted radical prostatectomy was performed on November 5th, 2025, using the MicroPort Toumai robotic platform. Total operative time was 90 minutes, with no intraoperative or postoperative complications. During active participation of the remote surgeon, mean network latency was 132 ms (range 129–137 ms), with 0% frame loss and no detectable jitter, indicating stable and reliable connectivity throughout the telementoring phase. Final pathology demonstrated Gleason 3+4, organ-confined disease involving both lobes, with approximately 10% tumor volume, negative surgical margins, no capsular invasion. At 45 days of follow-up, the patient reported undetectable PSA levels (<0.008 ng/mL), complete urinary continence, and full recovery of erectile function without the use of phosphodiesterase-5 inhibitors.

Beyond this individual urologic procedure, the project was conceived as a multispecialty study involving urology, gynecology, and general surgery. Although only the urologic case has been completed to date, subsequent procedures in gynecology and general surgery are planned under the same ethical, technical, and regulatory framework, highlighting the scalability of structured telementoring beyond a single specialty.

The innovation of this project lies not only in its geographic distance, but also in its concept. To our knowledge, this represents the first clinical telesurgery-related telementoring study performed in Brazil and the first live surgical collaboration between Africa and South America (7). More importantly, it demonstrates that telementoring can be safely implemented within a robust ethical framework that prioritizes patient autonomy, transparency, and institutional accountability. Rather than replacing local expertise or increasing predatory competition between remote experts and local surgeons, this approach promotes bidirectional learning and collaborative refinement of surgical practice, with potential to enhance robotic surgery training worldwide.

In summary, this telementoring experience during robot-assisted radical prostatectomy suggests that structured Telesurgery can be performed safely across Brazil and Africa. However, we still need more data under IRB-approved studies to establish these benefits in clinical settings and other specialties. In this context, although technology is innovative, it comes with clear responsibili-

ties, including strict ethical oversight, reliable connectivity, and transparent patient consent. When these elements are in place, telementoring can improve surgical training, facilitate real-time exchange of expertise, and connect multiple centers simultaneously. This approach may help expand access to specialized knowledge while maintaining patient safety and local surgical responsibility worldwide.

## CONFLICT OF INTEREST

None declared.

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# The Perioperative Revolution in Muscle-Invasive Bladder Cancer - Progress, Caution, and the Latin American Perspective

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## COMMENT

The therapeutic landscape of bladder cancer has evolved at an unprecedented pace over the past decade. From refinements in the management of non-muscle-invasive disease to transformative advances in muscle-invasive bladder cancer (MIBC), the field has shifted from a historically radical surgical paradigm to a biologically driven, multimodal approach (1). Radical cystectomy, once the unquestioned standard, is now integrated into perioperative systemic strategies that include neoadjuvant chemotherapy, perioperative chemo-immunotherapy, perioperative immunotherapy with antibody-drug conjugates, and, in selected cases, trimodal therapy, as endorsed by contemporary NCCN guidelines (2).

The NIAGARA trial marked a pivotal milestone in cisplatin-eligible patients with MIBC. The incorporation of perioperative durvalumab with gemcitabine-cisplatin demonstrated pathological complete response (pT0N0M0) rates of 37.3% and a 2-year overall survival of 82.2%, outcomes not previously achieved with chemotherapy alone in randomized settings. These results led to rapid guideline incorporation of perioperative chemoimmunotherapy and redefined expectations for curative-intent treatment (2, 3).

More recently, at the American Society of Clinical Oncology Genitourinary Cancers conference, the results of EV-304/KEYNOTE-B15 were presented, challenging a two-decade paradigm in muscle-invasive bladder cancer. For years, cisplatin-based neoadjuvant chemotherapy represented the cornerstone of systemic management in eligible patients. In this phase 3 trial, the combination of enfortumab vedotin plus pembrolizumab was evaluated in cisplatin-eligible patients and demonstrated a pathological complete response rate of 55.8%, compared with 32.5%



with standard chemotherapy. Two-year overall survival was 86.9% versus 81.3%, respectively (hazard ratio, 0.65;  $p=0.0029$ ), establishing a new benchmark for perioperative systemic therapy.

In parallel, KEYNOTE-905 (EV-303), recently published in the *New England Journal of Medicine*, extended this therapeutic advance to a historically underserved population: patients ineligible for cisplatin. In a high-risk cohort in which approximately 80% presented with stage III disease, perioperative pembrolizumab plus enfortumab vedotin achieved a pathological complete response rate of 57.1% and an estimated 2-year overall survival of 79.7%, with a hazard ratio for event-free survival of 0.50. These findings challenge the long-standing paradigm in which cisplatin-ineligible patients were directed to upfront cystectomy without systemic intensification.

Together, these studies redefine the perioperative landscape of muscle-invasive bladder cancer and signal a shift from chemotherapy-centered strategies to biologically intensified combinations capable of delivering unprecedented pathological and survival outcomes.

However, these advances warrant critical contextualization, particularly in Latin America. The region reports an incidence of approximately 4–5 cases per 100,000 inhabitants per year and a mortality rate of approximately 2.1 per 100,000, according to GLOBOCAN estimates (4). Despite this epidemiologic burden, Latin American populations remain underrepresented in landmark perioperative trials. In NIAGARA, only 9.6% of patients were enrolled from South America. In KEYNOTE-905, racial representation was similarly limited, with only 1.2% Black participants and 2.4% reporting multiple racial backgrounds (3,5).

This underrepresentation becomes more pronounced in subgroup analyses. In KEYNOTE-905, the magnitude of benefit appeared more pronounced among White participants, whereas confidence intervals for event-free survival (HR 0.29; 95% CI 0.24–1.02) and overall survival (HR 0.76; 95% CI 0.31–1.82) crossed unity in other racial groups. A similar phenomenon was observed in NIAGARA within South American subsets (EFS HR 0.55; 95% CI 0.29–1.03). While these analyses are exploratory and underpowered, they underscore the

need for broader representativeness before universal extrapolation (5).

A second critical consideration is financial toxicity. Bladder cancer is among the malignancies associated with the highest lifetime treatment costs (6). The integration of perioperative immunotherapy and antibody–drug conjugates further expand cumulative systemic exposure and intensifies resource utilization across the continuum of care. In NIAGARA, patients received four cycles of neoadjuvant therapy followed by eight cycles of adjuvant durvalumab. In KEYNOTE-905, three cycles of neoadjuvant pembrolizumab plus enfortumab vedotin were followed by up to one year of combination therapy. These strategies extend treatment duration well beyond conventional cisplatin-based neoadjuvant paradigms, with direct implications for drug acquisition costs, infusion capacity, monitoring requirements, and management of immune-related toxic effects.

The economic impact is particularly relevant in resource-constrained health systems. In Brazil, between 2019 and 2023, only one judicial claim within the public health system involved enfortumab vedotin for metastatic urothelial carcinoma; between 2024 and 2025, approximately 36 such claims were filed, representing a 36-fold increase. This surge reflects litigation-driven access to high-cost therapies and signals mounting fiscal pressure on both public and private payers. Such patterns illustrate how rapid therapeutic innovation, when not accompanied by structured incorporation policies, may shift decision-making from evidence-based allocation to judicial mandates.

Despite therapeutic advances, substantial disparities in access to contemporary oncologic care persist in Brazil, a country marked by pronounced geographic and socioeconomic heterogeneity. Limited availability of high-complexity treatments within the public system contributes to delays in diagnosis and definitive management, reinforcing inequities in oncologic outcomes. In this context, adoption of intensified perioperative regimens should be accompanied by rigorous pharmacoeconomic analyses, formal budget-impact modeling, and region-specific implementation strategies. Ensuring sustainability while preserving equitable

access will be central to translating these advances into meaningful population-level benefit (7, 8).

A lastly notable finding is that the EV-304/KEYNOTE-B15 population included a higher proportion of cT3-T4 tumors than in earlier perioperative chemotherapy trials. Patients with more advanced local disease and a higher risk of occult micrometastases may derive greater absolute benefit from systemic intensification. This difference in case mix provides important context for interpreting the magnitude of benefit without detracting from the trial's internal validity.

The next frontier must be biomarker-driven selection. Identifying molecular predictors of response could maximize oncologic benefit while limiting unnecessary exposure to immune-related and antibody-drug conjugate-associated toxicity, particularly given that adverse events were reported in 100% of patients treated with enfortumab vedotin plus pembrolizumab. Precision strategies may also support bladder-sparing approaches in carefully selected patients. However, longer follow-up remains essential: beyond early pathological and survival signals, durability of benefit, late toxicity, quality of life, and functional outcomes must define the true value of intensified perioperative therapy. Ultimately, success will be measured not only by hazard ratios, but by durable, patient-centered benefit.

The trajectory of bladder cancer management is undeniably optimistic. The magnitude of clinical gain is unquestionable. The field is advancing at unprecedented speed and with unprecedented biological sophistication. Yet progress must be accompanied by equity.

Innovation must not only change guidelines; it must change outcomes across populations..

## CONFLICT OF INTEREST

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# Repositioning the Digital Rectal Examination in the Era of Risk-Adapted Prostate Cancer Diagnostics: Right Tool to the Right Patient at the Right Time

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## COMMENT

Digital rectal examination (DRE) has long been a fundamental component of urological practice. Its attributes: low cost, safety, immediacy, and the ability to detect both prostate abnormalities and extra-prostatic findings, have historically justified its widespread use. However, the role of DRE in prostate cancer (PCa) detection has been substantially redefined, reflecting a broader shift toward precision-based, risk-adapted diagnostic pathways.

In the pre-multiparametric Magnetic Resonance Imaging (mpMRI) era, DRE played a more prominent role in the early detection of PCa. Approximately one-fifth of prostate cancers were identified solely based on abnormal DRE findings, and these tumors were often associated with higher Gleason grades and larger tumor volumes (1, 2). This observation suggested that DRE may have been inherently biased toward detecting clinically significant and biologically aggressive disease. Nonetheless, even in that context, its sensitivity remained limited, and its diagnostic contribution was highly dependent on patient characteristics and examiner experience.

The contemporary diagnostic landscape has evolved dramatically. Prostate-specific antigen (PSA) testing, combined with mpMRI and targeted biopsy strategies, now constitutes the backbone of early detection. These modalities offer superior sensitivity, improved risk stratification, and a more favorable balance between detection of clinically significant prostate cancer (csPCa) and avoidance of overdiagnosis. Consequently, DRE has progressively lost its role as a primary screening tool, especially in population screening.

This shift is now formally reflected in the 2026 updates of both the American Urological Association (AUA) and the European Association of Urology (EAU) guidelines, which no longer recommend DRE for routine screening in asymptomatic men. Instead, screening strategies are anchored in PSA-based risk assessment, with mpMRI subsequently used to guide biopsy decisions. This transition is supported by robust evidence demonstrating the

limited sensitivity and reproducibility of DRE, as well as its contribution to false-positive referrals and unnecessary biopsies (3, 4).

A key limitation of DRE is its inherently subjective, operator-dependent nature. Interobserver variability is substantial, particularly among less experienced clinicians, leading to inconsistent diagnostic performance. Moreover, DRE lacks the ability to reliably detect anterior, small-volume, or early-stage tumors, which are often better visualized with mpMRI. These shortcomings directly impact screening efficiency and contribute to both over- and under-diagnosis (5, 6).

From a patient-centered perspective, DRE also represents a recognized barrier to screening participation. Reluctance to undergo the examination has been consistently reported and may reduce adherence to early detection programs. Equally important, a "normal" DRE may provide false reassurance, potentially delaying further investigation in men who would otherwise benefit from PSA testing and imaging (7).

Despite these limitations, it would be a misinterpretation to consider DRE obsolete. Rather, its role has become more selective and context-dependent. When used judiciously, DRE continues to provide clinically meaningful information that complements modern diagnostic tools. One such role is in estimating prostate volume (8), which enables the ready calculation of PSA density (PSAD). PSAD has emerged as a critical parameter in risk stratification to determine which patients need further evaluation with mpMRI. In this context, DRE, although less precise than imaging, can offer a rapid, bedside approximation of prostate volume that informs clinical decision-making, especially in resource-constrained environments. Also, in men with equivocal mpMRI findings, the PSAD helps to identify patients with a higher chance of benefit from a prostate biopsy.

Furthermore, DRE retains value in identifying a small but clinically relevant subset of prostate cancers that may be missed by PSA- and MRI-driven pathways, informing biopsy strategies in selected cases, especially when physical findings and imaging results do not align. These cases, although uncommon, are often characterized by higher-grade disease and larger tumor burden.

Such observations reinforce the importance of maintaining clinical judgment alongside algorithm-based approaches (9).

From a diagnostic accuracy standpoint, DRE is best understood as a test with low sensitivity but relatively high specificity when findings are clearly abnormal. A distinctly suspicious DRE, such as nodularity, induration, or asymmetry, remains a strong indication for further investigation, regardless of PSA levels or imaging results. This characteristic supports its continued use in targeted clinical scenarios rather than population-wide screening.

DRE also maintains a role in clinical staging. Although mpMRI has improved local staging accuracy, DRE can still help identify extracapsular extension or locally advanced disease ( $\geq T3$ ), particularly when imaging findings are equivocal or discordant with clinical suspicion.

Importantly, the relevance of DRE is amplified in settings where access to high-quality mpMRI is limited. Global disparities in imaging availability and expertise mean that, in many regions, DRE remains a pragmatic and valuable component of the diagnostic pathway. In such contexts, its integration with PSA testing may still represent a reasonable and necessary approach.

While the repositioning of DRE reflects progress in prostate cancer diagnostics, it also highlights emerging challenges associated with increasing reliance on imaging. mpMRI, although highly valuable, is not without limitations. In addition to cost, variability in image acquisition, interpretation, and reporting continues to affect diagnostic performance and reproducibility. Interobserver variability among radiologists, differences in adherence to PI-RADS standards, and inconsistencies in training and quality assurance all contribute to heterogeneity in clinical outcomes (10).

Addressing these challenges requires robust standardization efforts. Structured training programs, certification processes, and quality control frameworks are essential to ensuring mpMRI delivers consistent, reliable results across institutions. Consensus initiatives, such as those led by the European Society of Urogenital Radiology, provide important guidance, but real-world implementa-

tion remains uneven (11). Without such standardization, the benefits of advanced imaging may be undermined, potentially reintroducing diagnostic uncertainty.

In this evolving landscape, the role of DRE should be understood within a broader framework of multimodal, patient-centered care. Rather than being abandoned, it should be selectively integrated into clinical pathways where it adds incremental value. This approach aligns with the fundamental principle of precision medicine: applying the right tool to the right patient at the right time.

In conclusion, DRE in 2026 is no longer a front-line screening modality but a complementary clinical instrument with specific indications. Its strengths lie in its accessibility, specificity when abnormal, and utility in selected diagnostic and staging contexts. As prostate cancer detection continues to evolve, the challenge is not to replace traditional tools outright but to refine their use within increasingly sophisticated diagnostic algorithms. The future of prostate cancer care will depend on the thoughtful integration of clinical examination, biomarkers, and advanced imaging to optimize outcomes while minimizing harm.

## CONFLICT OF INTEREST

None declared.

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# Editorial Comment: Analysis of the Current Surgical Anatomical Knowledge of Radical Prostatectomy: An Updated Review

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## COMMENT

Prostatic anatomy is one of the most important points in prostate cancer surgical treatment. Recently the advent of robotic surgery changes the radical prostatectomy, resulting in better outcomes and faster recovery (1-4). The objective in this paper of Mandel and colleagues (5) is to survey the existing peer-reviewed literature encompassing prostate anatomy and to consolidate its teachings to the surgeon trainee. The authors summarizes the key findings into a three-dimensional model, bringing the anatomy to life to help learners visualize the complexity of prostate anatomy. The paper conclude that the prostate is a dense organ with muscular and glandular features. Located within the true pelvis, the prostate is surrounded by several fascial planes that contain the neurovascular structures. Lumbosacral parasympathetic nerve root fibers of the pelvic plexus run posterolateral to the prostate gland in a neural hammock configuration. This anatomic understanding informs the NS technique. Finally, the anterior ligamentous structures play a role in continence and possibly erectile function too. We congratulate the authors for the interesting paper.

## CONFLICT OF INTEREST

None declared.

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# Transvesical Clipless Robot-Assisted Radical Prostatectomy Using a Multiport Platform: Technical Feasibility and Early Outcomes

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## ABSTRACT

**Introduction:** Robot-assisted radical prostatectomy (RARP) continues to evolve with surgical approaches aimed at preserving continence-related anatomy and optimizing postoperative recovery (1). Transvesical RARP has gained increasing interest, particularly with the advent of single-port platforms (2, 3). Building on our prior experience with clipless techniques and functional outcome optimization (4), we evaluated a multiport transvesical approach.

**Objective:** To describe, step-by-step, a clipless transvesical RARP technique and to report its feasibility and early functional and oncologic outcomes.

**Materials and Methods:** An intravesical, line-of-sight technique was employed, with abdominal trocars positioned similarly to conventional transperitoneal RARP. The surgical sequence included: posterior release; longitudinal cystotomy with suspension sutures; semicircumferential bladder neck incision; bilateral clipless lateral dissection (blunt and sharp); anterior and apical release with dorsal venous complex control; urethral transection; urethrovesical anastomosis using two 3-0 barbed sutures; and single-layer cystotomy closure. Three consecutive patients with localized prostate cancer and moderate prostate volumes were included.

**Results:** All procedures were completed as planned. Perioperative morbidity was low; one Clavien–Dindo grade II complication was managed conservatively. Early continence was observed in all patients, including at the first postoperative evaluation (45 days). One patient (Case 3) presented with a focal apical positive surgical margin on final pathology; prostate-specific antigen levels were undetectable in all cases during early follow-up. The approach was technically feasible and familiar to surgeons experienced in anterior RARP. Larger prostate volume may limit intravesical working space and apical visualization.

**Conclusions:** We describe a reproducible clipless transvesical RARP performed using a multiport platform, addressing a body of literature predominantly focused on single-port systems. The technique demonstrated encouraging early functional outcomes in carefully selected patients (5); however, larger prostate volumes and longer follow-up are required to further define its oncologic and functional durability. This video complements our previous publication on alternative RARP approaches supporting anterior-preserving strategies (6).

## CONFLICT OF INTEREST

None declared.

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# Robot-Assisted Sigmoid Colon Conduit for Urinary Diversion: Avoiding Bowel Anastomosis in a Patient with Prior Loop Colostomy and Pelvic Radiation

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## ABSTRACT

**Purpose:** Late radiation-induced genitourinary and gastrointestinal complications after multimodal treatment for pelvic malignancies frequently require complex reconstructive surgery, often necessitating both urinary and fecal diversion (1). In this setting, a colonic segment may provide an effective option for urinary diversion while avoiding bowel anastomosis (2, 3). Minimally invasive robotic approaches have increasingly expanded the feasibility of these complex reconstructions and may reduce morbidity, particularly in frail or previously irradiated patients (4–7). We describe a single-stage robot-assisted sigmoid colon conduit urinary diversion in a patient with a pre-existing loop colostomy.

**Materials and Methods:** A 46-year-old woman with prior pelvic chemoradiation developed a rectovaginal fistula requiring loop colostomy, followed by bilateral distal ureteral strictures, radiation cystitis, recurrent pyelonephritis, and a large parastomal hernia. After failed conservative management and preoperative nephrostomy placement, a single-stage robot-assisted procedure was performed. The operation included adhesiolysis, parastomal hernia repair, conversion of the loop to a terminal colostomy, and construction of a sigmoid colon urinary conduit. Ureterointestinal anastomoses were completed intracorporeally under indocyanine green fluorescence guidance.

**Results:** The procedure was completed robotically without intraoperative complications. Total operative time was 95 minutes, with an estimated blood loss of 100 mL. Oral intake resumed on postoperative day 1, and the patient was discharged on day 3. At 6-month follow-up, renal function was preserved, with no recurrent infections or evidence of ureteral obstruction.

**Conclusion:** Robot-assisted sigmoid colon conduit is a safe and reproducible option for urinary diversion in selected patients requiring concomitant bowel diversion, avoiding bowel anastomosis and reducing reconstructive morbidity.



## CONFLICT OF INTEREST

None declared.

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# Single Port Robotic Extraperitoneal Distal Ureterectomy and Ureteral Reimplantation via Lower Anterior Approach

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## ABSTRACT

**Purpose:** Single Port (SP) Robotic Extraperitoneal approach enhances maneuverability in the narrow extraperitoneal space while preserving peritoneal integrity (1, 2). First reports show reduced postoperative pain, fewer gastrointestinal complications and shorter hospital stay compared to multiport or open techniques (3-5). Recent experiences with robotic ureteral reconstruction have further supported the feasibility of advanced reconstructive procedures in selected patients (6-8) but literature on SP platform remains limited (9, 10), therefore we present this innovative technique.

**Materials and Methods:** We report the case of a 44-year-old female (BMI 29.1 kg/m<sup>2</sup>), with medical history of fibromyalgia, who presented with right-sided back pain and nausea. CT-urogram showed severe right hydroureteronephrosis with a distal ureteral stricture and diffuse ureteral thickening, without a clear obstructing lesion. Diagnostic ureteroscopy revealed luminal narrowing due to wall thickening, without papillary masses. Biopsies and urine cytology were negative for urothelial carcinoma. A double-J stent was placed, and SP robotic distal ureterectomy with ureteral reimplantation was scheduled.

**Results:** Low Anterior Access (LAA) was obtained through a 4-cm incision at the McBurney point. The retroperitoneal space was bluntly developed to identify the psoas muscle as anatomical landmark; the ureter was dissected caudally and resected at the level of the stricture. The bladder was then reached for cystotomy and ureteral reimplantation. Operative time was 160 minutes. No complications occurred and the patient was discharged on postoperative day 1. Final pathology revealed endometriosis. The ureteral stent was removed after 4 weeks; at 3-month follow-up the patient was asymptomatic, renal function was normal, and CT scan showed no right hydroureteronephrosis.

**Conclusion:** Robotic SP extraperitoneal approach appears safe, feasible, and promising for ureteral reconstruction, combining retroperitoneal access with SP system dexterity and potentially reducing postoperative morbidity and hospital stay.

## CONFLICT OF INTEREST

None declared.

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