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# The evolution of minimally invasive urologic surgery: innovations, challenges, and opportunities

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# The evolution of minimally invasive urologic surgery: innovations, challenges, and opportunities

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# Editorial: The evolution of minimally invasive urologic surgery: innovations, challenges, and opportunities

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**robotic surgery, urology, endourology, suction, artificial intelligence, chatGPT, kidney calculi, ureteroscopy**

Editorial on the Research Topic
The evolution of minimally invasive urologic surgery: innovations, challenges, and opportunities

Technological advances have had a great impact on the evolution of medicine and contributed to improvements in surgical technique. In this regard, the field of urology is no exception. Over the past decade, several technological innovations have led to new challenges and opportunities both in terms of diagnosing and treating benign and malignant urological conditions.

Large language models (LLMs) represent a rapidly expanding field, with many tested applications in the urological setting already. Talyshinskii et al. provide an insightful summary of one of the most widely used LLMs, ChatGPT. The authors emphasize its role in drafting clinical documents and notes, in facilitating communication with patients, while medical students and clinicians can benefit from an educational and research perspective Talyshinskii et al. of course, attention is needed to avoid use of misleading or even fake references, plagiarism, scientific fraud, issues with patients' data privacy and isolation between patient and physician Talyshinskii et al.

Social media (SoMe) is a means of expression, while it also represents a way to communicate concerns, experiences and perceptions, especially regarding several health issues. Juliebø-Jones et al. evaluated one of the most popular SoMe platforms, TikTok, regarding kidney stone surgery. The authors included the 100 most recent video posts and found that that the majority of posts were about recovery, pain and stents, while 51% showed a negative tone Juliebø-Jones et al.

Prostate cancer is one of the most common cancers in men, therefore it is reasonable that a lot of research focuses on this field. Haack et al. designed a comparative study to assess the ability of urologists to localize suspicious cancer lesions on multi-parametric (mp) magnetic resonance imaging (MRI), when having only mpMRI images, mpMRI images with radiological reports and mpMRI images with 3D printed model; they reported that radiology reports are still needed, while 3D models seem to be efficient, especially in younger residents Haack et al. Radical prostatectomy still represents a main form of management of localized disease and while it offers high survival rates, two of its associated sequelae, incontinence and erectile dysfunction, hinder its popularity. Leitsmann et al. assessed the impact of mpMRI-targeted biopsy on functional outcomes in patients undergoing robot-assisted radical prostatectomy Leitsmann et al. They reported that mpMRI-targeted biopsy compared to standard biopsy, led to fewer positive surgical margins, lower risk of erectile dysfunction at 1-year, lower rate of postoperative tumor upgrading and, in cases of nerve-sparing approach, fewer secondary nerve resection Leitsmann et al. Katsimperis et al. provided a concise summary with their narrative review on the approaches used to preserve continence after robot-assisted radical prostatectomy; bladder neck preservation, neurovascular bundle preservation, preservation of apical intraprostatic urethra, Retzius-sparing and hood techniques, anterior and/or posterior reconstructive stiches and newer techniques such as complete urethral preservation (CUP) and single port transvesical robotic prostatectomy Katsimperis et al. A critical step of radical prostatectomy, where a large amount of blood loss can occur, is deep vascular complex ligation. Chen et al. described a simulation platform for training of novice surgeons and residents on this step, showing good construct, face and content validity, while maintaining low costs Chen et al.

Partial nephrectomy is the treatment of choice in cases of T1 renal tumors and in selected cases in larger neoplasms, in order to maximize renal function preservation. Conventional technique, either performed via an open or minimally invasive approach, consists of clamping the renal arterial supply (warm ischemia) and subsequently excising the tumor and suturing the tissue defect, usually in two layers (inner and outer renorrhaphy). Several techniques have been described, with the sliding technique using clips to support the tissues and barbed sutures being the most commonly used one. Nguyen et al. performed an *in vivo* study to evaluate the use of off-clamp, microwave scissors-based and sutureless partial nephrectomy technique, compared to on-clamp conventional approach; they reported that the former one exhibited reduced surgical time and less normal nephron loss, while blood loss and urinoma formation were not significantly different Nguyen et al. Tumor characteristics play a major role in surgical complexity, while it also drives the complication profile in every patient. Gu et al. summarized existing evidence in their systematic review and meta-analysis regarding impact of completely endophytic renal masses Gu et al. They calculated based on six studies involving 2,126 patients that completely endophytic tumors compared to non-endophytic exhibit significantly higher rates of major complications, longer warm ischemia time, greater drop in renal function and lower rates of trifecta achievement Gu et al.

Urolithiasis in the upper urinary tract is a very common benign clinical condition affecting nearly 10% of population. Several advances have been performed in this field; Juliebø-Jones et al. provide an overview of controversies in endourology by evaluating the role of single use ureteroscopes and optimal use of laser for lithotripsy, comparing basketing vs. dusting techniques, assessing the impact of ureteral access sheath and the necessity of safety guidewires and finally providing a balanced conclusion for readers Juliebø-Jones et al. Achieving stone-free status (SFS) with minimal complications and reduced operative times are the main primary outcomes in endourological treatment of urolithiasis, thus also in ureteroscopy. During the last years we have seen an uprise in the use of suction via access sheaths, ureteroscopes or nephroscopes; use of suction achieves two main goals: minimizes intrarenal pressure and aids in removal of small fragments, thus avoiding repetitive extraction of fragments with baskets or forceps. Reduced intrarenal pressure minimizes complications by avoiding pyelovenous and pyelolymphatic backflow of urine and microorganisms. Zhang et al. evaluated a suctioning ureteral access sheath for removal of upper tract stones under local anaesthesia Zhang et al. In their study, authors described a feasible operating under local anaesthesia for a mean stone size of more than 2 cm and final SFS equal to 85.1% Zhang et al., thus showing clinical effectiveness of this technique. Endourological techniques have been applied also in cases of upper urinary tract urothelial carcinoma. Chen et al. assessed the clinical efficacy of an intelligent-pressure controlled ureteroscope with Thulium laser fiber (TFL) in treating patients with isolated upper urinary tract urothelial carcinoma Chen et al. This study focused on six patients, whose surgeries were smooth with no intraoperative complication, thus indicating that this technique might be feasible for this purpose.

Stress urinary incontinence in men can be observed mainly after treatments for prostate cancer, i.e., radical prostatectomy or radiation therapy and can lead to serious compromise of quality of life. In moderate-severe stress incontinence, surgical management is indicated, with male slings being one of the available choices. Adjustable transobturator male system (ATOMS$^{TM}$, A.M.I., Austria) is a treatment option for which a growing body of evidence exists. Juliebø-Jones et al. in their narrative review provide an updated summary on relevant evidence, showing that ATOMS may offer effectiveness similar to artificial urinary sphincter, while it provides the opportunity to replace certain parts of the device without replacing the device itself Juliebø-Jones et al.

Finally, several interesting case reports and case series are presented in this special issue. Yao et al. described their experience with an extrarenal renal cell carcinoma (RCC) in the adrenal region; a 48-year old lady and an isolated adrenal tumor had surgery, which revealed a clear-cell carcinoma, reminding us that RCC belongs to the differential diagnosis of adrenal masses Yao et al. Staying on the same subject of adrenal masses, Shi et al. described a solitary fibrous tumor of the adrenal gland, emphasizing the importance of this differential diagnosis in patients with low-density and uneven CT enhancement features Shi et al. Huang et al. published their technique of minimally-invasive single-port laparoscopic repair of vesicovaginal fistula through the vagina of a 53-year old female patient; this description represents the first "zero incision" technique for single-port laparoscopy in patients with high-position vesico-vaginal fistula and is accompanied by educational and explanatory figures Huang et al. Finally, Wang et al. presented their experience on paraganglioma of the urinary bladder Wang et al. They described 29 patients with a variety of clinical symptoms (hypertension, palpitations and micturition syncope) with some of them showing also increased 24-hour catecholamines and norepinephrine or positive metaiodobenzylguanidine or octreotide scans Wang et al. They also provide insights regarding treatment options and prognosis Wang et al.

Minimally invasive surgical techniques in endourology have been revolutionized by the advent of thulium fiber laser, low cost of treatment, use of suction for fragment removal and focus on patient reported outcome measures (1–4). Similarly, robotic surgery has pioneered new techniques in prostatectomy and partial nephrectomy Leitsmann et al., Katsimperis et al., Chen et al., Nguyen et al., Gu et al. These advances give patients more treatment choices and possibly better outcomes, contributing to personalized patient care. With the advent of artificial intelligence (AI), it is only a matter of time before AI influences all aspects of urological care too (5).

## Author contributions

LT: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. PJ-J: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. BS: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Flexible ureteroscopic lithotripsy with a suctioning ureteral access sheath for removing upper urinary calculi under local anesthesia

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**Objectives:** We aimed to probe the safety and effectiveness of flexible ureteroscopic lithotripsy (FURL) with a suctioning ureteral access sheath (S-UAS) for removing upper urinary calculi under local anesthesia (LA).

**Materials and methods:** The clinical data of 56 patients with upper urinary calculi treated by FURL with an S-UAS under LA during the period between September 2019 and November 2022 were analyzed retrospectively. For LA, intramuscular pethidine (1.0–2.0 mg/kg) and phenergan (25 mg) were administered 30 min prior to surgery, and oxybuprocaine hydrochloride gel was administered through the urethra at the start of the surgery. The S-UAS and flexible ureteroscope were used for FURL. Demographic characteristics, stone-related parameters, and clinical outcomes were analyzed.

**Result:** A total of 66 procedures were performed successfully on 46 patients (Group A), who underwent unilateral surgeries, and on 10 patients (Group B) who underwent same-session bilateral surgeries. All 56 patients were operated upon without altering the anesthesia strategy, and none required additional analgesia. The mean stone sizes of the Group A and Group B patients were 20.24 ± 5.45 mm and 29.40 ± 3.89 mm, respectively. The mean operative times of the two groups were 53.04 ± 13.35 min and 90.00 ± 15.81 min, respectively. In Group A, the stone-free rates (SFRs) were 76.1% (35/46) and 85.1% (40/46) at postoperative day 1 and day 30, respectively. In Group B, the SFRs were 80.0% (16/20) and 85.0% (17/20), respectively. Four (8.7%) patients in Group A suffered complications such as fever, stent pain, urosepsis, and steinstrasse. In Group B, one (10%) patient suffered from fever.

**Conclusion:** FURL, combined with an S-UAS under LA, is a feasible option and provides satisfactory clinical outcomes for appropriately selected patients.

KEYWORDS
local anesthesia, ureteral access sheath, flexible ureteroscopic lithotripsy, urinary calculi, stone-free rate

## 1. Introduction

Urinary calculus is a common worldwide urological condition, and the prevalence rates vary among different regions, ranging from 1% to 13% (1). Currently, the major minimally invasive endoscopic surgical methods for urolithiasis are flexible ureteroscopic lithotripsy (FURL) and percutaneous nephrolithotomy (PCNL). FURL is recommended as a first-line

Abbreviations
FURL, flexible ureteroscopic lithotripsy; S-UAS, suctioning ureteral access sheath; LA, local anesthesia; FURS, flexible ureteroscope; VAS, visual analog scale; SFR, stone-free rates; CR, complication rate; UAS, ureteral access sheath.

option for renal calculi smaller than 20 mm (2). However, with the advent of a miniaturized flexible ureteroscope (FURS) and innovative technologies, it can also be applied for removing high-burden renal stones beyond 20 mm with good outcomes (3, 4).

FURL is regularly performed under general or regional anesthesia (5) but rarely under local anesthesia (LA) predominantly because of the pain caused by surgical procedures or ureteral damage caused by painful movement (6). However, for patients with absolute or relative contraindications to general or regional anesthesia, LA is a selective method. Only a few studies have reported the successful application of ureteroscopic lithotripsy under LA (6, 7), and all procedures reported in these studies were performed on the unilateral side. For bilateral upper urinary stones, simultaneous bilateral FURL has been reported as a favorable less-invasive alternative (8). In this study, we first present our experiences with FURL, combined with a suctioning ureteral access sheath (S-UAS) under LA, for removing unilateral or bilateral upper urinary calculi.

## 2. Materials and methods

### 2.1. Patients

The medical records of patients with upper urinary calculi who underwent FURL with an S-UAS under LA at the First Affiliated Hospital of Gannan Medical University during the period between September 2019 and November 2022 were retrospectively reviewed, and these patients were included in the study. The exclusion criteria were as follows: (a) lower urinary tract calculi; (b) middle or distal ureteral stones; (c) preoperative ureteral structure or calculous pyonephrosis; (d) combined with upper urinary carcinoma. For two patients, the method of treatment was changed to PCNL under LA because of a narrow ureter. Finally, a total of 56 patients were included in our study. All patients were diagnosed by preoperative urinary non-contrast computed tomography (NCCT). For patients with normal renal function, intravenous urography (IVU) was recommended. The stone size was defined as the largest diameter measured by NCCT, and for multiple stones or bilateral upper urinary stones, the size was the sum of the largest diameter of each stone. Urinalysis and urine culture were routinely examined and the stones were treated with appropriate antibiotics preoperatively. Preoperative demographic characteristics such as gender, age, American Society of Anesthesiologists (ASA) score, body mass index (BMI), surgical side, ipsilateral surgical history, midstream urine culture result, stone parameters, hydronephrosis, and preoperative ureteral stent placement were obtained according to medical records.

Ethical approval for the study protocol was obtained from the Ethics Committee of the First Affiliated Hospital of Gannan Medical University (proof number: 2023032706), and the study was performed in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from all participants.

### 2.2. Surgical techniques

All patients were explicated with all alternative therapeutic strategies and anesthetic methods. Written informed consent was granted before the operation. For patients who selected FURL under LA, intramuscular pethidine (1.0–2.0 mg/kg) and phenergan (25 mg) were administered 30 min prior to surgery. After the patients were placed in the lithotomy position, the oxybuprocaine hydrochloride gel (10 ml gel containing 30 mg oxybuprocaine) was injected into the urethra for mucosal anesthesia and lubrication. A ureteroscopy inspection was performed by using a semirigid 6/7.5 Fr ureteroscope, and then a guide wire was inserted in the ureter. If a proximal ureter stone was detected, the stone was pushed retrogradely to the renal pelvis. Under the guidance of the wire, an 11/13 F or 12/14 F S-UAS (Shenzhen Kang Yi Bo Technology Development Co., Ltd., Shenzhen, China), combined with a vacuum aspiration device, was inserted depending on the condition of the ureter (**Figure 1**), and the S-UAS was placed in the pyeloureteral junction. Then, a single-use FURS (Guangzhou Red Pine Medical Instrument Co., Ltd., Guangzhou, China) was used for inspection. The FURS had a wide deflecting angle that ranged upward at 275° and downward at 275°, the outer diameter was 8.7 F, and the working channel inner diameter was 3.6 F (**Figure 2**). After a comprehensive inspection of renal calices and stones, a 200 -µm laser fiber was inserted through the FURS, and a holmium:yttrium aluminum garnet (Ho:YAG) laser was applied to pulverize calculi by interchangeably setting different parameters. A low-energy setting (0.2–0.6 J) and a high range of frequency

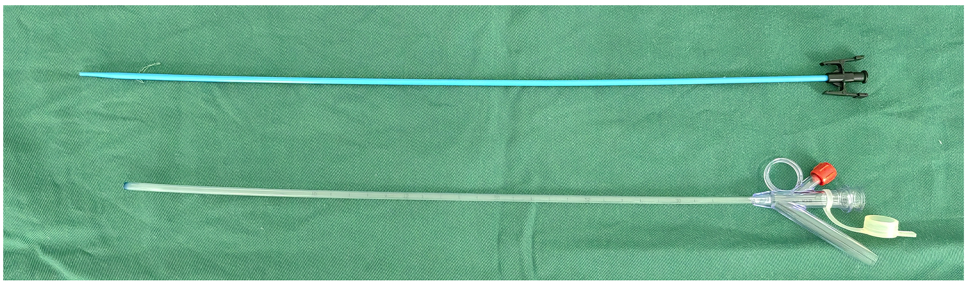

FIGURE 1
The suctioning ureteral access sheath.

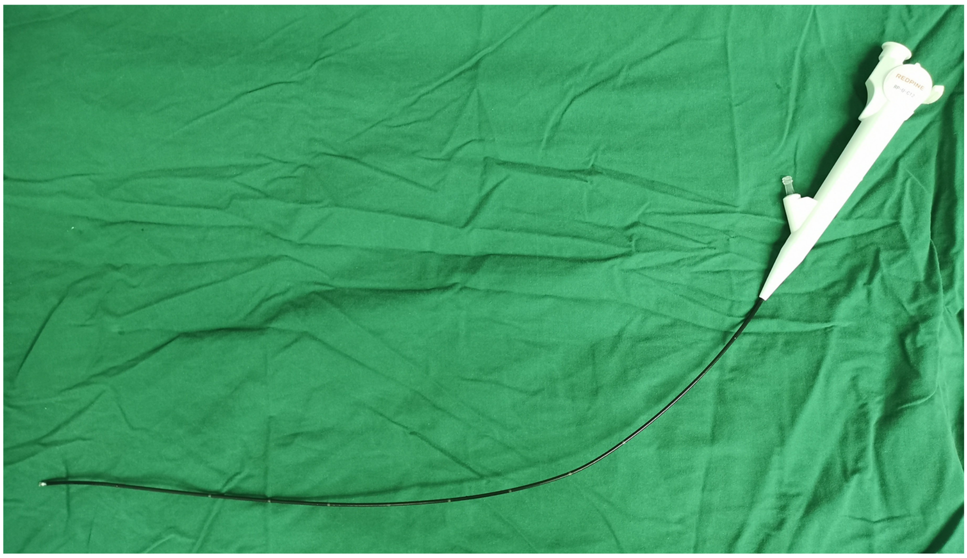

FIGURE 2
A single use flexible ureteroscope.

(20–30 Hz) was set for dusting, the fragmentation mode using higher energy ranged between 0.6 and 1.2 J, and the lower range of frequency was 5–20 Hz. A nitinol stone basket was applied to retrieve or relocate fragments when necessary. During the surgical procedure, the perfusion flow was set to 60–100 ml/min and the suctioning parameter of the vacuum device with negative pressure was set at −20 to −40 kPa. A part of the debris and dust was suctioned out through an S-UAS immediately. For some gravel particles, stone baskets or forceps were applied if necessary. After all renal stones were pulverized to the desired fragments and removed satisfactorily, a 5 F double-J stent was inserted routinely. Patients with bilateral upper urinary calculi underwent surgery in the same session, and the same surgeon operated on one side after completing another side. Figure 3 shows a patient who underwent

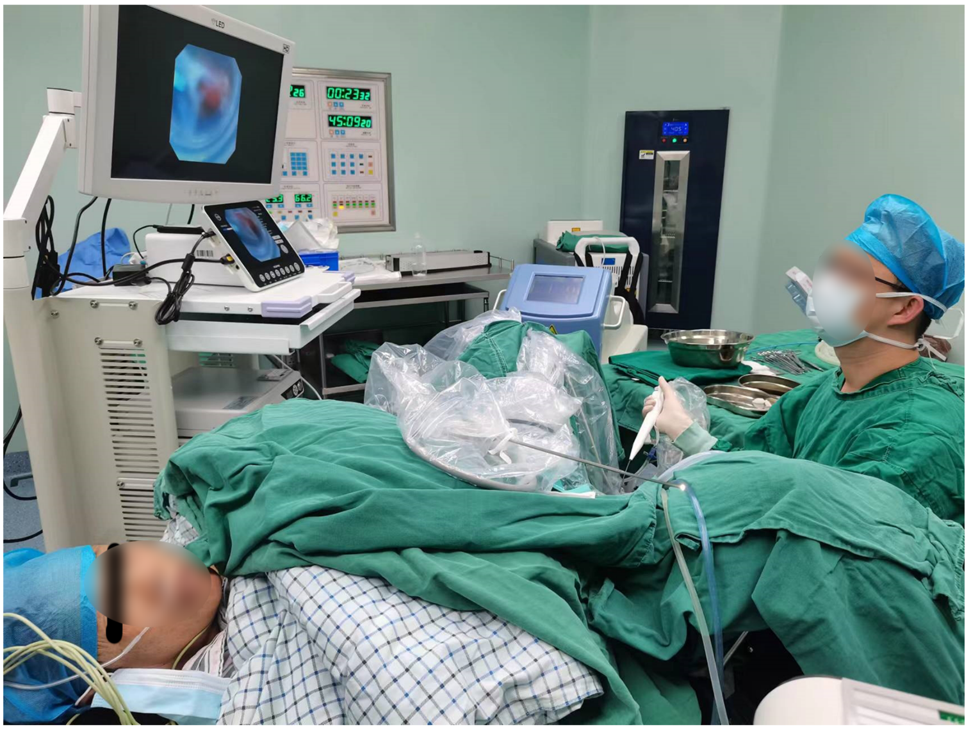

FIGURE 3
Patient was performed flexible ureteroscopic lithotripsy under local anesthesia.

FURL under LA. The procedures were performed by two expert surgeons, with each of them performing more than 250 FURL procedures per year.

The operative time, hemoglobin loss, visual analog scale (VAS) score, stone-free rate (SFR), and complication rate (CR) were analyzed. Kidney-ureter-bladder (KUB) graphy and/or urinary NCCT were performed at 1 day and 1 month after surgery, and a stone-free status was defined as "no remaining stone." For patients who underwent bilateral FURL, the operation time was defined as "the total surgical time of two sides." The double-J stent was routinely removed a month following surgery. For patients with ureteral stenosis or residual stones, a second procedure was performed 1 month after surgery.

## 3. Result

A total of 66 flexible ureteroscopic procedures were performed on 56 patients with upper urinary calculi, who included 46 patients (Group A) who underwent unilateral surgeries and 10 patients (Group B) who underwent same-session bilateral surgeries. In Group A, 22 patients underwent surgery on the left side and 24 patients on the right side. All procedures were successfully performed under local anesthesia without shifting to general or regional anesthesia, and none of them required additional analgesia during the performance of the surgeries.

Females constituted the majority of the two groupings. A total of nine patients in Group A and two patients in Group B were evaluated as high anesthesia risk (ASA III-V) patients. Comorbidities of the patients were hypertension, diabetes mellitus, coronary atherosclerotic heart disease, chronic obstructive pulmonary disease, renal insufficiency, and cerebral infarction. Two patients in Group A and one patient in Group B took daily aspirin, but there was no need to stop aspirin before FURL. The mean stone size was 20.24 ± 5.45 mm in Group A patients and 29.40 ± 3.89 mm in Group B patients. Preoperative ureteral stents on the surgical side were seen in 36 patients in Group A and 8 patients in Group B. The demographic characteristics and stone-related parameters are given in Table 1.

A total of 44 patients were prestented, including four patients with high general anesthesia risk who underwent regular replacement of a double-J stent because of calculous hydronephrosis, three patients who received a stent for sepsis; the remaining 37 patients were prestented for ureter dilation. In Group A, all prestented patients and two patients without preoperative stent were inserted with 12/14 F S-UAS, and the remaining patients were inserted with 11/13 F S-UAS. All 10 patients in Group B were treated with 12/14 F S-UAS. The mean operative time was 53.04 ± 13.35 min in Group A patients and 90.00 ± 15.81 min in Group B patients, and the mean hemoglobin loss was −4.78 ± 9.22 g/L and −4.10 ± 9.09 g/L, respectively. The intraoperative mean visual analog scale scores and scores at 6 and 24 h after surgery in Group A patients were 3.83 ± 0.53, 2.23 ± 0.64, and 1.22 ± 0.79, respectively. In Group B patients, the intraoperative mean visual analog scale scores and scores at 6 and 24 h after surgery were 3.10 ± 0.74, 2.20 ± 0.63, and 1.20 ± 0.63, respectively. The mean postoperative hospitalization time was 3.43 ± 1.70 days and 3.20 ± 1.40 days, and 35.7% (20/56) of patients had a postoperative hospitalization time of more than 3 days, predominantly because of the intrinsic features of our medical strategy and insurance policy and the tertiary hospital referral system and not because of surgery.

**TABLE 1** Demographic characteristics and baseline data of unilateral and bilateral groups.

| | Unilateral group | Bilateral group |
|---|---|---|
| Total number (*n*) | 46 | 10 |
| Age (years), mean ± SD | 54.74 ± 12.50 | 52.80 ± 13.44 |
| **Gender, *n* (%)** | | |
| Male | 5/46 (10.9%) | — |
| Female | 41/46 (89.1%) | 10/10 (100%) |
| BMI (kg/m$^2$), mean ± SD | 23.53 ± 3.48 | 24.07 ± 2.02 |
| **ASA score, *n* (%)** | | |
| I | 6/46 (13.0%) | 2/10 (20.0%) |
| II | 31/46 (67.4%) | 6/10 (60.0%) |
| III | 9/46 (19.6%) | 2/10 (20.0%) |
| **Comorbidities, *n* (%)** | | |
| Hypertension | 7/46 (15.2%) | 3/10 (30.0%) |
| Diabetes mellitus | 10/46 (21.7%) | 2/10 (20.0%) |
| Coronary atherosclerotic heart disease | 2/46 (4.3%) | 1/10 (10.0%) |
| Chronic obstructive pulmonary disease | 3/46 (6.5%) | 1/10 (10.0%) |
| Renal insufficiency | 11/46 (23.9%) | 4/10 (40.0%) |
| Cerebral infarction | 1/46 (2.2%) | — |
| **Operative side, *n* (%)** | | |
| Left | 22/46 (47.8%) | |
| Right | 24/46 (52.2%) | |
| Bilateral | | 10/10 (100%) |
| **History of surgery on the surgical ipsilateral side, *n* (%)** | | |
| ESWL | 2/46 (4.3%) | — |
| RIRS | 5/46 (10.9%) | 3/20 (15.0%) |
| PCNL | 2/46 (4.3%) | 4/20 (20.0%) |
| Laparoscopic surgery | 2/46 (4.3%) | 1/20 (5.0%) |
| **Midstream urine culture, *n* (%)** | | |
| Positive | 17/46 (37.0%) | 3/10 (30.0%) |
| Negative | 29/46 (63.0%) | 7/10 (70.0%) |
| Stone size (mm), mean ± SD | 20.24 ± 5.45 | 29.40 ± 3.89 |
| Stone hardness (HU), mean ± SD | 835.46 ± 318.28 | 819.6 ± 220.09 |
| **Stone location of the surgical ipsilateral side, *n* (%)** | | |
| Pelvis | 10/46 (21.7%) | 6/20 (30.0%) |
| Upper calyx | 3/46 (6.5%) | 1/20 (5.0%) |
| Middle calyx | 4/46 (8.7%) | 3/20 (15.0%) |
| Lower calyx | 7/46 (15.2%) | 2/20 (10.0%) |
| Proximal ureter | 8/46 (17.4%) | 2/20 (10.0%) |
| Multiple location | 14/46 (30.4%) | 6/20 (30.0%) |
| **Hydronephrosis at the surgical ipsilateral side, *n* (%)** | | |
| No | 11/46 (23.9%) | 5/20 (25.0%) |
| Mild | 20/46 (43.5%) | 5/20 (25.0%) |
| Moderate | 12/46 (26.1%) | 7/20 (35.0%) |
| Gross | 3/46 (6.5%) | 3/20 (15.0%) |
| **Preoperative ureteral stent existence at the surgical side, *n* (%)** | | |
| Yes | 36/46 (78.3%) | 16/20 (80.0%) |
| No | 10/46 (21.7%) | 4/20 (20.0%) |

ESWL, extracorporeal shock wave lithotripsy; RIRS, retrograde intrarenal surgery; HU, Hounsfield unit.

TABLE 2 Clinical outcomes of unilateral and bilateral groups.

| | Unilateral group | Bilateral group |
|---|---|---|
| Total number, (*n*) | 46 | 10 |
| Operative time (min), mean ± SD | 53.04 ± 13.35 | 90.00 ± 15.81 |
| Hemoglobin loss (g/L), mean ± SD | −4.78 ± 9.22 | −4.10 ± 9.09 |
| Postoperative hospitalization (days), mean ± SD | 3.43 ± 1.70 | 3.20 ± 1.40 |
| SFR of the surgical ipsilateral side at postoperative day 1, *n* (%) | 35/46 (76.1%) | 16/20 (80.0%) |
| SFR of the surgical ipsilateral side at postoperative day 30, *n* (%) | 40/46 (85.1%) | 17/20 (85.0%) |
| Intraoperative VAS score | 3.83 ± 0.53 | 3.10 ± 0.74 |
| VAS score at 6 h postoperatively | 2.23 ± 0.64 | 2.20 ± 0.63 |
| VAS score at 24 h postoperatively | 1.22 ± 0.79 | 1.20 ± 0.63 |
| Total complications, Clavien grade classification, *n* (%) | 4/46 (8.7%) | 1/10 (10.0%) |
| Fever (>38°C) (G I) | 1/46 (2.2%) | 1/10 (10.0%) |
| Stent pain (G I) | 1/46 (2.2%) | — |
| Urosepsis only needing additional antibiotics (G II) | 1/46 (2.2%) | — |
| Steinstrasse (G III) | 1/46 (2.2%) | — |

G, grade.

In our study, all patients received postoperative KUB. For patients with suspicious fragments based on KUB, a CT was done, and 30.3% (17/56) of patients were checked with NCCT. The SFRs of Group A patients at postoperative day 1 and day 30 were 76.1% and 85.1%, respectively. In Group B patients, the SFRs of the surgical ipsilateral side at postoperative day 1 and day 30 were 80.0% and 85.0%, respectively.

Four (8.7%) patients in Group A suffered from the following complications: 1 (2.2%) patient suffered from fever (Clavien grade I), 1 (2.2%) patient who had stent pain (Clavien grade I) was treated with a steroidal anti-inflammatory agent, 1 (2.2%) patient who had urosepsis only needed additional antibiotics (Clavien grade II), and 1 (2.2%) patient with steinstrasse was treated with ureteroscopic lithotripsy under LA. In Group B, 1 (10%) patient suffered from fever (Clavien grade I). No ureter injuries were observed in the two groups. More details of the clinical outcomes are given in **Table 2**.

## 4. Discussion

Because of the miniaturization of novel FURS and the development of lithotripsy devices, FURL is being increasingly performed nowadays because of its superior minimally invasive characteristics and satisfactory success rates. FURL is usually performed under general or regional anesthesia by anesthesiologists and urologists (5) but is rarely performed under LA. As the population is aging rapidly in China (9), the proportion of older patients with urolithiasis shows an increasing trend (10). Elderly people are associated with age-related functional decline of organ systems, decreased physiological reserve (11), and non-communicable diseases or comorbidities (9), which result in high anesthetic risk. For these patients with high-risk anesthesia, LA is a feasible option (7).

We first reported FURL, combined with S-UAS, for urinary calculi under LA. Unlike the LA method described in a previous study conducted by Pai et al. (7), which used only a lubricating gel per urethra, our LA procedures included two steps: intramuscular pethidine and phenergan were used half an hour prior to surgery for analgesia and sedation, and oxybuprocaine hydrochloride gel was infused into the urethra at the start of the surgery. Preoperative use of pethidine and phenergan could increase patient tolerance for surgical operations because of their analgesic and sedative effects (12). No patient in our study abandoned surgery because of pain or ureteral injury. Moreover, a second ureteroscopic lithotripsy under LA for a patient with postoperative steinstrasse was also successfully completed.

For patients who underwent LA, preoperative ureteral stenting was advised, and these patients constituted 78.3% in Group A and 80.0% in Group B. The benefits of prestenting were continuous relief of hydronephrosis and alleviation of obstructive pain caused by edematous mucosa (13). Stent placement dilates the ureter, facilitates insertion of the ureteral access sheath (UAS) (14), and improves the initial success rate (15). Although all patients in our study were successfully inserted an S-UAS, prestented patients were inserted large-caliber UASs.

In our study, we evaluated the intraoperative and postoperative VAS scores of patients who underwent FURL under LA. All procedures were successfully completed without additional analgesia, and the mean intraoperative VAS scores were 3.83 ± 0.53 in Group A and 3.10 ± 0.74 in Group B. A previous study indicated that high pelvis pressure was associated with intraoperative pain (16, 17). According to the working theory of suctioning design, the application of the S-UAS in our study can help maintain low intrarenal pressure (18), which can reduce intraoperative pain and decrease complications associated with high intrarenal pressure.

Except for one patient who needed an oral steroidal anti-inflammatory agent after surgery because of stent pain, all patients tolerated postoperative pain. Multiple studies have focused on factors related to postoperative pain after FURL (13, 19–22). Oğuz et al. observed that female patients, a large stone diameter, high residual fragments, and a prolonged dwell time of UAS in the ureter were main factors associated with postoperative pain in patients who underwent FURL (19). Tighe et al. reviewed 333,000 pain scores following surgery and detected that female patients experienced higher pain scores (20). Mustafa reported that ureteral stenting was associated with postoperative discomfort (13). In contrast, another study demonstrated that double-J stent placement might lessen postoperative discomfort or relieve loin pain after FURL (13, 21). Postoperative catheter indwelling could also increase postoperative VAS scores (22). Although risk factors such as being female, large stone size, and routine double-J stent placement were observed in our study, the mean postoperative VAS score was low. The reasons listed below can help explain our results. First, stone particles can be immediately suctioned out through the S-UAS, which can shorten the dwell time of the UAS and the total surgical time. Second, the application of S-UAS can drain renal fluid in time to maintain low renal pressure, even at high irrigation flow, which can help maintain clear surgical vision, improve the efficiency of the lithotripsy procedure, and reduce operation time. Third, a postoperative catheter was avoided in all patients under LA.

The SFRs at postoperative day 30 were 85.1% (40/46) in Group A patients and 85.0% (17/20) in Group B patients, which were consistent with the outcomes of the study conducted by Pai et al. (7). However, the median stone size in Pai et al.'s study was 8 mm, which was considerably smaller than that in our study (20.24 ± 5.45 mm). In addition, only 64.7% (55/85) patients in Pai et al.'s study had renal or proximal ureteral stones and underwent FURL (7). To our knowledge, except for our study and Pai et al.'s study, no research with regard to FURL under LA was seen in the PubMed database. Park et al. reported that the SFR was 83% (5/6) for patients with upper ureteral calculi, but all underwent ureteroscopic lithotripsy under LA. Compared with the SFR (88.8%) of FURL, combined with S-UAS under general anesthesia (23), our SFR was comparable.

The overall CR in our study was 8.7% in the unilateral group, which was comparable with outcomes reported in a previous study (7). No ureteral injury caused by painful movement was observed in the two studies. Infectious CR (fever, urosepsis, and septic shock) was 4.4% (2/46) in the unilateral group, which was comparable with a study in which an S-UAS was used under general anesthesia (23), but it was lower than in a study in which the traditional UAS was used (23). This difference was mainly due to the status of low intrarenal pressure maintained by the application of the S-UAS. Moreover, infectious substances can be suctioned in time, and the amount of infectious sources for pyelovenous backflow is reduced.

Same-session bilateral FURL is a favorable therapy with a satisfactory SFR and an acceptable CR; however, it may prolong operation time and cause renal damage (8). Ten patients underwent same-session bilateral FURL in our study, and the SFR (85%) and postoperative CR (10%) were similar to the outcomes of a previous study (8). These patients were strictly selected, and the total stone size of each patient was less than or close to 30 mm.

Our study had several limitations. A major limitation was that it was a retrospective study with a limited sample size, and therefore, potential patient selection bias could not be ruled out. Second, a control group was lacking in the study. Third, we recorded the intraoperative VAS score, but the VAS score of different surgical procedures were not recorded, these procedures included ureteroscopy inspection, UAS insertion, ureteroscopic manipulation, and lithotripsy procedures. Therefore, a professionally designed study with a large sample size is recommended for the future.

## 5. Conclusion

FURL combined with an S-UAS under LA is a feasible option and provides satisfactory clinical outcomes for appropriately selected patients. A professionally designed study with a large sample size is recommended for the future.

## Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

## Ethics statement

Our study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Gannan Medical University (proof number: 2023032706). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

## Author contributions

ZZ and SL acquired data, prepared the article, and wrote it. TX analyzed the data. YY revised the manuscript. XW designed the study and acted as a corresponding author. All authors contributed to the article and approved the submitted version.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2023.1242981/full#supplementary-material.

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# Expanding horizons and navigating challenges for enhanced clinical workflows: ChatGPT in urology

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**Purpose of review:** ChatGPT has emerged as a potential tool for facilitating doctors' workflows. However, when it comes to applying these findings within a urological context, there have not been many studies. Thus, our objective was rooted in analyzing the pros and cons of ChatGPT use and how it can be exploited and used by urologists.
**Recent findings:** ChatGPT can facilitate clinical documentation and note-taking, patient communication and support, medical education, and research. In urology, it was proven that ChatGPT has the potential as a virtual healthcare aide for benign prostatic hyperplasia, an educational and prevention tool on prostate cancer, educational support for urological residents, and as an assistant in writing urological papers and academic work. However, several concerns about its exploitation are presented, such as lack of web crawling, risk of accidental plagiarism, and concerns about patients-data privacy.
**Summary:** The existing limitations mediate the need for further improvement of ChatGPT, such as ensuring the privacy of patient data and expanding the learning dataset to include medical databases, and developing guidance on its appropriate use. Urologists can also help by conducting studies to determine the effectiveness of ChatGPT in urology in clinical scenarios and nosologies other than those previously listed.

KEYWORDS
chatGPT, generative AI, healthcare, urology, workflow

## Introduction

In this modern day and age medical practitioners are challenged with a significant amount of administrative tasks and documentation. Unfortunately, these duties frequently require more time to complete than actual medical procedures on patients (1). Sadly, the present healthcare system in most countries neglects to address the challenges faced by physicians and aide workers. Recent research exhibited that bureaucratic duties, inadequate pay for additional hours worked, and sporadic working hours were found to be detrimental associated factors identified by doctors (2). One worrying issue regarding doctors' well-being is job-related stress manifesting into a very concerning issue referred to as "burnout". Amongst medical specialists, urologists appear to be most heavily afflicted by this problem. Research indicates that rates of reported burnout among urologists go up as high as 68% and 54% across America and Europe respectively, something that calls for prompt and effective measures from healthcare institutions globally (3). The need of the hour is thus to improve efficiency and optimize the workload on urologists. The potential applications for generative artificial intelligence (AI) within the context of healthcare are numerous. From facilitating doctors' workflows to enhancing patient interactions and providing decision-support tools, this exciting technology presents myriad possibilities (4). ChatGPT, developed by Open AI in San Francisco, CA, USA, is a widely accepted generative AI representative (5, 6). The literature's evident benefits and prospects of ChatGPT are complimented by controversial research, underscoring the lack of a thorough understanding of this technology's current state. Moreover, when it comes to applying these findings within urological contexts, well-thought-out studies have not been many (7). Thus, our primary objective is rooted in analyzing available works cited by scholars on this topic with a keen focus on delineating pertinent issues such as what aspects are beneficial or disadvantageous in using ChatGPT systems. Also if they are efficiently exploited by professionals specializing in fields such as urology.

## Overview of applications of ChatGPT in healthcare

OpenAI established ChatGPT in November 2022 to construct conversational AI systems that can understand and respond to human language. Over its different iterations response accuracy and human likeness have been improved. ChatGPT's zero-shot learning allows it to respond coherently to novel inputs. Encoders and decoders comprise ChatGPT's transformer architecture. The transformer design relies on the attention mechanism, which lets the model focus on different parts of the input text while generating output (8). **Figure 1** shows an overview of the ChatGPT architecture and the training process needed to process the input and deliver the output.

The potential implications of employing ChatGPT in various medical areas have been explored through numerous articles. Many useful insights are featured within the work of D'Amico et al. (9). They evaluated how ChatGPT can assist with neurosurgical health data collection and processing according to their logic and increasing efficiency among health professionals. Having such access will enable better quality patient monitoring by allowing them immediate access to historical patient records whenever needed. It can also help in creating a credible source for counseling self-help tips much like a therapist or physician and can get help in real-time during an emergency without any delay. ChatGPT assistance for decision-making was found to expedite sorting and prioritizing patients who have a pressing medical situation. ChatGPT can potentially provide patients with accurate information about various illnesses and related symptoms that may prevent unnecessary and premature appointments with the doctor. The remote sharing of medical information can contribute to lowering the burden of healthcare professionals by enabling remote contact between doctors and patients, thereby significantly reducing waiting times in the process.

Investigating advancements in emergency medical technology, Bradshaw (10) explored the implications of implementing ChatGPT in a medical context. By streamlining data input procedures through optimized automation, this innovative tool may save healthcare providers a significant amount of time. In addition to reducing instances where human error is possible, ChatGPT also offers clear benefits related to improved communication between physicians and patients, which ultimately results in greater levels of satisfaction overall.

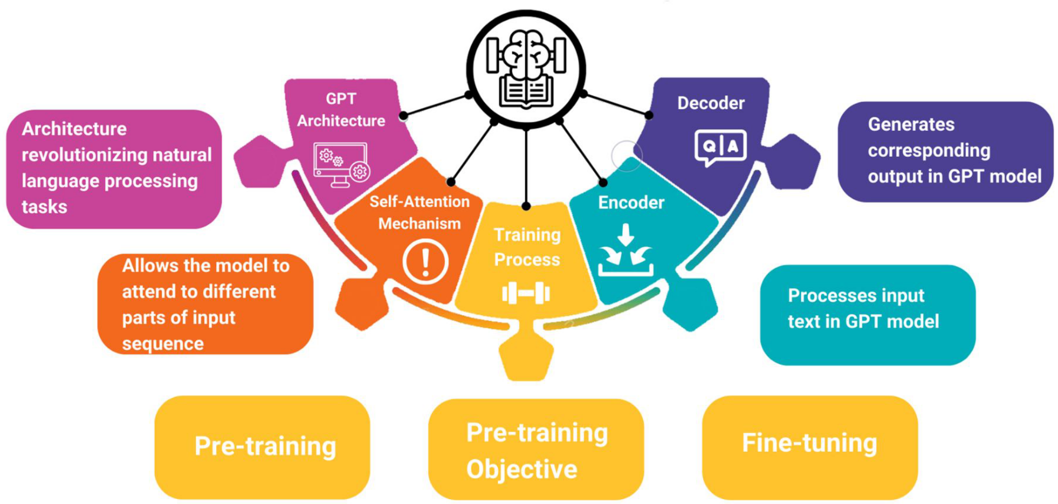


FIGURE 1
Overview of ChatGPT architecture and training process.

In the field of clinical oncology, ChatGPT holds tremendous potential by maximizing patients' personalized information gathered from case histories and medical records (11). This technology streamlines screening processes while allowing healthcare practitioners to make informed judgments based on detailed patient-specific data analysis.

However, the opinion on ChatGPT immaturity in physicians' assistance also exists. Farhat (12) assessed ChatGPT's effectiveness in providing support for issues related to anxiety and depression, based on the chatbot's responses and cross-questioning. According to the findings, there were significant inconsistencies and ChatGPT's reliability was low in this specific domain. Cao et al. (13) reported that Six liver cancer specialists had found ChatGPT unreliable in answering 20 questions concerning monitoring and diagnosis. Inaccurate answers sometimes included inconsistent or deceptively comforting, if not erroneous, information about individual LI-RADS categories. Potential scenarios, where ChatGPT could be used with associated risks and benefits are briefed in **Table 1**.

## Clinical documentation and note-taking

ChatGPT assumes a text-oriented strategy that can facilitate the management of medical data entry and note-taking processes based on individualized analysis of symptoms and test outcomes specific to patients. As a result of this, there is potential for reduced time taken on this aspect, which implies more time dedicated to patient conversation and counseling. More so, structuring intricate information consistently via the use of ChatGPT serves as a tool for reinforcing comprehension and the overall message among its users. In their research article, Singh et al. (14) point out the various abilities of ChatGPT, from generating ocular extracts to offering operational notes for healthcare providers. Based on these findings, ChatGPT has the potential to provide tailored prescription information, consultation time, and follow-up advice as appropriate. Additionally, Zhou et al. (15) indicated that the model can furnish an elaborate overview of medical history as well as the patient's current health status via test

TABLE 1 Current scenarios to use chatGPT in medicine, their potential advantages and shortcomings.

| Domain | Feature | Potential advantages | Disadvantages |
|---|---|---|---|
| Clinical documentation and note-taking | Structuring of medical history<br>Medical history summarizing<br>Notes creation<br>Follow-up advices<br>Real-time documentation assistance<br>Decision support | Potential for reduced time expenditure on these duties which implies more significant periods dedicated towards conversations with patients as well as treatment coursing; Enhanced collaboration between physicians and patients | Lack of contextual understanding; Misinterpretation of ambiguous inputs; limited clinical experience; Lack of personalized data privacy |
| Patient communication and support | Self-evaluation of symptoms<br>Language barriers<br>Emotional support<br>Non-judgmentality<br>Confidentiality<br>24/7 availability and accessibility<br>Educational tool | Providing patients with reliable information pertaining to their health state, treatment alternatives available and foreseeable implications; Providing communication with physicians and high quality patient care for patients with language barriers; Alleviate patients' emotional stress by acknowledging their concerns | Misunderstandings since patients may not clearly explain condition and write input; Inability to perform physical examination, estimate non-verbal signs, provide hands-on care; Lack of knowledge on recent advancements in healthcare; Lack of personalized data privacy; Lack of empathy |
| Medical education and preparation for medical entrance exams | Interactive education platform<br>Knowledge in all medical disciplines<br>Real-time errors analysis<br>Advices on further education | ChatGPT has vastly knowledgeable user base caters to students and experts who can access various topics; Serves as reliable and dynamic platform for online learning experiences where it immediately analyses errors made by its users after each response attempt with advices for further improvement. As containing vast medical knowledge, can aid and help users when preparing for specific medical entrance exams | Knowledge are limited by 2021 year; The absence of a certified medical source training dataset; Variation in ChatGPT's medical test accuracy across different countries; Lack of clinical experience; Insufficient explanation; |
| Literature review and research support | Generating completely original content<br>Correct manually-written references in various styles<br>Statistical data processing<br>Editing services for english-language texts<br>Brainstorming | ChatGPT has proficient capacity for processing copious amounts of information quickly provides clients with succinct summaries; ChatGPT is able to simplify the process of preparing manuscript; It is possible to generate medical paper from scratch; It is possible to identify potentially fruitful research ideas through the clarification of problematic issues that require scientific analysis | Inaccurate references search; No up-to-date text generation; Inability in web search; The absence of a certified medical source training dataset; Lack of critical thinking; Risk of accidental plagiarism; Potential for loosing of analytical potentials by users; |

results analysis. What is more remarkable is that this model is knowledgeable enough to give sound clinical suggestions while presenting a summary report about a patient's current well-being, both grounded in its comprehensive database. Lastly, given its vast skillset and experience base thereof, doctors may avail themselves of real-time documentation assistance via ChatGPT.

## Patient communication and support

Patients using ChatGPT can get reliable information about their health, treatment alternatives available, as well as foreseeable implications, as demonstrated by Yeo et al. (16) indicating an impressive accuracy rate for ChatGPT knowledge on cirrhosis (79.1%) and HCC (74.0%). To complement the platform's capabilities, ChatGPT structures patient questions to aid in symptom evaluation and provides preliminary suggestions based on responses given by the patients themselves, ideas that can assist in establishing their symptom severity while also determining when they require emergency medical treatment or if self-care practices are sufficient (17).

Addressing language barriers is paramount in ensuring that high-quality patient care can be delivered, and one solution is the use of translation software. As reported by Yeo et al. (18) GPT-4 outperformed ChatGPTs response accuracy when answering questions in English, Korean, Mandarin, and Spanish. Moreover, sentimental support provided via ChatGPTs empathic dialogue can help alleviate patients' emotional stress by acknowledging their concerns while guiding them on managing their mental well-being. In an assessment of ChatGPT's ability to detect emotional subtleties using the Levels of Emotional Awareness Scale (LEAS), Elyoseph et al. (19) discovered that the chatbot performed significantly better than most humans during both initial and follow-up evaluations.

## Medical education

Optimizing medical education appears promising with the use of ChatGPT because its vastly knowledgeable user base caters to students and experts who can access various topics concerning this field. Oh et al. (20) attested to ChatGPT's efficiency in providing surgical teaching through its analysis of various responses submitted, resulting in a 76.4% accuracy percentage on tests administered by the Korean Board of General Surgery. Li et al. (21) reflected even better results when they scored this tool with an average score of 77.2% accuracy on virtual objective structured clinical exams administered within Singapore, surpassing human averages at a ratio of over 4% superiority. Also notable is that some human evaluators found it challenging to distinguish between replies from people and those from ChatGPT because of the program's smart learning capability. However, Alfershofert et al. (22) evaluated the performance of ChatGPT on six different national medical licensing exams and investigated the relationship between test question length and ChatGPT's accuracy. They discovered significant variation in ChatGPT's test accuracy across different countries, with the highest accuracy seen in the Italian exam (73 percent correct answers) and the lowest accuracy seen in the French exam (22% correct answers). Moreover, they discovered that queries requiring multiple correct responses, such as those on the French examination, presented a greater challenge to ChatGPT.

## Medical literature review and research support

ChatGPT continues to amaze the scientific community due to its exceptional capabilities in streamlining medical article composition and literature appraisal (23). Holly Els assessed ChatGPT's textual output and highlighted its exceptional performance regarding generating completely original content. A highly rated component was its ability to produce machine-generated texts that could even fool human reviewers in over a third of attempts during her test analysis (24). However, the opposite opinion also exists. As stated by Arif et al. (25) ChatGPT can be used as a supplement to constructive writing, examining information, and rephrasing the text rather than as a replacement for a complete original blueprint. Because medical literature is a constant process of updated research, there is growing worry that ChatGPT may now be easily utilized for authoring articles that may lack clinical reasoning and critical thinking.

In addition to generating the finished text using ChatGPT, it is also possible to simplify the process of preparing your manuscript. ChatGPT can quickly overwrite manually-written references in various styles, such as Vancouver, MLA, or Chicago, but not create those *de novo* (26). ChatGPT can function as a proficient biostatistician for statistical data processing, determining the most informative methods of statistical analysis, while also advising visual support (27). This advanced technology excels beyond the capabilities of commonly accessible translators, offering exceptional editing services for English-language texts at a C1 level of language proficiency (28).

This technology allows for not only the direct examination of the text but also the identification of potentially fruitful research ideas through clarification of problem-solving issues that require scientific analysis. Users can also chat with ChatGPT to discuss principal concepts and potential developments, promoting critical thinking among young professionals and motivating them to test certain hypotheses (29).

## Implications for urology practice

Several investigations have explored the application of ChatGPT in the domain of medical expertise and urological patient care. One study conducted by Tung et al. (30) involved using ChatGPT as a virtual healthcare aide for preoperative TURP concerns. The tool provided succinct yet reassuring responses regarding potential dangers along with encouraging individuals to seek input from expert physicians for additional clarification, while also offering post-operative relief by advising on identifying alarming symptoms and providing detailed guidance on physical activity as well as easing constipation.

In another inquiry carried out by Ilie et al. (31), researchers examined the role played by AI technology specifically through ChatGPT in medico-education settings. The reviewers interviewed ChatGPT to provide an overview of localized prostate cancer treatment plans and established that it was particularly reliable for delivering accurate medical information. However, its usage was primarily based on US data which could lead to such findings being slightly biased.

The prevention and screening of prostate cancer were explored by Zheng et al. (32) in evaluating the AI-powered system ChatGPT-4's effectiveness in offering advice on the matter through NCCN recommendations-based questions alongside clinical data points given to them. According to urologists involved with the research project, most of ChatGPT's responses were deemed appropriate. However, a few responses were not suitable or inaccurate underlining the need for exhaustive review before accepting AI-generated information unquestionably.

Another research paper conducted by Zhu et al. (33) analyzing several language models' capacities for addressing issues surrounding prostate cancer found that AI tools such as ChatGPT can be used effectively to provide patients with relevant information about screening procedures, prevention measures as well as treatment options, drawing insights from clinical expertise records alongside established patient educational standards. This facilitates informed decisions between doctors and their patients, ultimately empowering them with medical knowledge and allowing them to reach a shared decision making.

ChatGPT's proficiency in urology and its potential benefits for residents were observed by Deebel et al. (34). The American Urological Association (AUA) Self-Assessment Study Program ratings varied for ChatGPT. To broaden its educative scope, ChatGPT must increase its wealth of knowledge. Additionally, Schuppe et al. (35) utilized AI-based writing support from ChatGPT to draft a Nelson syndrome case study post-bilateral adrenalectomy. In this way, ChatGPT assisted in outlining, developing, and concluding the case study. As mentioned earlier, in every aspect of the application of ChatGPT, there is both confirmation and refutation of the usefulness of the technology. Medical Education is not an exclusion. Huynh et al. (36) evaluated the utilization of ChatGPT as an educational supplement for urology trainees and practicing physicians in the American Urological Association Self-assessment Study Program. ChatGPT correctly answered 36/135 (26.7%) open-ended questions and 38/135 (28.2%) multiple-choice questions. Indeterminate replies were obtained in 40 (29.6%) of the cases and in 4 (3.0%). Although regeneration reduced uncertain replies, it did not raise the number of accurate responses. ChatGPT gave consistent reasons for erroneous responses and remained concordant between correct and incorrect answers for open-ended and multiple-choice questions. The same opposite results were found by Whiles et al. (37) When evaluating ChatGPT's ability to provide patient counseling answers based on clinical care recommendations in urology. The authors stated that when evaluating healthcare-related recommendations from present AI models, users should exercise caution. Additional training and changes are required before these AI models can be trusted by patients and doctors. Also, Misheyev et al. (38) characterized the information quality and detected misinformation regarding prostate, bladder, kidney, and testicular malignancies from four AI chatbots: ChatGPT, Perplexity, Chat Sonic, and Microsoft Bing AI. The results indicate that AI chatbots produce information that is generally accurate and of moderate to high quality in response to the top urological malignancy-related search queries. However, the responses lack clear, actionable instructions and exceed the recommended reading level for consumer health information.

## Challenges and risks of using ChatGPT in healthcare

An analysis of ChatGPT limitations should come first before explicating further the positive aspects, especially because our understanding of them might be incomplete.

One primary challenge facing ChatGPT is its lack of web crawling capabilities which currently limits access solely to information acquired before 2021. Ayoub et al. (39) conducted a cross-sectional analysis to evaluate ChatGPT's capabilities as a source of medical knowledge, using Google Search as a comparison, and discovered that ChatGPT performed better than Google Search when providing general medical knowledge, but worse when providing medical recommendations. Manolitis et al. (40) assessed the efficacy of a ChatGPT API 3.5 Turbo model to a standard model in supporting urologists in getting precise, reliable medical information. The API was accessed using a Python script written particularly for this study and based on 2023 EAU guidelines in PDF format. This custom-trained model provides clinicians with more exact, rapid responses concerning specific urologic issues, thereby assisting them in providing better patient care rather than the existing standard model.

Using deceptive or inaccurate data to train, ChatGPT could also pose a significant risk, leading to inconsistent or untrue medical responses. Tung et al. (34) observed that ChatGPT gave inaccurate information, such as a percentage risk of retrograde ejaculation based on current research. ChatGPT did not offer clarifying questions to improve diagnosis, and replies were also inconsistent. Skewed training data can result in skewed output, and excessive reliance on ChatGPT can reduce patient adherence and promote self-diagnosis. To ensure the accuracy, validity, and reliability of ChatGPT-generated content, rigorous validation and ongoing updates based on clinical practice are necessary.

"Hallucination" in writing, where it is influenced more by learned patterns rather than scientific facts, is what leads to these mistakes (41). Generative ChatGPT can show signs of this phenomenon due to being trained on large amounts of unsupervised data. Farhat et al. (42) assessed the performance of ChatGPT in creating an abstract and references for bibliometric analysis. Despite the well-written quantitative data display, ChatGPT offered incorrect information regarding major authors, countries, and avenues. Moreover, ChatGPT provided either non-existent or unrelated to the study references. When ChatGPT was questioned about the sources, it apologized and provided a fresh set of references, however, the references were similarly non-existent following further inquiry. These data show that ChatGPT is configured to react to any enquiry, regardless of correctness, and it accepts no responsibility for any inaccuracies. Summarizing the above, the following ChatGPT-associated intrinsic issues can be distinguished: hallucination, biased content, not real-time, misinformation, and inexplicability. Some authors proposed adaptive steps to combat them. So, Sohail et al. (8) discussed that algorithmic improvement, inputting the queries properly, verifying generated responses, and human feedback, and refining the training data to remove or mark the biased content might help overcome these problems.

ChatGPT can be a valuable tool for literature review and research. Nevertheless, we must recognize its limitations since it cannot replace human critical thinking, knowledge acquisition, or peer review processes (43). Presumably using AI technology may have serious unintended consequences, leading young scientists especially into losing their analytical potential over time. Additionally "knowledge homogenization" could result if every individual merely receives data from an unbiased "collective consciousness" without any supervision exercised (44). Generative AI researchers like ChatGPT risk accidental plagiarism while carrying biases, emphasizing the need for responsible ethical conduct on their part. Finally, it is important to mention that ChatGPT fails to meet either GDPR or HIPAA standards, creating issues regarding safeguarding patient health information (PHI) and personal data. As stated by Cacciamani et al. (45) patient safety, cybersecurity, transparency and interpretability of the data, inclusivity and equity, fostering responsibility and accountability, and the preservation of providers' decision-making and autonomy are among the potential ethical issues that must be taken into account when implementing AI in clinical practice.

While the majority of the medical community's concentration is on ChatGPT, other Large Language Models (LLMs) should be kept in mind and investigated to determine whether ChatGPT's shortcomings are unique or shared by the entire LLMs industry. Dao (46) compared ChatGPT, Microsoft Bing Chat, and Google Bard using the VNHSGE (Vietnamese High School Graduation Examination) dataset. The performance of BingChat, Bard, and ChatGPT (GPT-3.5) is 92.4%, 86.4%, and 79.2%, respectively, confirming the increased accuracy with BingChat use in English language education due to the incorporation of up-to-date information.

However, when it comes to the medical field, obvious advantages become hidden. Agarwal et al. (47) compared the applicability of ChatGPT, Bard, and Bing in generating reasoning-based multiple-choice questions (MCQs) for undergraduate students on the subject of physiology and found that BingChat generated significantly the least valid MCQs, while ChatGPT generated significantly the least difficult MCQs. Rahsepar et al. (48) compared the accuracy and consistency of responses generated by ChatGPT, Google Bard, and non-expert questions related to lung cancer prevention, screening, and terminology and found that Although ChatGPT had higher accuracy in comparison with the other tools, neither ChatGPT nor Google Bard, Bing, or Google search engines answered all questions correctly and with 100% consistency.

Thus, it is evident that the issues associated with the use of ChatGPT reflect the state of LLMs in general, emphasizing the need to improve all publicly accessible ChatBots powered by generative AI.

## Future directions and opportunities for research

As ChatGPT hinges on the data it obtains, certain key details must be manually inputted. However, potential advancements may allow for ChatGPT to independently extract data from digital archives sans human guidance (49). Additionally, the training database should be up-to-date and include relevant guidelines, as opposed to being limited to the year 2021 as it is currently. This strategy will equip ChatGPT with the necessary skills and reduce the likelihood of patients and medical students receiving incorrect information. Indeed, training with clinical guidelines significantly improves the accuracy of ChatGPT responses, as was confirmed by Manolitis et al. previously (40). UroChat (https://urochat.streamlit.app) was recently developed using the GPT 3.5-turbo model and 2023 EAU Guidelines. The presence of such chatbots is already a solution to several of ChatGPT's limitations. Nevertheless, future studies are needed to estimate its value for clinical decision-making, medical education, and patient counseling.

The potential of ChatGPT in aiding personalized therapy is considerable. Temsah et al.'s study indicates that by integrating the findings from the extensive global burden of disease research with advanced AI via open AI chat and utilizing the power of conversational ChatGPT-4, healthcare planning could be transformed at an individual level. With such integration, medical practitioners will have an improved ability to develop specially designed treatment plans based on patient's specific lifestyles and preferences (50).

The progress in AI has brought transformative benefits across various human endeavors, and scientific research is no exception. However, we must acknowledge potential risks from certain AI innovations like ChatGPT, specifically regarding fraudulent use, that may pose threats to scientific integrity. We must therefore take necessary measures and precautions against any emerging types of deceit linked with ChatGPT. Amongst current approaches include building diversified analytical tools capable of detecting instances of potentially fraudulent text produced through platforms like ChatGPT. Despite this approach, it is important to note an ongoing debate on ethical issues surrounding the extensive use of ChatGPT for purposes such as enhancing writing efficiency vs. interfering with original scientific inquiry.

Although banning ChatGPT might seem like a quick and easy solution, such actions could thwart progress in today's rapidlyevolving world. Instead, researchers must prioritize ethical considerations and aim for academic rigor despite any obstacles they face. Plagiarism can be avoided by refraining from copying and pasting unattributed content generated with AI tools into manuscripts. Prohibiting these instruments completely isn't necessary, it would be sufficient to simply document their usage within acknowledgments or methods sections when publishing research work, as stated by a recent article from Nature (51). Furthermore, credit should not be given to AI tools since they do not contribute to research outcomes but instead support revisions for original works only (45).

## Conclusion

Despite the many advantages offered by ChatGPT, it is not puzzling as to why urologists have yet to adopt this technology in their clinical and academic practice. The existing limitations mediate the need for further improvement of ChatGPT. These include measures such as algorithmic improvement, verifying generated responses, human feedback, refining the training data to remove or mark the biased content, ensuring the privacy of patient data, and developing guidance on its appropriate use to provide honest and reliable use of ChatGPT. Moreover, to determine the effectiveness of ChatGPT in urology, further studies in clinical scenarios and nosologies other than those previously listed are needed.

### Key points

- ChatGPT has emerged as a potential tool for facilitating doctors' workflows.
- Despite the benefits of ChatGPT, several of its drawbacks, such as the lack of web crawling, the risk of accidental plagiarism, and concerns about patient data privacy, limit its reliable use.
- Studies on ChatGPT's potential in urology have not been many and are mainly focused on virtual healthcare aides for benign prostatic hyperplasia concerns, educational and prevention tools for prostate cancer, educational support for urological residents, and as an assistant in writing urological papers.
- Further improvements to ChatGPT should encompass the privacy of patient data, the possibility of independently extracting data from digital archives without human guidance, including medical databases, and the development of guidance on its appropriate use.

## Author contributions

AT: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. NN: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. BH: Conceptualization, Formal Analysis, Methodology, Writing – original draft. UZ: Conceptualization, Data curation, Formal Analysis, Methodology, Writing – original draft. GK: Formal Analysis, Investigation, Methodology, Supervision, Writing – review & editing. BG: Investigation, Methodology, Supervision, Validation, Writing – review & editing. PJ: Conceptualization, Methodology, Software, Supervision, Writing – review & editing. LT: Conceptualization, Project administration, Supervision, Validation, Writing – review & editing. BS: Conceptualization, Project administration, Supervision, Validation, Writing – review & editing.

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# Controversies in ureteroscopy: lasers, scopes, ureteral access sheaths, practice patterns and beyond

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Ureteroscopy has become an increasingly popular surgical intervention for conditions such as urinary stone disease. As new technologies and techniques become available, debate regarding their proper use has risen. This includes the role of single use ureteroscopes, optimal laser for stone lithotripsy, basketing versus dusting, the impact of ureteral access sheath, the need for safety guidewire, fluoroscopy free URS, imaging and follow up practices are all areas which have generated a lot of debate. This review serves to evaluate each of these issues and provide a balanced conclusion to guide the clinician in their practice.

KEYWORDS
ureteroscopy, ureteral access sheath, fluroscopy, laser, lithotripsy

## Introduction

Ureteroscopy (URS) stands beside shockwave lithotripsy (SWL) and percutaneous nephrolithotomy (PCNL) in the trilogy of minimally invasive therapies performed in patients with urolithiasis. Since the early descriptions by Marshall et al. in 1964, it has undergone many modifications, both in terms of the equipment used as well as the surgical techniques applied (1–3). These advances have elevated the position of URS to that of a treatment of choice in a wide variety of clinical scenarios and complex stones, and the patient selection has expanded accordingly. To this end, URS has been demonstrated in clinical studies to be not only safe but also a preferred option in certain situations such as pregnancy, patients at the extreme of age and stones in the lower pole (4–8). The abovementioned modifications include technological advancements such as the energy sources employed for stone lithotripsy, the development of digital and single use ureteroscopes as well as novel accessories such as anti-retropulsion devices and more recently, real time intra-renal pressure monitoring systems (9). While it is a luxury for the modern-day surgeon to have such an array of technologies at their disposal, which have certainly contributed to the improved outcomes associated with URS, it has led to a wide range of practice patterns as well as ongoing debate regarding the actual advantages and disadvantages they may actually yield for the patient (10). While there is an increasing volume of studies which have sought to evaluate these individual areas, it can be difficult for the time pressured clinician to maintain a balanced and informed viewpoint on these areas of debate and controversy. Our aim was therefore to review the literature and deliver such information.

## Methods

A non-systematic literature review was performed in order to gain evidence to allow for evaluation of the following key topics: Role of single use ureteroscopes, optimal laser for stone lithotripsy, basketing versus dusting, the impact of ureteral access sheath (UAS), the need for safety guidewire (SGW), fluoroscopy free URS, imaging and follow up practices are all areas which have generated a lot of debate over the last few years and are reviewed in the present study. Each of the specific words were used as search terms. Bibliographic databases searched included Medline, Google Scholar and the Cochrane Library. Only articles in the English language were assessed but all article types were included. The findings have been presented in a narrative format.

## Single use ureteroscopes

Until recently, all flexible ureteroscopes have been reusable. In October 2015, the first fully disposable single use (SU) and commercially available flexible ureteroscope was introduced (Lithovue$^{TM}$, Boston Scientific, Marlborough, MA). Approximately 30 models are now available from different companies. Reducing the infection and contamination risk, potential cost benefit and preservation of reusable (RU) ureteroscope represent the main arguments for their adoption (11). Newer generation models are now available, and a recent meta-analysis of clinical studies reveal a non-inferior status regarding outcomes such as stone free rate (SFR) and complication burden when compared to RU scopes (12). The trajectory of their uptake appears likely to rise further owing to favourable physical properties. This includes ergonomic advantages such as lighter weight (some models are less than 100 g including cable) and novel modifications such as left and right-handed versions. Mixed conclusions have been put forward regarding the true cost efficiency of SU models and the reason for this is largely due to the different inputs used for the calculations such as the average life cycle of RU ureteroscope (range: 8–29 procedures) and the individual contract for repair costs between hospitals and suppliers (13). A proposed disadvantage of SU models has been the generally larger outer diameter sizes compared to RU scopes and more specifically, fibre-optic models. This has the potential to lead to sequalae such as lower rates of success at overcoming the ureteral orifice and a narrower space between the scope and the ureteral wall, which may result in a poor irrigation outflow and consequently increases the risk of high intrarenal pressure. Also, a larger scope calibre can result in the need for larger sized UAS. While the newer generation models are slimmer, they do not yet match the dimensions of RU alternatives such as the Olympus P7, which has a tapered 4.9Fr tip. The durability of SU ureteroscopes for surgeries of longer duration has also been questioned, given the issue of sudden image loss (14). To this end, a recent analysis of national registry of device failures associated with SU ureteroscopes found that image loss accounted for more than 75% of reported problems associated with their clinical use (15).

## The optimal laser source: holmium:yttrium-aluminium-garnet vs. thulium fiber laser vs. pulsed thulium:yttrium-aluminium-garnet

Holmium:yttrium-aluminium-garnet (Ho:YAG) is the current standard when performing URS and stone lithotripsy. This has been the case for over 30 years and while alternatives have been introduced, none of these were able to demonstrate superiority in the clinical setting (3). Thulium fiber laser (TFL), that also has a pulsed action, is arguably the first alternative that has challenged the dominant status of Ho:YAG (16–18). Several clinical studies now support the superiority found in earlier pre-clinical studies (19, 20). This includes a randomised trial by Ulvik et al. that found significantly higher SFR for renal stones associated with TFL use as well as fewer intra-operative adverse events and shorter operative times (21). However, SFRs for ureteral stones were the same (100%) and this highlights that in many scenarios (e.g., uncomplicated distal ureteral stone), even a low power holmium laser machine is still sufficient. Of note, while it was a 60 W TFL machine and 30 W Ho:HAG machine, the power setting of 2,4 watts used for both, which is well within the range of the machines. Another recent randomised study by Haas et al. found no differences in SFRs between these two lasers, regardless of stone location (22). However, in that study, the stone burden was comparatively extremely low with mean lasering times of 2.7 min for the Ho:YAG and 3.6 min for the TFL, while the per protocol power analysis assumed 6 min differences between the two groups. Additionally, follow up imaging was ultrasound (US) and plain x-ray (XR) rather than computed tomography (CT). That study also supports that any low power pulsed laser may be adequate when facing small stone burden.

Recently, the pulsed Thulium:YAG laser has been proposed as a further alternative to the Ho:YAG, with promising stone dusting proprieties (23). Two clinical studies are available to date and reveal the pTm:YAG as an efficient and safe laser for lithotripsy (24, 25).

No comparative studies evaluating the Ho:YAG against the TFL and pTm:YAG are available to date, therefore no clear recommendation can be made as to whether either to TFL or the pTm:YAG may become the new gold standard for lithotripsy.

## Basketing versus dusting

Regardless of type, laser has become an established energy source for stone lithotripsy. However, the laser strategies employed by surgeons do vary. More specifically, continued debate exists regarding whether the more traditional approach of fragment and basketing is superior to dusting (26). Although no difference between the two strategies was found in the EDGE study from North America, it is important to point out, though, that almost none of the patients had a CT scan for follow-up

(27). A recent meta-analysis of 10 studies found no significant difference for SFR, re-treatment rate or complications (28). In that study, the most popular dusting settings were 0.2–0.5 J and 15–20 Hz (3–10 Watts). In addition to the predominant use of plain XR to assess SFR, none of the studies to date have employed TFL, which lends itself to dusting. Consensus is still lacking regarding what constitutes dust and definitions currently range between 200 and 400 µm sized particles (28, 29). In practical terms, it could be considered the particles of such size that can be aspirated through the working channel of the ureteroscope. Proponents for dusting may also argue that accessories such as the basket are becoming obsolete and adverse events can occur during their use (30). However, in a recent randomised trial by Yaghoubian et al., where lower pole stones were either displaced with a basket before lithotripsy or treated in site, patients in the former group achieved significantly higher SFR (95% vs. 74%, $p = 0.003$) (31). Arguably, basketing may remain as a primary choice according to the clinical scenario and personal preference of surgeons, but current trends have confirmed an emphasis towards dusting techniques (32).

## Ureteral access sheath

Application of UAS holds potential advantages including reduction of intra-renal pressure and subsequent infectious complications, as well as improved irrigation and endoscopic vision accordingly. A statewide study of over 5,000 URS procedures by Meier et al., revealed that use of UAS among surgeons varied between 1.8% and 96% (33). That particular study highlighted not only the contrasting personal preferences of surgeons towards this accessory, but also potential limitations as the authors found a significantly increased likelihood of increased emergency department (ED) presentation and hospitalization associated with use of UAS. It is indeed these concerns regarding the adverse events why UAS hold a controversial status. This includes intra-operative complications such as ureteral perforation and late sequelae such as ureteral stricture formation (34). Improved dusting capabilities that are enabled with newer laser platforms arguably reduce the need for the relay of fragments out of the kidney via UAS. At the same time, it can be argued that the smaller dimensions of newer ureteroscopes allow for smaller diameter UAS to be used and hence, there is a reduced risk of associated ureteral injury. Of note, using a smaller diameter UAS, diminishes the effect on intrarenal pressures (35). Furthermore, the smaller sized laser fibers available with TFL, allow for more irrigation to be delivered via the working channel and therefore improved vision. There are numerous individual studies where the findings either support or disfavour UAS, but when the literature is reviewed as a whole, it seems the data is still inconclusive (36).

## Safety guidewire in routine URS

A safety guidewire (SGW) is a guidewire that is introduced during initial cystoscopy and kept in the ureter adjacent to the ureteroscope throughout the procedure. In the advent of the ureteroscopic era, the SGW was a valuable tool aiding in maneuvering the large diameter endoscope up to the ureter. Since then, despite miniaturisation of the ureteroscopes, the SGW has been considered a formal requirement when performing URS by many experts. They offer an exit strategy when faced with unforeseen intra-operative complications such as ureteral perforation. While there is agreement regarding their merits in scenarios such as difficult ureteric anatomy or heavily impacted stone with a clear risk for worsening any ureteral damage, debate exists regarding whether they should be mandatory in URS determined to be routine or uncomplicated. That is because their employment can hinder the surgeon in terms of advancing up the ureter alongside a SGW. In fact, a randomised trial demonstrated that the forces needed to introduce and retract the ureteroscope in the ureter increased more than 100% when a SGW was in place compared to when omitted (37). In a comparative trial with 500 URS with SGW and 500 URS without SGW, the same group also studied the proposed benefits of using an SGW, that is increased success of entering the ureteral orifice, easier maneuvering up the ureter in terms of reaching the stone level, and most importantly preserve the ability to place a stent at the end of the procedure (38). The study showed no difference between the groups in any of the suggested benefits of using an SGW, and the authors concluded that routine use of SGW during URS should not be mandatory. Opponents to this might argue that one does not know if a case will really be a routine operation until it is too late. The European Association of Urology (EAU) guidelines do recommend their use, however the level of evidence to support this is only expert opinion (39). Interestingly, all studies that have evaluated the topic have revealed no increased association with complications, although these studies were arguably underpowered, since the event of a SGW that is going to be used for safety is extremely rare. Moreover, this includes two randomised trials that not only support this finding but also reveal longer operation times associated with use of a SGW (40–42).

## Fluoroscopy free URS

There is agreement among surgeons to follow the “as low as reasonably achievable” (ALARA) principles regarding intra-operative use of fluoroscopy (43, 44). Active measures can be taken by the surgeon including use of pulsed fluoroscopy and image collimation (45). Several studies have sought to determine an association of higher dosages when control of the C-arm is primarily by surgeon or an assistant/radiation technologist, and overall there appears to be no difference (42). This includes a recent randomised trial by Kokorowski et al. (46). There has been more attention recently towards zero use of fluoroscopy. Adaptations can be made to the standard technique such as marking length on ureteroscope once positioned in the pelvic ureteric junction to facilitate insertion of UAS. Here too, ureteral stents are inserted using tactile feedback rather than fluoroscopy control. Use of real time ultrasound has also been presented as a tool (47). There is a number of cohort studies reporting this approach in large patient samples and without an increased complication burden. However, these are usually highly experienced, single surgeon series and more difficult patient groups such as urinary diversions are usually excluded (48). Of note, almost all case reports on unintentional DJ-stent insertion into large vessels report the lack of fluoroscopy during the intervention (49). By analogy, fluoroscopy free ureteroscopy might cause rare, but disastrous events. A simple and effective method of reducing fluoroscopy time during URS is to increase awareness of the topic, and the surgeon should ask him- or herself whether there really is a need for fluoroscopy *every time* the pedal is activated. The most recent systematic review and meta-analysis on this topic including 24 studies, among which 12 have been randomized, revealed that no significant differences exist in stone-free rates, length of stay and operative time between fluoroscopy-free and fluoroscopy-guided procedures, with complications been higher in the fluoroscopy-guided group (50). These findings were similar when URS and PCNL was analysed separately, while the overall conversion from fluoroscopy-free to fluoroscopy-less procedure was 2.84%.

### Imaging for assessment and follow up

Beyond the surgery itself, there is debate and differing practice patterns regarding both work up and follow up of urolithiasis patients. Imaging type and timing form a large part of this debate. CT delivers the highest sensitivity and specificity for diagnosing urolithiasis compared to alternatives such as US and plain XR. Low dose versions also allow the dosage to be reduced further while still providing necessary information. Such are the merits of CT for assessing stone burden that some scientific journals have started requiring it as a standard for submission (51). This does present difficulties in less resource rich areas as well as special populations such as children, in addition to the argument about higher radiation dosages. Related to imaging type is how stone size is reported. The current standard in guidelines is based on the maximal diameter (39). However, two stones with the same maximal dimensions can in fact have quite different overall sizes if the volume is measured (52). Measurement of stone volume has therefore been recommended as a means to give more accurate assessment of stone burden. From a research perspective, it could also allow for more accurate evaluation of laser energy consumption (Joules/$mm^3$), e.g., when comparing Ho:YAG and TFL (53). However, adopting stone volume is not without problems as there several methods to calculate it. Even when the formula has been decided upon, manual measurement of three dimensions increases the risk for inaccuracy for each one that is subsequently multiplied. It can also be a relatively time intensive process. Automated calculation with software represents one solution to this but these are not yet available as an integrated tool within hospital systems and can be expensive. Exporting patient sensitive information also presents privacy concerns.

## Future directions

For all these contested topics, more randomised trials will help guide future clinical practice. Part of the reason why it can be so challenging to compare outcomes across different studies, regardless of their type, is the heterogeneity in reporting that is present. Implementation of reporting tools such as the Adult-Ureteroscopy (A-URS) Checklist could serve to help address this (54). This tool offers an overview of suggested study details and parameters to be reported.

## Strengths and limitations

This narrative review has certain limitations to acknowledge. Firstly, the literature search was non-systematic and therefore not unabridged. A large number of the studies reviewed were of a low level of evidence including expert opinion. To this end, the conclusions need to be considered in light of this. However, this review offers the reader an overview of the core issues surrounding each topic. The findings in this review can therefore serve as a useful aid to the time pressured clinician.

## Conclusion

In the field of URS, there are many controversies. Technological advances allow for improved patient outcomes but adoption of a particular technique over an another is largely based on surgeon preference. Surgeons are encouraged to explore and understand the advantages and disadvantages of each of these so as to enable a tailored approach for their patients and practice as a whole.

## Author contributions

PJ-J: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. EK: Conceptualization, Writing – original draft, Writing – review & editing. VC: Conceptualization, Methodology, Writing – review & editing. SU: Data curation, Methodology, Writing – review & editing. LT: Conceptualization, Data curation, Methodology, Writing – review & editing. MÆ: Conceptualization, Data curation, Writing – review & editing. CB: Methodology, Resources, Supervision, Writing – review & editing. BS: Supervision, Writing – original draft, Writing – review & editing. ØU: Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2023.1274583/full#supplementary-material

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# Comparison of off-clamp microwave scissors-based sutureless partial nephrectomy versus on-clamp conventional partial nephrectomy in a canine model

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**Objectives:** To compare the usefulness and safety of off-clamp microwave scissors-based sutureless partial nephrectomy (MSPN) with on-clamp conventional partial nephrectomy (cPN) in dogs.
**Methods:** We performed off-clamp MSPN using microwave scissors (MWS) in six dogs, and on-clamp cPN in three dogs, in two-stage experiments. The bilateral kidney upper poles were resected via a midline incision under general anesthesia. After 14 days of follow-up, the lower pole resections were performed. The renal calyces exposed during renal resections were sealed and transected using MWS in off-clamp MSPN and were sutured in on-clamp cPN. In the off-clamp MSPN group, the generator's power output of MWS was set as either 50 W or 60 W for each kidney side. We compared the procedure time (PT), ischemic time (IT), blood loss (BL), and normal nephron loss (NNL) between the two techniques using the Mann–Whitney *U*-test.
**Results:** We successfully performed 24 off-clamp MSPNs and 12 on-clamp cPNs. The off-clamp MSPN was significantly superior to on-clamp cPN in avoiding renal ischemia (median IT, 0 min vs. 8.6 min, $p < 0.001$) and reducing PT (median PT, 5.8 min vs. 11.5 min, $p < 0.001$) and NNL (median NNL, 5.3 mm vs. 6.0 mm, $p = 0.006$) with comparable BL (median BL, 20.9 ml vs. 23.2 ml, $p = 0.804$). No bleeding and major urine leakage were noted during the reoperations.
**Conclusions:** Off-clamp MSPN outperforms on-clamp cPN in lowering the risks of postoperative renal function impairment in dogs.

KEYWORDS

partial nephrectomy, off-clamp, microwaves, renal function, renal ischemia

Abbreviations
%KVR, percentage of kidney volume resected; BL, blood loss; cPN, conventional partial nephrectomy; EKV, estimated kidney volume; IT, ischemic time; KVR, kidney volume resected; MSPN, microwave scissors-based sutureless partial nephrectomy; LPN, laparoscopic partial nephrectomy; MWS, microwave scissors; NNL, normal nephron loss; PN, partial nephrectomy; RF, renal function; PT, procedure time.

## Introduction

Partial nephrectomy (PN) has become the "treatment of choice" for T1 renal cell carcinoma (1) since it achieved a similar oncologic outcome (2) to that of radical nephrectomy. Whereas, PN was superior to radical nephrectomy in preserving renal function (RF) (3) and reducing risks of cardiovascular disorders, which could contribute to the superiority of overall survival reported in large real-world databases (4).

PN conventionally involves hilar clamping and tumor removal followed by renorrhaphy (5). Hilar clamping can reduce blood loss and bring a clear surgical view that helps in accurate tumor excision. However, reducing renal ischemia and reperfusion injury demands a short clamping time and thus requires resecting the renal parenchyma quickly, repairing the collecting system if needed, and closing the parenchyma by suturing in a short time. Such fast suturing occasionally injures renal vessels, causing delayed bleeding, artery pseudoaneurysms, and arteriovenous fistula formation (6). Although hemostatic agents are used conveniently in renorrhaphy to reduce hemorrhage (7), their effects on other renovascular complications are limited. Moreover, they are foreign materials and still carry risks of infection and allergic reactions.

Sutureless PN is an alternative procedure in which the resected bed is ablated and sealed using energy devices such as radiofrequency sealers (8) and coagulators (9), ultrasound sealers (10), laser probes (11), microwave probes (12, 13), and so on, to control renal bleeding. These devices obtained effective outcomes for patients with small and superficial tumors. However, sutureless PN with a short clamping time for large and highly complex tumors is still challenging due to their suboptimal device tip shapes and insufficient sealing function.

Recently, microwave scissors (MWS), which install a microwave irradiation function into mechanical scissors (14), have enabled operators to perform tissue microwave coagulation, vessel sealing, and mechanical cutting smoothly. The MWS was designed as a scissor-shaped surgical instrument, suitable for use in both open and laparoscopic surgery. Therefore, operators can naturally employ their skills and techniques, similar to using traditional scissor instruments. Excellent clinical track records have been reported in partial pancreatectomies (15), lung segmentectomies (16), colectomies (17), and thyroidectomies (18). Microwaves intrinsically induce dielectric heat by oscillating the dipoles such as water molecules in tissues. This heating process is more direct and faster than that induced by other energy forms, making them an excellent energy source for tissue coagulation (19). These reports suggest a hypothesis that the MWS could have a sufficient sealing function in organs with high blood perfusion, such as kidneys, and the use of MWS can enable PN to be performed in short/zero ischemic time.

We propose and evaluate a novel sutureless PN technique without hilar clamping using MWS. In this study using a canine model, we evaluate the feasibility of off-clamp microwave scissors-based sutureless partial nephrectomy (MSPN), compare its usefulness and safety with on-clamp conventional partial nephrectomy (cPN), and assess the histopathological changes of renal tissue after thermal injury induced by MWS.

## Methods

### Microwave scissors

The MWS (Acrosurg Revo S, Nikkiso Co., Ltd., Tokyo, Japan) is shown in Figure 1. The fixed and rotational scissor blades are the extension of the inner and outer conductors (14) of the microwave-

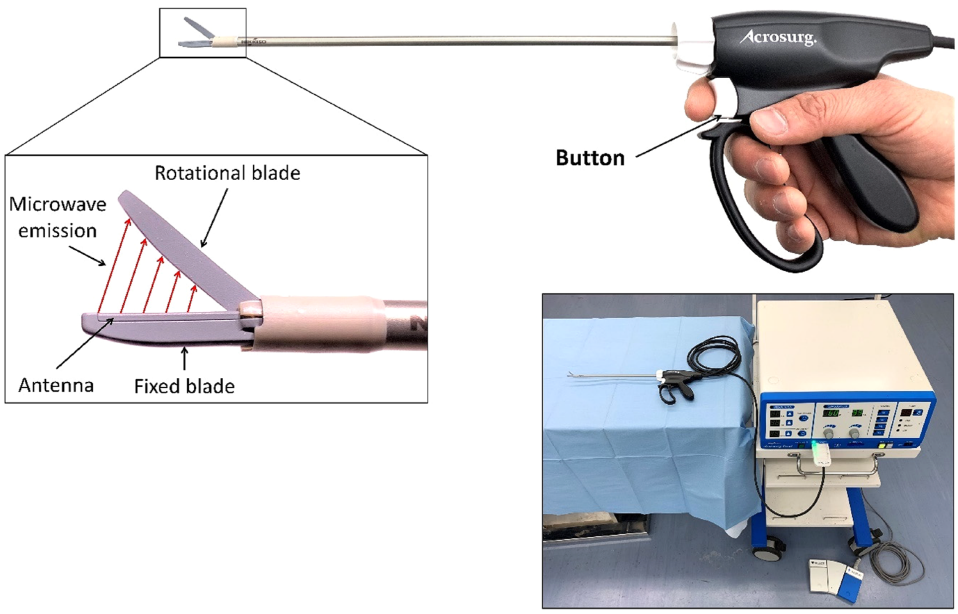


FIGURE 1
The microwave scissors and their generator (right-lower corner).

transmitted coaxial cable connected to a 2.45 GHz microwave generator. Microwaves are emitted from the fixed blade to the rotational blade while pushing the button or the footswitch, creating an alternating electric field on the tissue placed between the scissor blades. This electric field intrinsically induces dielectric heat by oscillating the dipoles such as water molecules at a frequency of 2.45 GHz, causing direct tissue coagulation without heat sink effects (19). The microwave irradiation time and cutting timing can be arbitrarily adjusted (14), allowing the MWS to be used flexibly and adaptively as cold scissors, scissors for cutting with seamless sealing, or a simple microwave coagulator without cutting. When the operators gently grasp tissue using scissor blades, irradiate microwaves, and then mechanically cut them, the MWS can seamlessly seal the tissue like bipolar radiofrequency and ultrasonic sealers (18, 20). When the operators close or partially open the scissor blades, and touch the scissor-blade side to the bleeding tissue while irradiating microwaves (18, 21), the interblade microwave irradiation induces an electric field around the scissors, causing dielectric heat that can coagulate tissue and stop bleeding.

## Animals and surgeries

Eleven beagles weighing approximately 10 kg each raised in a pathogen-free environment were used for this study. We used the first two dogs to assess the feasibility of off-clamp MSPN and to determine the generator's power outputs that are suitable for the kidneys. The pilot-phase data was not included in this article. In the main-phase study, nine dogs were divided into two groups: (1) the off-clamp MSPN group in which PN without hilar clamping or renorrhaphy using MWS was performed in six dogs, and (2) the control group involving three dogs for on-clamp cPN.

The experiments were performed in two stages under general anesthesia. For the first stage, each dog was placed in a supine position. The upper poles of both kidneys were resected via a 15-cm-midline incision. After 14 days of follow-up, we reoperated the dogs to inspect for postoperative complications and perform bilateral lower pole resections as the second stage. All procedures were performed at the level of either the upper or lower polar line of each kidney. At the end of the second stage, we performed euthanasia for remnant kidney sampling.

For off-clamp MSPN, we performed renal resections using only MWS without hilar clamping or renorrhaphy, as shown in **Figures 2A–C**. The generator's power output of MWS was alternately set at either 50 W or 60 W for each kidney side. We subgrouped every three dogs to perform off-clamp MSPN with or without precoagulation. In the non-precoagulation subgroup, we used the MWS to bite and seal the renal parenchyma and then cut them mechanically while slightly lifting the resected tissue using forceps with the other hand. The renal calyces and vessels exposed during renal resections were sealed and transected using MWS. The resected bed, if oozing, was recoagulated using MWS to consolidate hemostasis. In the precoagulation subgroup, we coagulated the excision line using MWS before performing the same manner described above to minimize the BL.

For on-clamp cPN, we performed hilar clamping and renal resection followed by suturing as shown in **Figures 2D–F**. Initially, we separately clamped the renal artery and vein using bulldog clamps (FB330R, Aesculap B-Braun, Melsungen, Germany). The renal parenchyma was resected using Metzenbaum scissors. Finally, we performed renal suturing in two layers. We sutured the renal medulla and the opening of renal calyces using a running suture (Monodiox 3-0, Alfresa Pharma, Osaka, Japan). The renal parenchyma was reconstructed using interrupting sutures (Opepolyx-N 2-0, Alfresa Pharma, Tokyo, Japan). Additional sutures were carried out if bleeding persisted after hilar declamping.

## Outcome measurements

We recorded kidney size, kidney volume resected (KVR), ischemic time (IT), procedure time (PT), blood loss (BL), and normal nephron loss (NNL) of the remaining kidneys. The estimated kidney volume (EKV) was calculated using the ellipsoid sphere volume formula, $V = \frac{4\Pi}{3} d_1 d_2 d_3$; where $d_1$, $d_2$, and $d_3$ indicate the length, width, and thickness of an ellipsoid sphere, respectively. The percentage of kidney volume resected (%KVR) was determined by dividing the KVR by the EKV. The PT was counted from the beginning of renal resection until the bleeding from the resected bed was completely controlled, using MWS in off-clamp MSPN or by renorrhaphy in on-clamp cPN, respectively. The IT was the clamping time in on-clamp cPN. The BL was determined by subtracting the preoperative weight of dry gauze from the postoperative weight of the corresponding blood-soaked gauze after each procedure. The NNL was determined as the largest depth measured from the resection line to the edge of either the thermal injury zone in the renal remnants induced by MWS-based coagulation in off-clamp MSPN or the suturing zone in on-clamp cPN, as observed in histopathological images.

The dogs were monitored for postoperative complications during 14 days of follow-up after the first-stage experiment. During the second stage, aspects of the intra-abdominal condition, such as remnant kidney status, ascites, hematoma, and internal bleeding from the upper pole resections in the first stage, if any, were recorded.

## Histopathological evaluation

To assess the macroscopic features of the lateral thermal injury induced by MWS in off-clamp MSPN and the devascularization zone induced by renorrhaphy in on-clamp cPN, the renal remnants were sectioned perpendicular to the resected bed. Hematoxylin and eosin staining was performed for histopathological evaluation.

## Statistics

Data were analyzed using SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). The non-parametric Mann–Whitney *U*-test was used to confirm the differences in medians between the two quantitative groups. Statistical significance was defined by a $p$ value <0.05.

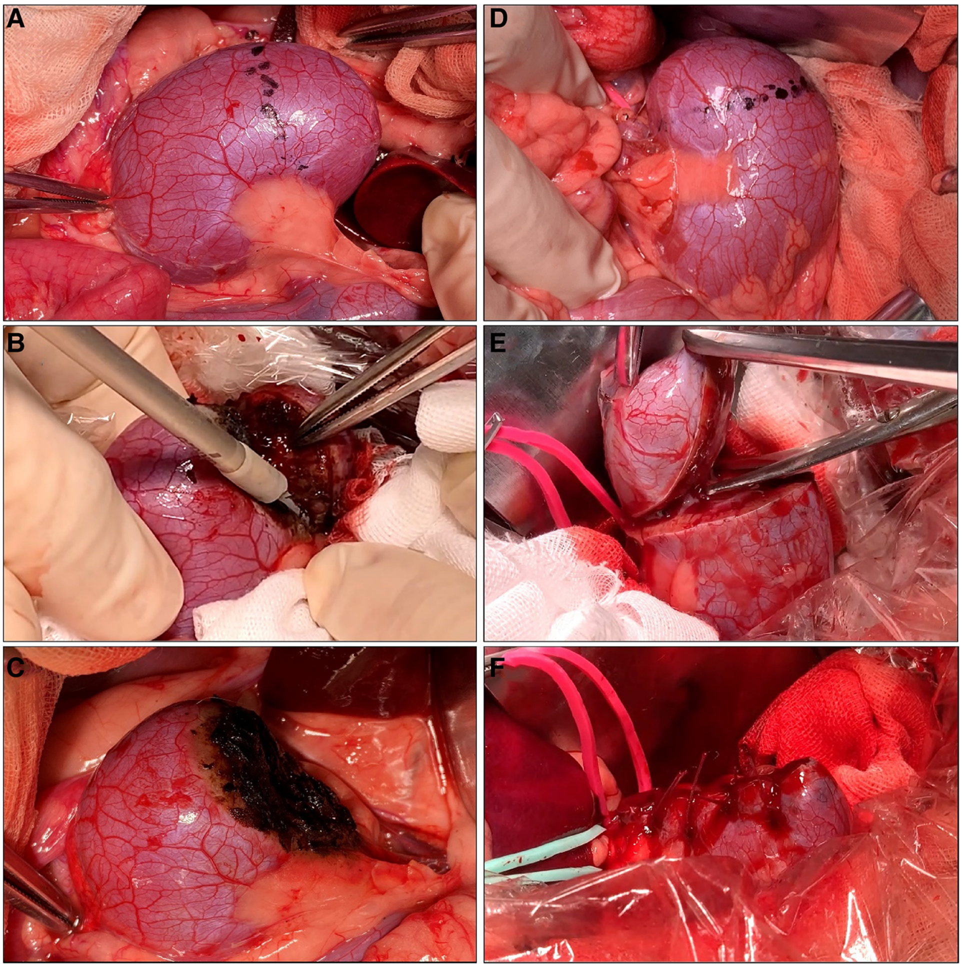


FIGURE 2
Off-clamp microwave scissors-based sutureless partial nephrectomy (MSPN) (A–C) and on-clamp conventional partial nephrectomy (cPN) (D–F) for upper pole resections. The excision line was marked at the level of the upper polar line (A,D). The kidney's upper poles were resected using microwave scissors (MWS) (B) without hilar clamping in off-clamp MSPN or using Metzenbaum scissors (E) after hilar clamping in on-clamp cPN. The resected beds were coagulated using MWS without renorrhaphy (C) in off-clamp MSPN, or sutured (F) in cPN.

# Results

## Perioperative results

We successfully performed 24 off-clamp MSPNs and 12 on-clamp cPNs. The perioperative outcomes of the two groups are presented in Table 1. All dogs survived after 14 days of follow-up. Off-clamp MSPN was significantly superior to on-clamp cPN in avoiding renal ischemia (median IT, 0 min vs. 8.6 min, $p < 0.001$), shortening PT (median PT, 5.8 min vs. 11.5 min, $p < 0.001$), and reducing NNL (median NNL, 5.3 mm vs. 6.0 mm, $p = 0.006$) with comparable BL (median BL, 20.9 ml vs. 23.2 ml, $p = 0.804$).

Except for two procedures in the non-precoagulation subgroup that had an outlier BL (68.2 ml and 130.4 ml), all other off-clamp MSPNs had BL of <45.2 ml. The renal parenchyma was torn during renorrhaphy in one on-clamp cPN, and required additional sutures, resulting in a deeper NNL (8.7 mm). The renal calyx was seamlessly sealed using MWS or sutured to prevent urine leakage in 16 off-clamp MSPNs (66.7%) and 7 on-clamp cPNs (58.3%). No complications such as bleeding and major urine leakage (recognized by ascites appearance) were noted during the reoperations.

**TABLE 1 Perioperative outcomes of off-clamp MSPN and on-clamp cPN in dogs.**

| Parameter | Off-clamp MSPN (*n* = 24) | On-clamp cPN (*n* = 12) | *p* value* |
|---|---|---|---|
| KVR (g), median (range) | 4.5 (2.9–6.0) | 4.6 (3.5–6.0) | 0.402 |
| %KVR (g), median (range) | 15.2 (9.4–24.0) | 16.2 (11.1–20.6) | 0.908 |
| PT (min), median (range) | 5.8 (3.1–13.4) | 11.5 (8.2–13.5) | <0.001 |
| IT (min), median (range) | 0 (0–0) | 8.6 (7.8–10.6) | <0.001 |
| BL (mL), median (range) | 20.9 (8.0–130.4) | 23.2 (13.1–45.7) | 0.804 |
| NNL (mm), median (range) | 5.3 (3.8–6.6) | 6.0 (5.2–8.7) | 0.006 |
| Calyceal sealing/suturing, *n* (%) | 16 (66.7) | 7 (58.3) | – |
| Urine leakage, *n* | 0 | 0 | – |
| Postoperative bleeding, *n* | 0 | 0 | – |

KVR, kidney volume resected; %KVR, percentage of kidney volume resected; PT, procedure time; IT, ischemic time; BL, blood loss; NNL, normal nephron loss.
*Mann–Whitney *U*-test.

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Subgroup comparison demonstrated that precoagulation caused a significantly lesser BL compared to non-precoagulation in off-clamp MSPN (median BL, 17.5 ml vs. 33.5 ml, $p = 0.028$). The PT and BL in the 50-W subgroup were greater than those in the 60-W subgroup, albeit without statistical significance. Off-clamp MSPN resulted in a significantly shallower NNL compared to cPN, as observed on both day 0 (median NNL, 5.4 mm vs. 6.2, $p = 0.049$) and day 14 (median NNL, 5.1 mm vs. 5.9 mm, $p = 0.049$) postoperatively.

## Tissue changes after MWS-based coagulation and renorrhaphy-induced devascularization

Both microwave coagulation and renorrhaphy result in tissue necrosis. Figure 3 shows the hematoxylin and eosin staining of the resected specimen and the remaining kidney after off-clamp MSPN. The MWS-induced thermal injury included two zones: (1) the near zone, which had closer contact with the scissor

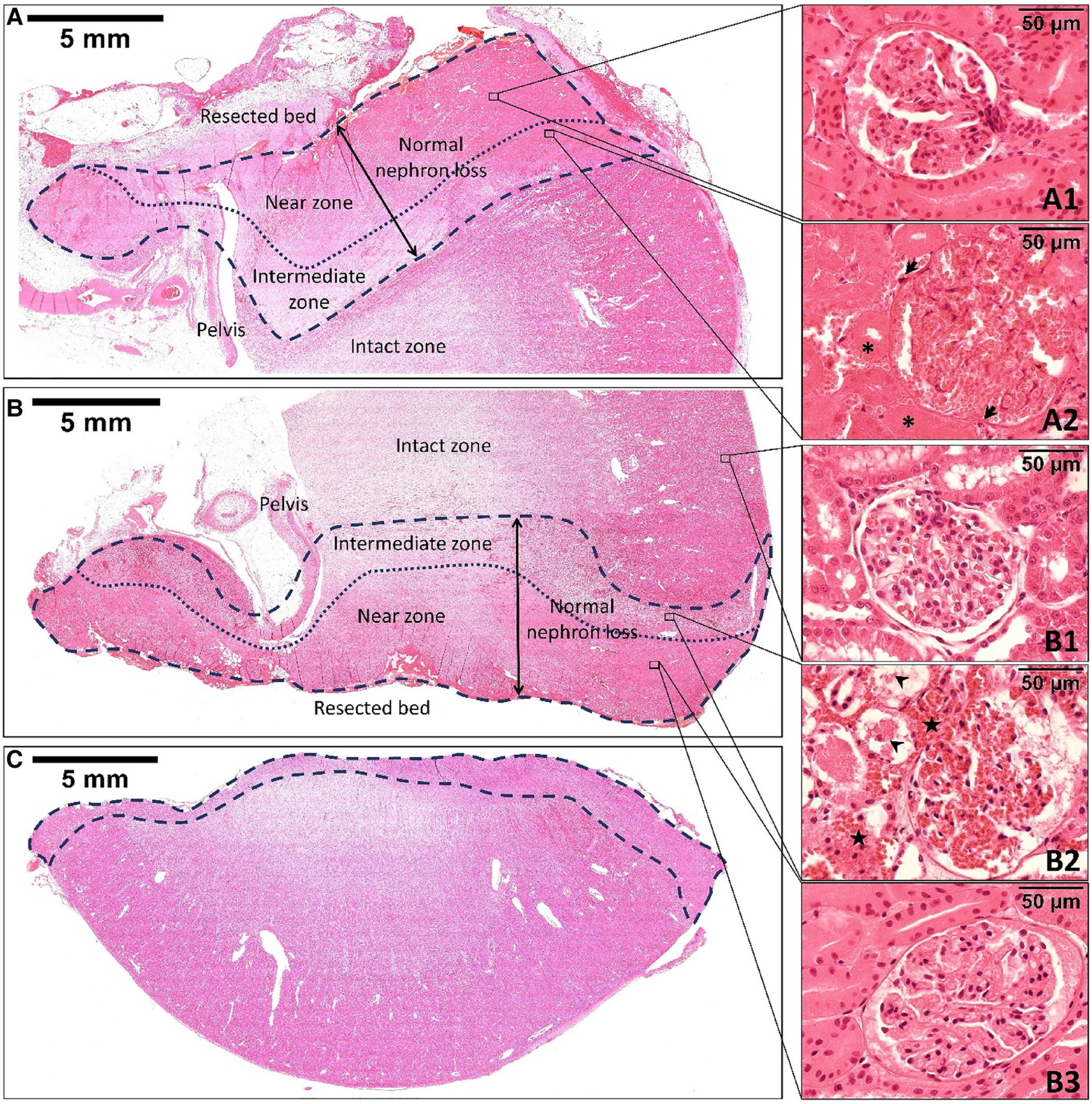


FIGURE 3
The hematoxylin and eosin staining of the remnant kidney's upper pole at the two-week follow-up (A), the remnant kidney's lower pole (B), and the resected specimen (C) immediately after off-clamp microwave scissors-based sutureless partial nephrectomy. The area limited by the dashed line indicates the thermal injury zone. The dotted line divides the thermal injury zone into two zones: the near zone and the intermediate zone. The morphology of the renal tissue in the near zone was well maintained for up to two weeks postoperatively (A1, B3). However, the renal tubular cells and glomeruli were slightly smaller than those in the intact zone (B1). The intermediate zone (B2) was characterized by the extravasation of erythrocytes (stars) into interstitial spaces. The renal tubular cells were sporadically ruptured and detached into the lumen (arrowheads). Two weeks postoperatively, the intermediate zone (A2) exhibited coagulative necrosis that was characterized by the disappearance of tubular cells' nuclei (asterisks), infiltration of macrophages and neutrophils (arrows), and fibrosis formation.

blades, and (2) the intermediate zone, which separated the near zone from the intact zone. Although the morphology of renal glomeruli and tubules including nuclear staining (Figures 3A1, B3) was well maintained for up to two weeks postoperatively in the near zone, we noted that the cell membranes disappeared, the cytoplasm looked homogeneous, and erythrocytes were completely disrupted. These properties were not found in the intact zone (Figure 3B1). The intermediate zone (Figure 3B2) was characterized by the extravasation of erythrocytes into interstitial spaces, and the renal tubular cells that were sporadically ruptured and detached into the lumen. Two weeks postoperatively, the intermediate zone exhibited coagulative necrosis that was characterized by the infiltration of macrophages and neutrophils, as well as degeneration of the renal glomeruli and tubules with nuclear disappearance, and fibrosis (Figure 3A2).

On the other hand, the suturing zone observed two weeks after operations (Figure 4) exhibited blood congestion and tissue necrosis with the infiltration of macrophages and neutrophils, degeneration of renal glomeruli and tubules, and fibrosis. We noted that the nuclei of renal tubular cells were completely lost.

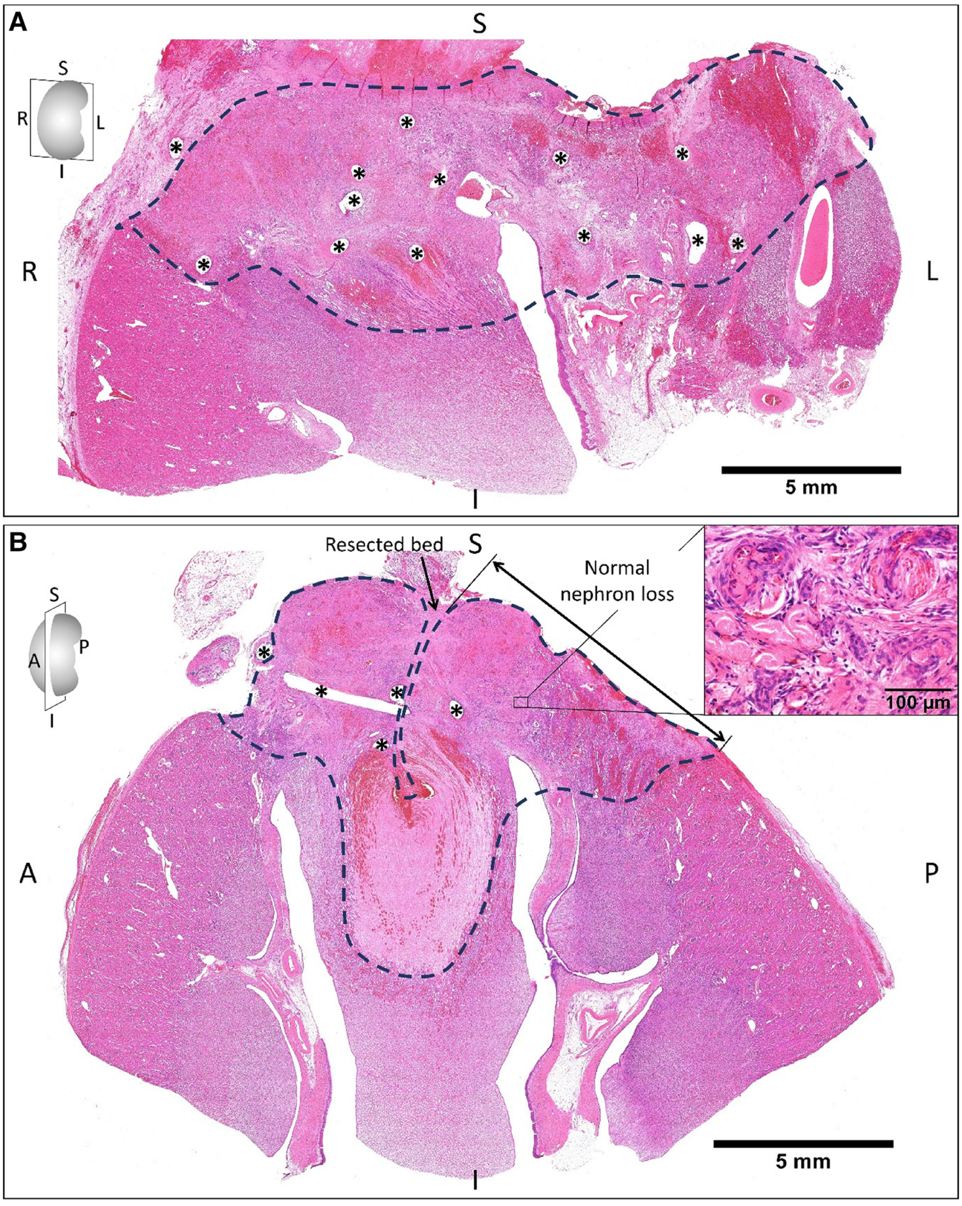


FIGURE 4
The hematoxylin and eosin staining of the remnant kidney sectioned on coronal (A) and sagittal planes (B) two weeks after on-clamp conventional partial nephrectomy. The areas limited by the dashed line indicate the devascularization zone induced by renorrhaphy (asterisks are suturing holes), which exhibited blood congestion and tissue necrosis (B, right-upper corner) with the infiltration of macrophages and neutrophils, degeneration of renal glomeruli and tubules, and fibrosis. S, superior; I, inferior; R, right; L, left; A, anterior; P, posterior.

## Discussion

In this initial assessment in dogs, off-clamp MSPN was performed faster than on-clamp cPN with comparable BL and lesser NNL, albeit without hilar clamping. These findings demonstrated that MWS-based coagulation can adequately control renal bleeding in canine off-clamp PN without the requirement for renorrhaphy or hemostatic agents. In addition, we provided an understanding of the two-week renal tissue changes after thermal injury induced by MWS compared to the devascularization caused by renorrhaphy.

### Off-clamp sutureless PN vs. on-clamp cPN with renorrhaphy

In on-clamp cPN, the hilar clamping-induced renal injury and the healthy parenchyma loss after surgery are responsible for the RF decreases (22), and were considered modifiable targets to preserve postoperative RF. Although no differences in RF decreases were found between off-clamp and on-clamp robotic PN in patients with two kidneys, regular baseline function, and tumors with a RENAL score ≤10 (23, 24), off-clamp is superior to on-clamp PN in preventing acute kidney injury and new-onset stage ≥3b chronic kidney disease in solitary kidney patients (25, 26). These findings suggest that on-clamp PN with limited renal ischemia is acceptable in patients with two normal kidneys (24). However, hilar clamping should be avoided when technically feasible for patients with solitary kidneys or low baseline RF (25, 26).

Mir et al. (27) analyzed pre- and postoperative renal parenchymal volume using computed tomography imaging and reported that a median of 83% (interquartile range: 75–91) of functioning parenchyma was preserved after PN. A strong correlation was observed, with the percentage of parenchymal volume saved being the strongest predictor ($p < 0.001$) of the percentage of glomerular filtration rate saved. In other words, healthy parenchyma loss is primarily responsible for RF decrease after surgery. Healthy parenchyma loss involves non-neoplastic parenchyma excised with the tumor and normal volume loss induced by devascularization/ablation in the renal remnant (22). Currently, enucleation or resection of a thin rim along the plane of the tumor pseudo-capsule is sufficient to achieve a negative surgical margin (28). As a result, non-neoplastic parenchyma excised with the tumor does not significantly impact postoperative RF (29). Therefore, normal volume loss induced by devascularization/ablation may dominantly contribute to RF decrease after PN. Indeed, modifying the reconstruction technique, ideally reducing normal volume loss, significantly improves postoperative RF (30).

In our study, the calculation of normal volume loss was not technically feasible because of limited facilities. Therefore, we evaluated the parameter "NNL"—the largest depth of normal volume loss measured from the resection plane, as shown in **Figures 3**, 4. The present study demonstrated that coagulation of the resected bed using MWS significantly reduced NNL compared to renorrhaphy. Consequently, we consider that off-clamp MSPN can reduce the risks of RF impairment by avoiding renal ischemia and preserving healthy parenchyma. On the other hand, renorrhaphy might be hastily terminated in the race against the clamping time without adequate hemostasis of the resected bed. The renal parenchyma might be torn during renorrhaphy, requiring additional deeper suturing. Furthermore, the suture needle occasionally transects the renal vessels, resulting in renovascular complications (6). Considering these challenges, we believe that employing MWS to control renal bleeding in off-clamp MSPN could reduce the procedural burden, time consumed for suturing, and perioperative complications by eliminating the need for renorrhaphy.

### The microwave thermal effects on renal tissue

We note that the histopathological changes of renal tissues after MWS-based coagulation are similar to those found in the livers after microwave ablation therapy (31, 32) reported previously, in which the morphology of the hepatocytes near the microwave coagulator was well maintained under light microscopy. However, the electron microscopy revealed serious damage to the nuclear and cytoplasmic membranes, with no apparent organelle structures such as mitochondria or endoplasmic reticulum (32). These findings could be explained that because the microwave dielectric heating was so rapid (19), tissue temperature in the near zone quickly reaches ablation range (33, 34) of 50°C–95°C. This immediately causes protein denaturation, rupture of phospholipid membranes, and destruction of cytoplasmic organelles and enzymes, resulting in irreversible cell death, whereas the tissue's structural outline was fixed. We believe that this fixation effect has relevance to the excellent hemostasis ability of MWS on kidneys observed in the present study. The absence of enzymic digestion (32) in the near zone resulted in the well-maintenance of renal tissue morphology for up to two weeks postoperatively.

In the intermediate zone, although the thermal effect gradually attenuates based on the negative temperature gradient, tissue temperature in the hyperthermia range (33) of 40.5°C–47°C, which is majorly induced by heat conduction (34), results in changing of the cell membrane permeability, leading to overaccumulation of metabolites and intracellular fluid shifts, subsequently causing cytolysis (33). Moreover, DNA and cytoplasmic organelle dysfunction secondary to protein aggregation and unfolding induced by hyperthermia (33) leading to cell death.

### The perspective and limitations of PN using MWS

Sutureless PN, which reduces technical burden by eliminating the need for renorrhaphy, is worthy of further research and development. Although several studies (8–13, 35, 36) have reported the feasibility of off-clamp sutureless PNs, these techniques limit the targets to small and low-complexity renal tumors. Brassetti et al. (36) demonstrated that the sutureless approach significantly increases trifecta achievement (negative surgical margin, no major complications, and no significant RF deterioration) compared to renorrhaphy in off-clamp robotic PN. However, the selection bias, where most patients in the sutureless group had small and uncomplex tumors, limits the generalizability of these findings. Currently, no off-clamp sutureless PN techniques are widely accepted by most urologists. On the other hand, on-clamp cPN can adequately achieve oncologic control with limited BL, for most patients with localized renal tumors, remaining the gold standard approach in nephron-sparing surgery (5).

We investigate a novel sutureless PN utilizing only MWS for renal resection and bleeding control. In this experimental study, we compared off-clamp MSPN vs. on-clamp cPN to primarily assess the capacity of MWS for controlling renal bleeding without renorrhaphy. Although the usefulness of off-clamp MSPN was demonstrated, its procedural success might be attributed to the open-surgery modality because the MWS was omnidirectionally manipulated, facilitating tissue coagulation and bleeding control in a short time. To inspect the impact of degrees of freedom on MWS manipulation in the minimally invasive surgery modality, we conducted a preliminary experiment in five kidneys from three pigs (21) following the present study. It demonstrated that off-clamp sutureless laparoscopic partial nephrectomy (LPN) using MWS is feasible for both middle and lower pole resections, mimicking various tumor locations in clinical scenarios. All pigs survived after three days of follow-up.

Even though hilar clamping was not performed, the off-clamp sutureless LPN using MWS (21) recorded shorter PT and lesser BL compared to porcine on-clamp LPNs (37, 38), in which renal bleeding was controlled with renal suturing (37, 38), renal suturing with hemostatic agents (38), or electrocautery with hemostatic agents (37), respectively. In addition, its BL (21) was lesser than that of off-clamp open PN using ultrasonic (39) or radiofrequency ablation devices (39), in similar porcine renal resections reported previously. To our knowledge, the cost of MWS is lower than that of other devices usually employed for dissection in conventional LPN, such as bipolar radiofrequency or ultrasonic devices. Consequently, we consider that the use of MWS can provide an affordable surgical treatment to improve patients' outcomes not only in open PNs but also in LPNs. Moreover, if the MWS was installed into surgical robots, the realized "off-clamp MWS-based sutureless robotic PN" could provide dexterous and precise manipulation of MWS like MSPN in open surgery shown in this study with microwave coagulation-based excellent renal bleeding control.

It is crucial in MSPN that the surgeons sufficiently coagulate the tissue before cutting and meticulously control the renal bleeding to maintain a clear surgical view during resections because the MWS does not have a feedback mechanism to monitor tissue conditions during the coagulation process. The lack of tissue-condition monitoring might result in the possibility of cutting tissue after premature coagulation, leading to improper vessel sealing and bleeding. Furthermore, stopping massive bleeding might require most of the irradiated microwave energy, which can diminish the coagulation effects of the MWS on tissues and eventually obscure the resection line.

This study remains several limitations. First, we did not evaluate the pre- and postoperative RF. It is necessary to evaluate the RF decrease of the affected kidneys to reach a definite conclusion on the functional benefits of the novel method. Second, a pyelogram was not performed. Although no major urine leakage confirmed the postoperative calyceal sealing effects, the pyelogram may provide further information such as extravasation, and pelvic stenosis complications. Third, it is necessary to compare off-clamp MSPN with off-clamp PN without MWS to evaluate the advantages of MWS compared to other devices and bleeding control methods. Finally, dog kidneys are smaller and not as well vascularized as human kidneys, limiting the translation of these findings to clinical scenarios. Therefore, additional studies in human-size animals are warranted.

In conclusion, the present study provides fundamental knowledge of renal tissue changes after thermal injury induced by microwaves. In this assessment in dogs, off-clamp MSPN outperforms on-clamp cPN in shortening PT and lowering the risks of RF impairment. MWS-based coagulation can adequately control perioperative renal bleeding in off-clamp canine PN without the need for renorrhaphy. We believe that PN using MWS is a promising surgical treatment modality for patients with localized renal tumors.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The animal study was approved by The Ethical Research Committee for Animal Life Science at the Shiga University of Medical Science. The study was conducted in accordance with the local legislation and institutional requirements.

## Author contributions

HN: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. AY: Data curation, Funding acquisition, Methodology, Writing – review & editing, Investigation. SN: Data curation, Investigation, Writing – review & editing. KM: Writing – review & editing. TT: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing, Investigation.

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## Conflict of interest

HN and TT belong to the joint research department of Shiga University of Medical Science and Nikkiso Co., Ltd. TT declares that he is the representative of Micron Shiga Inc. and the inventor of microwave scissors. Micron Shiga Inc. receives royalties provided by intellectual property of microwave scissors from Nikkiso Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note



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# Understanding tumor localization in multiparametric MRI of the prostate—effectiveness of 3D printed models

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**Introduction:** Understanding tumor localization in multiparametric MRI (mpMRI) of the prostate is challenging for urologists but of great importance in mpMRI-fused prostate biopsy or radical prostatectomy. The aim was to evaluate the effectiveness of 3D printed models of the prostate to help urologists to locate tumors.
**Methods and Participants:** 20 urologists from University Medical Center Mainz (Germany) were asked to plot the location of a cancer suspicious lesion (PI-RADS ≥ 4) on a total of 30 mpMRI on a prostate sector diagram. The following 3 groups (as matched triplets) were divided into: mpMRI only, mpMRI with radiological report and mpMRI with 3D printed model (scaled 1:1). Statistical analysis was performed using one-way and two-way ANOVA (with bonferroni post-test).
**Results:** Overall, localization of the suspicious lesion was superior with the radiological report (median of max. 10 [IQR]: MRI 2 [IQR 1;5], MRI + report: 8 [6.3;9], MRI + 3D model 3 [1.3;5.8]; $p < 0.001$). Residents with <1 year of experience had a significantly higher detection rate using a 3D printed model [5 (5;5.8)] compared to mpMRI alone [1.5 (1;3.5)] ($p < 0.05$). Regarding the estimation of index lesion extension, the 3D model showed a significant benefit (mean percentage difference [95% CI]: MRI alone 234% [17.1;451.5], MRI + report 114% [78.5;149.6], MRI + 3D model 17% [−7.4;41.3] ($p < 0.01$).
**Conclusion:** Urologists still need the written radiological report for a sufficient understanding of tumor localization. The effectiveness of the 3D printed model regarding tumor localization is particularly evident in young residents (<1 year) and leads to a better overall assessment of the tumor extension.

KEYWORDS
prostate, prostate carcinoma, prostate biopsy, MRI of the prostate, PI-RADS, 3D printed prostate model

## Introduction

Multiparametric Magnetic Resonance Imaging (mpMRI) of the prostate has become a standard diagnostic method for patients with suspected prostate cancer. The resulting mpMRI targeted prostate biopsy significantly increased the detection rate of clinically significant prostate cancer (1, 2). Therefore, mpMRI of the prostate has been implemented in several urological guidelines as mandatory diagnostic before prostate biopsy (2, 3). However, understanding mpMRI regarding tumor localization remains a major challenge for urologist and even radiologists worldwide (4–6). Physician's experience with mpMRI has shown to be an important factor for the reliable reporting of mpMRIs (7, 8). This is also reflected in a prolonged learning curve for reliably performing mpMRI targeted prostate biopsies (9).

Since these procedures are usually performed by residents it is crucial that they can gain a comprehensive understanding of mpMRI of the prostate quickly to ensure a sufficient detection rate of the prostate biopsy. This is particularly crucial for the indication of nerve sparing in the context of radical prostatectomy, as the quality of the preoperative biopsy represents a significant risk factor for a positive surgical margin (10). The use of printed three-dimensional (3D) prostate models or virtual 3D models of the prostate for surgical planning or education has been evaluated in several studies (7, 11, 12). It has shown to improve physicians' orientation and localization of suspicious lesions in mpMRI (7, 11) and can help with patient education as well (13).

Our study aimed to investigate the effectiveness of 3D printed prostate models regarding tumor localization in mpMRI. Furthermore, the study focuses on the impact of the 3D model on different levels of experience of urologists.

# Methods and participants

## Study design and population

A total of 20 urologists of different levels of experience (4 residents <1 years, 4 residents >3 years, 8 specialists >6 years and 4 senior specialists >10 years) were reviewed in this single-center, prospective study from June 2022 to December 2022. Each participant was asked to locate a singular suspicious lesion in the prostate-mpMRI of 30 cases in total. The localization was carried out by marking the lesion on the prostate sector diagram used by the European society of Urogenital Radiology and American College of Radiology (14). The 30 cases were divided into three equally sized groups as matched triplets. The first group included only the mpMRI sequences, so that the physician had no further information. The second group represented the clinical standard with mpMRI-sequences and radiological report. In the third group mpMRI-sequences were supplemented by a corresponding printed 3D model of the prostate (scaled 1:1) where the tumor was highlighted with red color. The duration of the survey was recorded with a stopwatch. At the end, each participant received a 10-item questionnaire (5-point Likert scale; 1: very poor; 2: poor; 3: fair; 4: good; 5: excellent) that asked about the perceived usefulness of the 3D model and the perceived certainty in mpMRI reporting.

## mpMRI of the prostate

All mpMRI sequences were realized using 3-Tesla mpMRI at our center, which included T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), diffusion weighted imaging (DWI) and dynamic contrast-enhanced MR imaging (DCE-MRI). A special T2WI sequence with 1 mm layer thickness was created for a more seamless printing of the 3D prostate models. Assessment of the mpMRI studies was performed according to the Prostate Imaging and Reporting Data System (PI-RADS) version 2.1. Only singular target lesions found with PI-RADS 4 or 5 were used for this study. In each of the three groups, we collected 7 cases with PI-RADS 4 and 3 cases with PI-RADS 5. There was no limitation in target lesion size. The target lesion size ranged from 3 to 408 $mm^2$. Same side, level, zone and PI-RADS score of the lesion, as well as similar prostate size were used to create matched triplets. Cases with multiple lesions and a prostate volume of >100 ml were excluded.

## Printed 3D models

Segmentation of the 3D prostate models was realized with the DICOM files (Digital Imaging and Communications in Medicine) of the mpMRI sequences with 1 mm layer thickness using Materialise Mimics® (Version 24.0.0.427) and 3-matic® (Version 16.0) (Materialise NV, Leuven, Belgium). The digitalized 3D model was then exported and printed using the UltiMaker® 3 Extended with dual extruder (released 2015, Ultimaker®, Utrecht, Netherlands). Prostate and both seminal bladders were printed continuously with a transparent polylactic acid filament (PLA), whereas the tumor was printed into the prostate using a PLA-filament in bright red color (**Figure 1**).

## Data acquisition

For the interviews, the mpMRI sequences were sorted alphabetically by patient name. Thus, the matched triplets were not comprehensible for the participant. For data analysis, the cases were reorganized according to the matched triplets so that a comparison was possible. Primary Outcomes were side (left or right), level (basis, midgland, apex), zone (e.g., lateral peripheral) and exact location of the lesion (if all previous outcome items were correct). Location of the index lesion was marked on the prostate sector diagram (14). The score for each outcome item was binary (correct or false), so that the maximum score for each outcome item was 10. The scoring system is further explained in **Figure 2**. Secondary Outcome was the duration of the interview as well as the percentage deviation of the area of the lesion, but only in those cases where the exact location was correct. The area extension was measured from the markings on the prostate sector diagram (14) by of the participant and compared with the radiologist's markings (**Figure 3**).

## Statistical analysis

Statistical analysis was performed using one-way and two-way ANOVA (with bonferroni post-test). All data were analyzed using GraphPad PRISM® 5 (Version 5.01, 2007, GraphPad Software Inc., Boston, USA). Statistical significance was defined as $p < 0.05$.

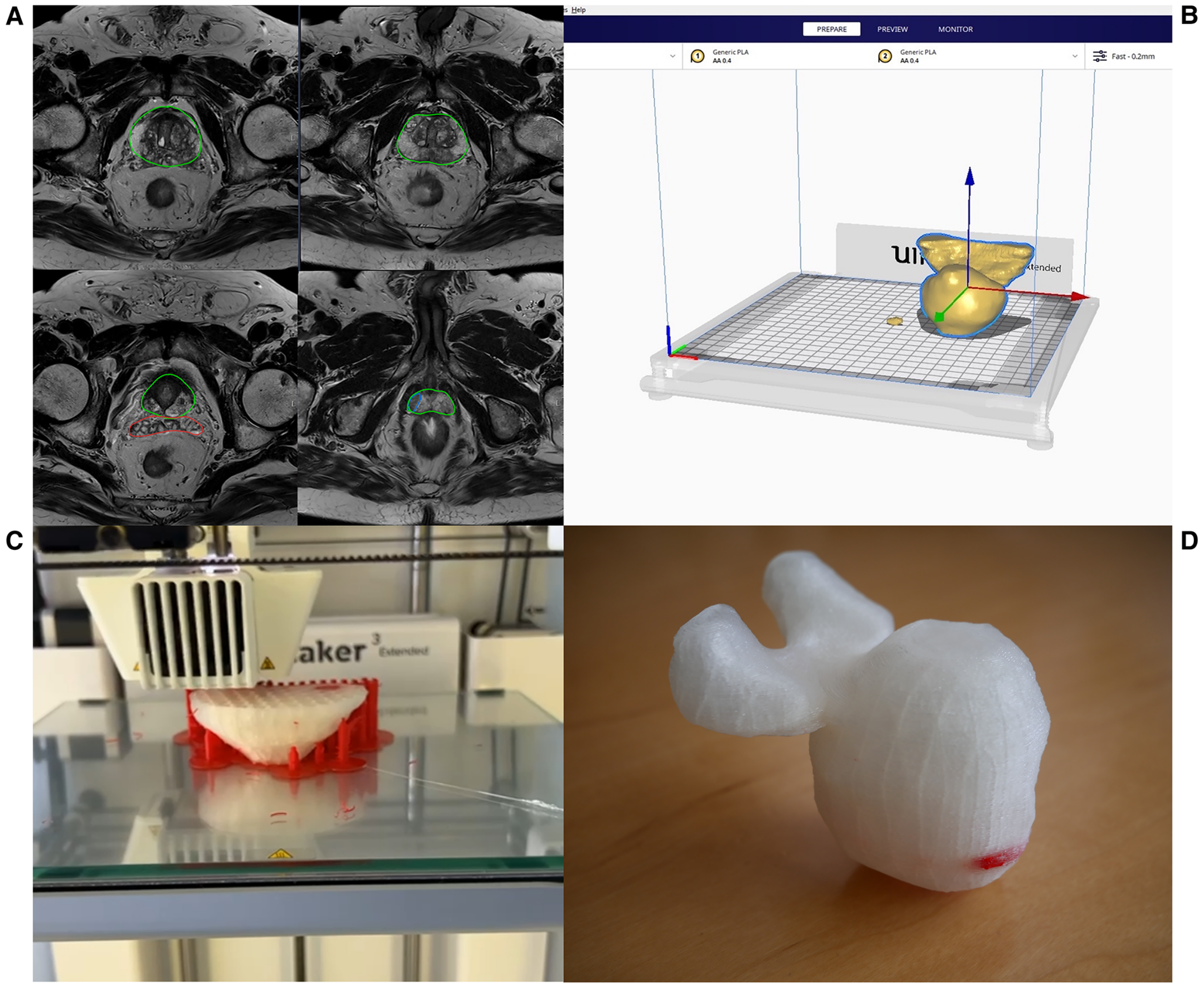


FIGURE 1
Prostate segmentation from mpMRI series (A), digitalizing the 3D model (B), 3D printing (C), finished 3D printed prostate model with the tumor indicated in bright red color (D).

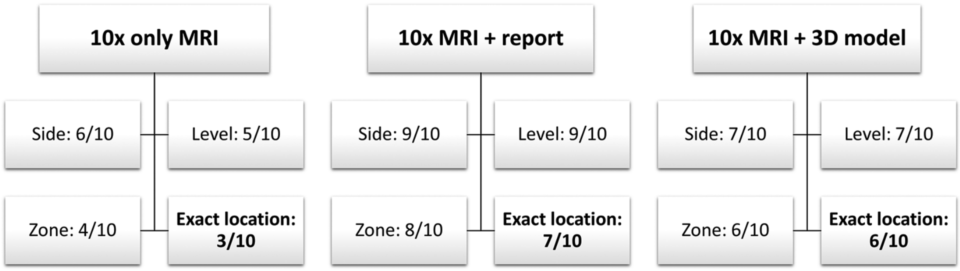


FIGURE 2
Exemplary scoring of primary outcomes (side, level, zone and exact location) of one participant in all 3 groups (only MRI, MRI + report and MRI + 3D model).

# Results

## Tumor localization and extension

Overall, tumor localization was superior in all primary outcome items when using mpMRI and radiological report: side [6 (5;7) vs. 10 (10;10) vs. 8 (6.3;10); $p < 0.001$], level [4 (2.3;6) vs. 10 (9;10) vs. 5 (4;6.8); $p < 0.001$], zone [5 (4;6.8) vs. 8 (7;9) vs. 5.5 (3;8); $p < 0.001$] and exact location [2 (1;5) vs. 8 (6.3;9) vs. 3 (1.3;5.8); $p < 0.001$] (Table 1). The most correct localization was achieved by the >10-year senior specialists with the additional use of the radiological findings (Figure 3). The >3-year residents

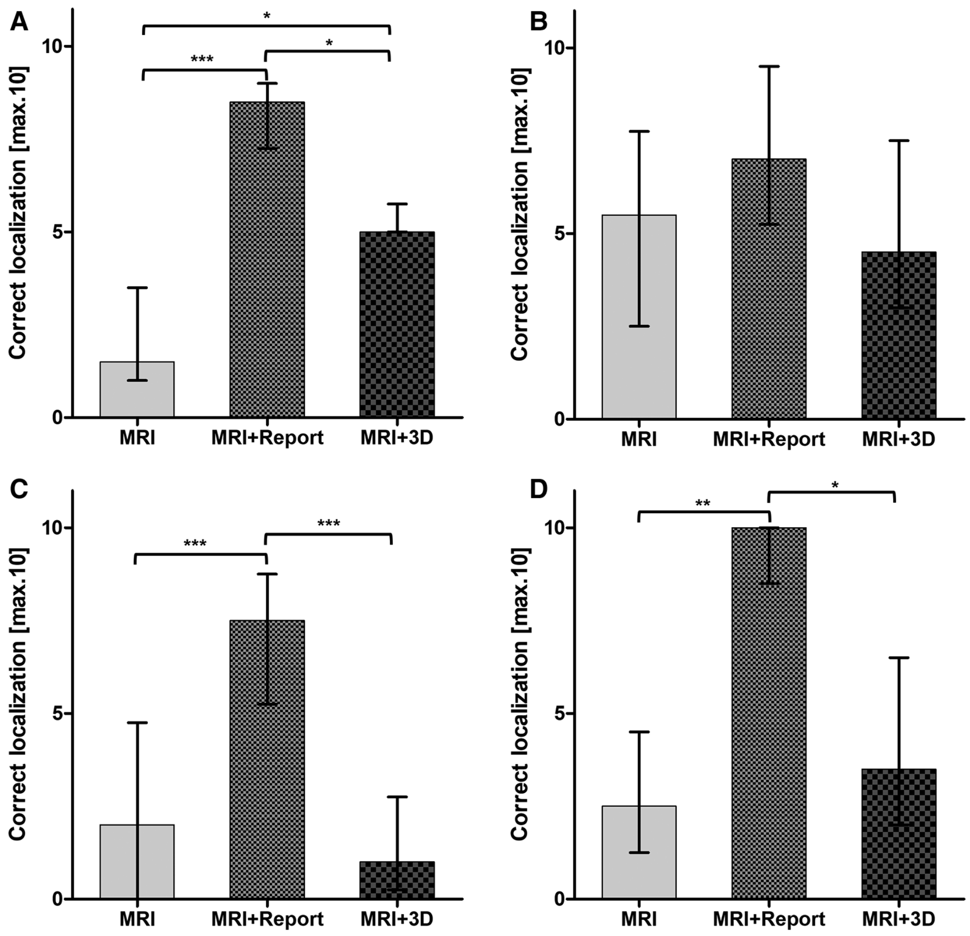


FIGURE 3
Correct localization of the index lesion in all three modalities differentiated into four groups of experience: (A) <1 year residents; (B) >3 year residents; (C) >6 year specialists; (D) >10 year senior specialists. Statistical significance was $p < 0.05$.

TABLE 1 Localizations and deviation of the lesion extension in the three modalities.

| $n = 20$ | MRI | | MRI + report | | MRI + 3D-model | |
|---|---|---|---|---|---|---|
| | Median [IQR] | Mean [95% CI] | Median [IQR] | Mean [95% CI] | Median [IQR] | Mean [95% CI] |
| Side | 6 [5;7] | | 10 [10;10] | | 8 [6.3;10] | |
| Level | 4 [2.3;6] | | 10 [9;10] | | 5 [4;6.8] | |
| Zone | 5 [4;6.8] | | 8 [7;9] | | 5.5 [3;8] | |
| Exact location | 2 [1;5] | | 8 [6.3;9] | | 3 [1.3;5.8] | |
| <1 year ($n = 4$) | 1.5 [1;3.5] | | 8.5 [7.3;9] | | 5 [5;5.8] | |
| >3 year ($n = 4$) | 5.5 [2.5;7.8] | | 7 [5.3;9.5] | | 4.5 [3;7.5] | |
| >6 year ($n = 8$) | 2 [0;4.8] | | 7.5 [5.3;8.8] | | 1 [0.3;2.8] | |
| >10 year ($n = 4$) | 2.5 [1.3;4.5] | | 10 [8.5;10] | | 3.5 [2;6.5] | |
| Area deviation [%] | | 234 [17.1;451.5] | | 114 [78.5;149.6] | | 17 [−7.4;41.3] |

showed no significant difference between all 3 groups and performed best when given only the mpMRI sequences (Table 1; Figure 3). A significant benefit of the 3D prostate model compared with mpMRI reporting alone could be shown within the <1-year residents [5. (5;5.8) vs. 1.5 (1;3.5); $p < 0.05$] (Figure 3).

Participants overestimated the lesion extension by a mean of 234% with mpMRI alone. The overestimation decreased to 114% with the radiological report. The most accurate assessment of the tumor extension was achieved with the 3D model (17%) (Figure 4).

Mean survey duration was 47.7 min [38.9;56.6]. Fastest completion time with 31.7 min on average [27.9;35.5] was recorded in the >3-year residents. Unsurprisingly, the <1-year residents took the longest time to complete the survey [58.6 (19.2;97.8)]. However, the times did not differ significantly between the experience categories ($p = 0.394$).

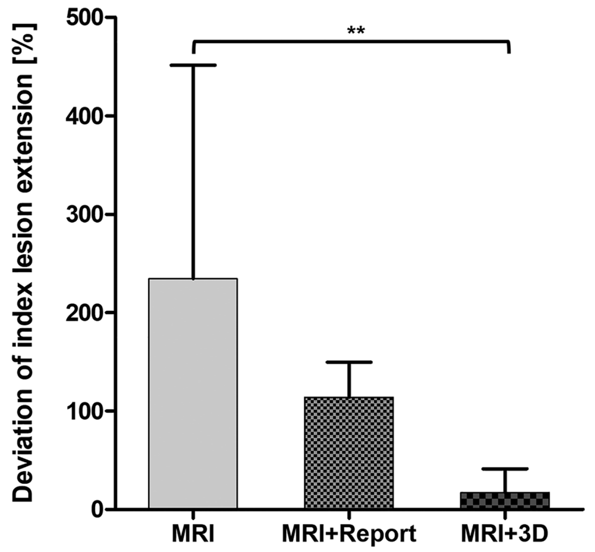


FIGURE 4
Deviation of index lesion extension marked on the prostate sector diagram. Statistical significance was $p < 0.05$.

## Perceived usefulness and certainty in reporting

Most participants found the use of the 3D model in locating the lesion very useful [4.4 (4;4.8)] (Table 2). However, estimated benefits of the 3D prostate model on pre- or intraoperative usage regarding radical prostatectomy was moderate [3.6 (3.1;4.1) vs. 3.9 (3.4;4.3)]. The 3D prostate model was perceived to be useful regarding training of inexperienced surgeons or biopseurs as well as patient education [4.6 (4.3;4.9) and 4 (3.4;4.6)]. The certainty in localizing the index lesion was the same using the radiological report and the 3D prostate model [4.2 (3.9;4.5) vs. 4.2 (3.7;4.6)]. However, the uncertainty in the localization increased when only the mpMRI was available [2.5 (2;3.1)].

TABLE 2 Questionnaire for perceived usefulness and certainty in reporting on a 5-point Likert scale (1: very poor; 2: poor; 3: fair; 4: good; 5: excellent).

| Number | Question | Mean [95% CI] |
|---|---|---|
| 1 | How helpful do you find the use of the 3D model in locating the index lesion? | 4.4 [4;4.8] |
| 2 | How well do you think the 3D model reflects the anatomical conditions? | 4.5 [4.2;4.9] |
| 3 | How great do you see the benefit of the 3D model in preoperative planning (e.g. in relation to nerve sparing)? | 3.6 [3.1;4.1] |
| 4 | How useful do you think the 3D model is intraoperatively? | 3.9 [3.4;4.3] |
| 5 | How well do you think the 3D model can be implemented in the training of inexperienced surgeons/biopseurs? | 4.6 [4.3;4.9] |
| 6 | How useful do you consider the 3D model in terms of patient education and preoperative preparation? | 4 [3.4;4.6] |
| 7 | How high do you see the benefit of the 3D model in terms of time efficiency? | 3.7 [3.1;4.2] |
| 8 | How confident do you feel in locating the index lesion with radiological findings and MRI sequences? | 4.2 [3.9;4.5] |
| 9 | How confident do you feel in locating the index lesion with 3D-prostate model and MRI sequences? | 4.2 [3.7;4.6] |
| 10 | How confident do you feel in locating the index lesion using only the MRI sequences? | 2.5 [2;3.1] |

# Discussion

A precise knowledge of the tumor localization in mpMRI is mandatory for an accurate targeted prostate biopsy. In many cases, the biopseur has to transmit the region of interest onto the ultrasonic image for a mpMRI-Ultrasound fusion biopsy or perform a cognitive targeted biopsy (9, 15). Even in radical prostatectomy, a detailed understanding of the tumor localization in mpMRI as well as a high quality prostate biopsy is essential for safe resection margins and nerve sparing (10, 16). However, achieving a comprehensive understanding of mpMRI is still a major challenge for many urologists worldwide (4, 5) and requires a high level of experience (4, 7, 9, 17). After implementation of mpMRI and targeted prostate biopsies into the EAU-guidelines as the gold standard diagnostic for prostate cancer (3) the demand for targeted prostate biopsies has increased drastically. With a progressing shortfall of healthcare workers relative to population growth the number of highly trained urologists is declining as well (18–21). This effect is especially aggravating in rural areas, as specialists tend to gravitate towards urban settings (20). The divergence in demand and resources could lead to inexperienced urologists performing targeted prostate biopsies. To address this issue, technologies have evolved to help with three-dimensional orientation, planning and education, such as printed 3D models and virtual reality (7, 11, 22). The effectiveness of these tools has been demonstrated in several studies before, but there is still too little data to justify a more widespread use.

Therefore, the aim of this study was to provide more data on the effectiveness of 3D printed models of the prostate and focus on the impact on different levels of urologists' experience. Consistent with some previous findings (4), urologists of different levels of experience were found to require written radiological findings for reliable interpretation of mpMRIs (Table 1). Interestingly residents with >3 years of experience performed best between all groups when interpreting mpMRI only with the mpMRI-sequences (Table 1). This result could be explained by the fact that biopsies are performed most frequently at this level of training in our clinic. As Lee and Mager et al. have already shown, there is a learning curve of 40-50 targeted biopsies, after which the detection rate is sufficient and sometimes even higher than the expert standard of the institution (9, 17). This is likely a practice effect, which makes those who perform many biopsies at the time of the survey perform better. This is also supported by the short duration time to complete the interview of the >3-year residents. Interestingly there was a significant benefit of the printed 3D model within the <1-year residents (Table 1). This underlines the great usefulness of the 3D model in three-dimensional orientation since they have not had much exposure to mpMRI imaging in their career. Therefore, this result is consistent with the results from other studies (7, 23). Surprisingly, the >6-year specialists performed worse when using the printed 3D model compared to no additional aids (**Table 1**). This remains unclear and requires further investigation. As expected, the senior specialists (>10 years of experience) performed best overall when using the radiological reports (**Table 1**). The impact of the 3D model was similar compared to the >3-year residents but we could not detect a significant difference to the sole mpMRI interpretation as was only within the <1-years residents (**Figure 3**). The assessment of index lesion extension was significantly decreased when using the 3D model (**Figure 4**). Interestingly the participants overestimated the area in all three groups (**Figure 4**). However, the variance was greatest when only the mpMRI sequences were available. This reflects the limited experience with mpMRI assessment that still exists among many urologists (4). This emphasizes a great need for more training and visual aids. The overall uncertainty of the participants in interpreting mpMRI sequences when no other tools are available supports this even more (**Table 2**). The printed 3D model was perceived to be very useful in terms of anatomical resemblance, three-dimensional orientation and localizing, training and patient education (**Table 2**). However, it was rated only moderately useful in preoperative and intraoperative use (**Table 2**). This contradicts with some other studies, where the pre- and intraoperative utility of the 3D prostate model in prostate-specific surgery was considered to be useful (12, 24). 3D printed prostate models could also improve accuracy of targeted biopsies of PSMA-positive areas within the prostate since biopsy fusion software is mostly designed for mpMRI and post radiation effects reduce accuracy of mpMRI (25). Hereby, diagnostic certainty of PSMA-PET-CT for prostate cancer recurrence after curative prostate radiation could be improved.

In summary, our study provides significant data that supports the effectiveness of printed 3D models of the prostate in the localization of the tumor in mpMRI, especially with inexperienced urological residents (<1 year). However, urologists still need radiological reports to sufficiently locate the index lesion in mpMRI. Furthermore, our study showed a significant benefit of the printed 3D model of the prostate regarding assessment of the extension of the index lesion. The utility of the 3D model was considered useful regarding spatial orientation, training of inexperienced physicians and patient education. With the help of technological advances and more accessible 3D visualization tools the challenge of interpreting mpMRI of the prostate could become less in the future and improve prostate cancer diagnostics as well as patient care.

Our study also has some limitations. Study population was relatively small, especially in each of the four experience-categories. The effect of the 3D prostate model could be further evaluated in a multicentered follow-up-study. Furthermore, we only included singular index lesions with a PI-RADS score ≥4. To evaluate the impact of the 3D model in a more realistic scenario multiple lesions and PI-RADS 3 lesions would need to be included. Moreover, the transparent PLA-filament used for prostate and seminal bladders turned out to be partially transparent after printing. Hereby, lesions that were located more central were hard to see from the outside. As a solution, an acrylic filament could be used for complete transparency.

## Conclusion

Understanding tumor localization in multiparametric MRI of the prostate still requires written radiological reports for sufficient interpretation. However, life-sized 3D printed models show great benefit in young residents (<1 year) regarding tumor localization and lead to a significantly more precise assessment of tumor extension.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

## Author contributions

MH: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Software, Supervision, Visualization, Writing – original draft. KR: Data curation, Visualization, Writing – review & editing. AG: Conceptualization, Methodology, Software, Supervision, Writing – review & editing. KS: Methodology, Software, Writing – review & editing. LF: Writing – review & editing. PS: Writing – review & editing. GD: Writing – review & editing. RM: Writing – review & editing. AH: Writing – review & editing. HB: Conceptualization, Project administration, Supervision, Writing – review & editing.

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# Surgical techniques to preserve continence after robot-assisted radical prostatectomy

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Radical prostatectomy significantly impacts the inherent anatomy of the male pelvis and the functional mechanisms of urinary continence. Incontinence has a considerable negative influence on the quality of life of patients, as well as their social and psychological wellbeing. Numerous surgical techniques have been demonstrated to support the preservation of continence during robot-assisted radical prostatectomy (RARP). In this in-depth analysis, we give a general summary of the surgical techniques used in RARP and their impact on incontinence rates.

KEYWORDS
prostate cancer, robot-assisted radical prostatectomy (RARP), continence recovery, preserving reconstruction techniques, functional outcomes

## Introduction

Prostate cancer (PCa) is the second most common cancer among men (after skin cancer), with an estimated 1.4 million diagnoses worldwide in 2020 (1, 2). Robot-assisted radical prostatectomy (RARP) is considered one of the first-line treatment options for localized PCa. It is indubitably a challenging operation that has been refined through the years to achieve three main goals, namely, cancer treatment, preservation of urinary continence, and recovery of sexual function. These outcomes, referred to as trifecta, are of utmost importance for a patient (3). Apart from oncological efficacy, which is the most critical endpoint, urinary incontinence is a significant and long-term consequence that substantially decreases the quality of life (QoL) of patients (4).

While most men will remain continent at 12 months post-op (defined as no use of pads), early urinary continence rates vary with up to 70%–80% of men requiring the use of pads at 6 weeks and 20%–40% at 6 months and are, in turn, linked to low self-esteem and deterioration of psychological wellbeing (5–7). Multiple technical modifications have been proposed to improve urinary continence, such as bladder neck preservation (BNP) approaches (8), subapical urethral dissection (9), anterior and posterior reconstruction (10, 11), and nerve-sparing and Retzius-sparing (12). In this article, we review the available literature, summarizing the surgical techniques of RARP and their impact on incontinence rates.

## Surgical anatomy of the prostate

During RARP, the key goal is to leave the inherent anatomy of the male pelvis and the functional mechanisms of urinary continence undisrupted. The main anatomical landmarks are considered the detrusor apron, neurovascular bundles (NVBs), and Denonvilliers' and endopelvic fascia.

For many years, there has been a common misconception that the bladder ends in front of the prostate. On the contrary, the bladder continues caudally in front of the prostate as an entity called detrusor apron, which is fixed to both the pubic bone and apex of the prostate. Puboprostatic ligaments are parts of the bladder apron (13). The detrusor apron is considered of major importance as it interconnects the two sphincteric mechanisms, namely, the vesical internal sphincter and external urethral sphincter, into one functional unit. The vesical internal sphincter, which is the circular part of the bladder continuing inside the prostate also covers the prostate from the outside (14). During bladder neck sparing, this musculature is stripped down until the bladder neck to help preserve as much bladder neck as possible. The external sphincter has two main parts. One is a circular horseshoe-shaped smooth muscle, responsible for continence preservation, and the other is an external striated muscle (14). The striated muscle ventrally overlaps the prostate way above the end of the apex. The lower boundary of the Santorini venous plexus is way under the anterior boundary of the striated sphincter (15). Knowledge of the anatomy helps preserve the external urethral sphincter during the control of the dorsal vein complex (DVC) (**Figure 1**).

In the past, the NVBs were considered two strains of nerves located in the posterolateral side of the prostate. Newer concepts in neural anatomy demonstrate that they are not two strains but a complete network of neurons interconnected from one side to the other. They form a surface at the level of Denonvilliers' fascia (16). Denonvilliers' fascia is one of the fascial components that surround the prostate gland, along with the prostatic capsule and lateral or endopelvic fascia. Like endopelvic fascia, Denonvilliers' fascia is potentially not a single-layered structure but is composed of multiple sheets of tissues (17). This knowledge obtained from the advantage of magnification that laparoscopic surgery provided permitted the development of intra-, inter-, and extrafascial dissection during RARP. Avoiding the removal of Denonvilliers' fascia during RARP is crucial for continence preservation. This tendinous structure continues from the base to the apex of the prostate and is considered to support the urethra and prostate as a fulcrum (18). The rest of

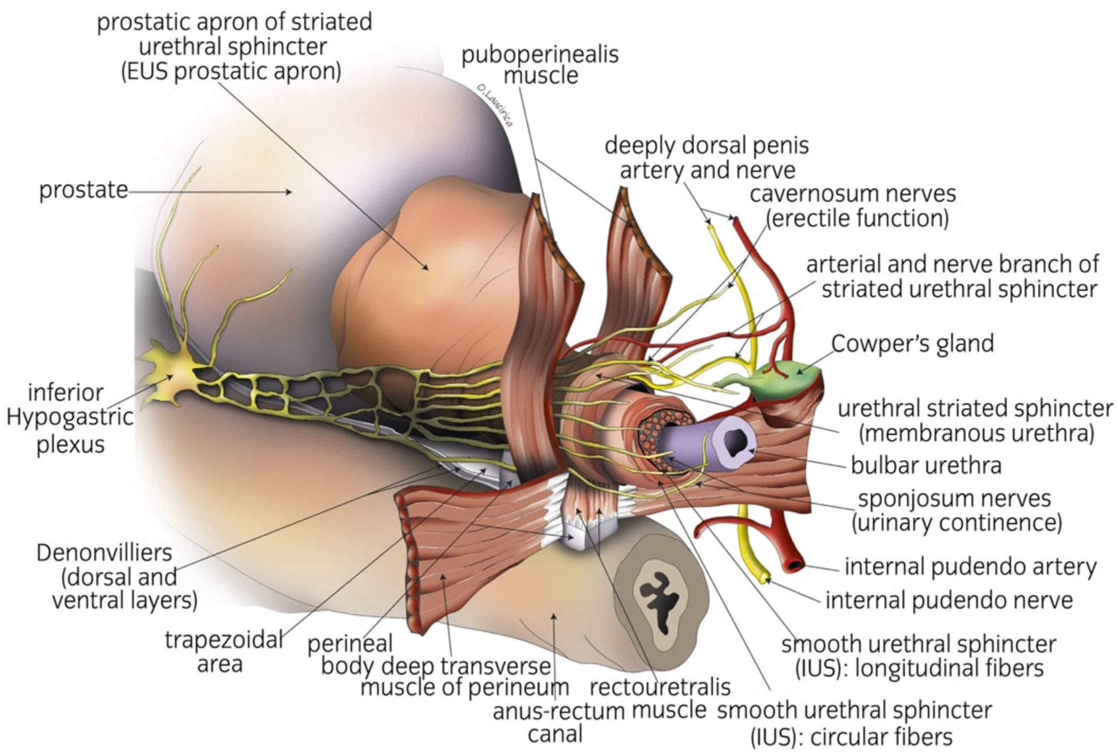


FIGURE 1
Anatomical landmarks to achieve early urinary continence.

Denonvilliers' fascia across the posterior prostatic surface is considered to act as a hammock to support vesicourethral anastomosis (19).

## Surgical techniques to improve urinary continence rates

### BNP approaches

Different approaches have been proposed to protect bladder neck circular fibers during RARP to achieve the preservation of urinary continence. Anterior, lateral, and anterolateral dissection planes are most commonly utilized. Regardless of the chosen technique, protecting the bladder neck as high as possible has been found to preserve urinary continence. Deliveliotis et al. (20) described the first reported cases of BNP that resulted in improved continence rates in patients who underwent open radical prostatectomy. Freire et al. were the first to describe a technique of BNP in RARP (21). In their series of 347 patients who had undergone the BNP technique vs. 271 patients who had undergone a standard RARP, they reported significantly better continence rates at 4 and 12 months with BNP (65.6% vs. 26.6% at 4 months; 86.4% vs. 81.4% at 12 months) (21). Hashimoto et al. performed a retrospective multivariate analysis on predictors of continence in patients undergoing RARP with BNP and found that BNP was significantly associated with early continence (22). In a relatively recent systematic review and meta-analysis, BNP was associated with significantly better urinary continence outcomes at 3–4 months compared with patients who underwent RARP without BNP [odds ratio (OR), 2.88; 95% confidence interval (CI), 1.52–5.48; $p = 0.001$], 12 months (OR, 2.03; 95% CI, 1.10–3.74; $p = 0.02$), and 24 months (OR, 3.23; 95% CI, 1.13–9.20; $p = 0.03$) after RARP (23). The risk of increased positive surgical margin (PSM) still remains controversial regarding BNP. In the former meta-analysis, there was no difference in the rate of overall PSM (OR, 1.00; 95% CI, 0.72–1.39; $p = 0.99$) and that of PSM at the prostate base (OR, 0.49; 95% CI, 0.21–1.13; $p = 0.09$) between the two groups. A newer described technique of extended bladder neck sparing is complete urethral preservation, during which the intraprostatic urethra is preserved in cases with no central zone tumors. During this technique, the bladder neck is not dissected until the level of the verumontanum, where the urethra is usually thinner and essentially permits a urethra–urethral instead of a vesicourethral anastomosis. Initial oncological and functional outcomes are very encouraging, with reported immediate continence rates of nearly 50% after removing the catheter (24).

### Neurovascular bundle preservation

When NVB techniques were first adopted by surgeons, their main goal was to preserve erectile function. Through the years, a better understanding of the anatomical localization of the prostatic nerves has led some urologists to theorize that damage to the NVB might affect the continence mechanism. For instance, the cavernosal nerves of the NVB have been shown to directly innervate the membranous urethra. On the other hand, some surgeons contend that it is the meticulous dissection during nerve-sparing rather than the NVB itself that is responsible for improved outcomes of urinary continence (25, 26). Regardless of the real reason behind this, NVB preservation seems to be strongly associated with improved continence recovery after RARP. Reeves et al. conducted a systematic review and meta-analysis involving 13,749 patients and showed that NVB sparing compared with non-NVB sparing resulted in improved early urinary continence rates up to 6 months postoperatively (27). Park et al. (28) demonstrated similar results. In their study, 84.6% of the patients treated with nerve-sparing RARP were continent at 12 months compared with 74.6% of those having non-nerve-sparing RARP. Nerve-sparing was also significantly associated with recovery of urinary continence on multivariate analysis (hazard ratio, 0.713; 95% CI, 0.548–0.929; $p = 0.012$).

Nerve-sparing techniques are categorized, based on fascial dissection, into intrafascial, interfascial, and extrafascial. The working plane in the intrafascial dissection is between the prostatic capsule and the several layers of periprostatic fascia. It allows total NVB preservation but with a greater risk for PSM. In the interfascial dissection, the working plane is between the prostatic fascia and the lateral pelvic fascia and medial to the NVB. The prostatic fascia is retained intact, which allows a greater safety margin decreasing the PSM. In the extrafascial approach, the dissection is carried over the prerectal fat and the endopelvic fascia. It is important to plan the level of dissection based on the preoperative multiparametric MRI and biopsy, to allow for more accurate local staging.

The classic nerve-sparing RARP technique involves the dissection of NVB from the posterolateral arc between the prostate and Denonvilliers' fascia. This technique has been further refined, leading to the development of newer techniques. Such a technique is the so-called Veil of Aphrodite (29), where the initial plane of dissection is between the prostatic fascia and lateral pelvic fascia from the base of the seminal vesicles. The interfascial dissection then proceeds between the 1 and 5 o'clock positions for the right side and between the 6 and 11 o'clock positions for the left side, leaving the detached prostatic fascia as a supportive structure. Kaul et al. (29) reported that 29% of patients who underwent RARP with Veil of Aphrodite were continent at the time of catheter removal, 97% were continent at the 12-month follow-up, and the median time to continence was 14 days, demonstrating an advantage in regaining early continence. Ghani et al. then modified this technique, extending the interfascial dissection more anteriorly between the 11 and 1 o'clock positions (30). The idea behind this procedure called super Veil is that 25% of the NVBs can be found on the anterior surface of the prostate. Due to its greater complexity, this procedure is usually preserved for low-risk patients. Galfano et al. presented another modified nerve-sparing technique in which NVBs are preserved by releasing them retrogradely (31). In his technique, after reaching the space of Retzius, the anterior neck of the bladder is dissected without entering the endopelvic fascia or ligating the DVC. The vas deferens and seminal vesicles are then dissected through an incision made in the posterior neck of the bladder. Using this technique, the NVB can be released easily from below, achieving a good avascular plane between the prostatic fascia and NVB. The main goal is to connect the space created by separating the NVB from the anterior prostate surface with the previously created Denonvilliers' space. The presented results were very promising as continence was reached immediately in 85.9% of the patients and 98.4% were continent at 1 year. However, these results were deeply questioned by experts in the field (32). In 2017, Cochetti et al. (33) presented another novel neurovascular sparing technique called the PERUSIA technique (PERUSIA stands for Posterior, Extraperitoneal, Robotic, Under Santorini, Intrafascial, Anterograde). In their technique, after inducing pneumo-Retzius, they follow an anterograde–intrafascial dissection approach in a lateral manner with enlargement of the retroprostatic space toward the prostatic pedicles. Following the medial aspect of the Veil of Aphrodite they reach the anterior periprostatic tissue and detouch it bluntly from the fascia, without damaging the accessory neurovascular plate. This technique has proved its feasibility and efficacy, with reported continence rates of 69% the day after the removal of the catheter, 92% at 3 months, and 97% at 12 months after surgery (34).

### Subapical urethral dissection and preservation of the external sphincter and membranous urethral length

As we have previously mentioned, a big part of the external sphincter is placed inside the prostate between the apex and the verumontanum (35, 36). Due to the anatomical variations of the shape of the apex, a considerable part of the sphincter is covered by apical tissue (37–39). For that reason, preserving the full functional length of the urethra also helps preserve part of the external sphincter. Mungovan et al. demonstrated that each extra millimeter of urethral length, which was measured preoperatively via MRI, was associated with early continence recovery (40). These findings were also justified by Song et al., who showed that the preoperative and postoperative maximum urethral length was significantly associated with urinary continence at 6 and 12 months after RARP (41). Michl et al. demonstrated that careful dissection of the apex had a beneficial effect on early and long-term urinary continence rates compared with a wide excision (26). In a recent retrospective study by Hoeh et al., implementing full functional-length urethral sphincter and NVB preservation in patients undergoing RARP resulted in improved long-term (12 months) continence rates (defined as no pad or one pad) of 91% (42).

### Preservation of supporting anatomical structures: Retzius-sparing and hood technique

In 2010, Galfano et al. described Retzius-sparing RARP, a posterior approach to the prostate via access through the Douglas space (12). In Retzius-sparing RARP, a transverse incision is first made at the peritoneal reflection underlying the rectovesical pouch. The vas deferens and seminal vesicles are then recognized and mobilized. Antegrade dissection begins at the posterior and posterolateral surfaces of the prostate, and the NVBs are swept laterally. The bladder neck is divided, and the DVC is released with sharp dissection. The urethra is cut below the apex, and the prostate is freed. This approach preserves all the anatomical structures anterior to the prostate such as the DVC, pubovesical and puboprostatic ligaments, detrusor apron, and endopelvic fascia, providing anterior bladder support and leading to better continence rates. Galfano et al. demonstrated immediate continence in >90% of the patients. Numerous later publications (43–45) supported these findings. One common critic for this technique is that the benefit of continence does not exist after 6 months when continence rates equalize with those of the standard approach. However, in a systematic review and meta-analysis published in 2020, higher continence recovery was seen up to 12 months (46). Another major concern regarding Retzius-sparing RARP is that existing studies have consistently reported higher PSM rates (47). In the MASTER study, a systematic review and meta-analysis of four randomized controlled trials (RCTs) and six prospective observational studies, PSM rates in ≤pT2 tumors were statistically significantly higher following Retzius-sparing RARP as compared with standard RARP (47). In another study coming from Japan, the authors demonstrated that Retzius-sparing RARP is associated with higher PSM rate in anterior tumors, but not in posterior tumors, compared to conventional RARP (48). The preservation of Santorini plexus and detrusor apron probably makes the distance between the tumor edge and the resection plan a lot smaller, which, in turn, affects PSM. The steep learning curve involved to achieve optimal outcomes is also worthy of mention when talking about Retzius-sparing RARP (49, 50).

In 2021, Tewari et al. demonstrated their own RARP technique, preserving periurethral anatomical structures in the space of Retzius and sparing the pouch of Douglas, which they called the hood technique (51). The contents in the space of Retzius are preserved anteriorly, and the preserved tissue after prostate removal has the appearance of a "hood" comprising the detrusor apron, arcus tendineus, puboprostatic ligament, anterior vessels, and some fibers of the detrusor muscle. This hood surrounds and safeguards the membranous urethra, external sphincter, and supportive structures. Among patients receiving the "hood technique," the continence rate exceeded 80% at 4 weeks following catheter removal. By 48 weeks post-catheter, the continence rate rose to 95%. The technique also had a low rate of PSM (6%).

## Reconstructive techniques to improve urinary continence recovery

### Posterior reconstruction (Rocco stitch)

In 2001, Rocco et al. first presented their technique of posterior reconstruction in open retropubic prostatectomy, aiming to achieve improved continence recovery (52). During posterior reconstruction, the surgeon sutures the remaining Denonvilliers' fascia to the posterior aspect of the rhabdosphincter and the posterior median raphe. Then, the posterior layer of the rhabdosphincter is sutured to the posterior surface of the bladder. This transfers the urethral sphincter cranially, lessens the stress in the anastomosis, and also gives the bladder neck pelvic support. Bearing these in mind, preserving Denonvilliers' fascia seems to be of utmost importance for the success of this technique. In 2007, Rocco et al. adapted their technique to RARP, demonstrating significantly shortened time to continence recovery and feasibility of the technique laparoscopicaly (53). Since its introduction, other surgeons have used and slightly modified the Rocco stich. Rocco et al. tried to synthesize the evidence in a systematic review, showing improved continence recovery at 30 days postoperatively (54). In a more recent review, Rosenberg et al. demonstrated that posterior reconstruction in RARP may result in better continence 1 week after removal of the catheter compared with RARP without reconstruction (although it is also possible that it is no better). However, it may make little to no difference at either 3 or 12 months after surgery (55).

### Anterior reconstruction (Patel stich)

Similar to what Walsh first described in open retropubic prostatectomy, Patel suggested his technique of anterior reconstruction in RARP (56, 57). After ligating the DVC, Patel placed a periurethral retropubic stitch to the pubic bone in a figure of eight pattern, providing suspension to the rhabdosphincter. The suspension technique resulted in significantly greater continence rates at 3 months after RARP compared with the group without the Patel stich (92.8% vs. 83%, $p = 0.013$).

### Combined anterior and posterior reconstruction

Urologists mostly preferred using combined anterior and posterior reconstruction or referred by many as total reconstruction as it has shown better results regarding continence rates. In the first RCT comparing RARP with total reconstruction (group A) to standard RARP (group B), Koliakos et al. showed improved continence recovery (58). At 7 weeks, the continence rates were 65% and 33% for groups A and B, respectively. In two more RCTs that followed, Hurtes et al. and Student et al. presented similar results (59, 60). In 2019, Porpiglia et al. presented a large series of >1,000 procedures of RARP with total reconstruction showing excellent results in the early recovery of urinary continence with 79.66% of the patients being continent at 3 months after catheter removal (61). Furthermore, a systematic review by Checcucci et al. showed that total reconstruction facilitates a faster and higher continence recovery compared with the standard approach or posterior reconstruction or anterior reconstruction only (62).

### Newer concepts: single port transvesical robotic radical prostatectomy

In 2021, Kaouk et al. demonstrated a totally different approach in RARP utilizing the new da Vinci single port surgical system (63). In their technique, after placing the patient in a supine position, a suprapubic incision, two fingerbreadths above the pubic symphysis, is made. The bladder is then identified, and the new da Vinci SP access port is used for robot docking. The bladder is insufflated to 12 mmHg pressure, and the robot is docked.

The operation starts with the incision of the posterior bladder neck in a semilunar fashion, extending to 5 and 7 o'clock, respectively (64). The dissection is proceeded posteriorly to reach the vasa deferentia and seminal vesicles bilaterally. After transecting the vas deferens, Denonvilliers' fascia is incised, and the posterior plane is developed between the prostate and the rectum. Next, the incision of the bladder neck is completed anteriorly to reach the endopelvic fascia. The urethra is divided distal to the apex of the prostate, preserving a long urethral stump (64). Prior to urethrovesical anastomosis, a posterior reconstruction is performed. With their technique, Kaouk et al. have reported excellent continence rates. The median time using a Foley catheter after surgery was 4 days, 56% of the patients had immediate continence after Foley removal, and the continence rate was 96.7% at 3 months postoperatively (64). Even though more studies are needed, this approach seems very promising.

## Conclusions

RARP is a procedure that has undergone numerous modifications to improve patient outcomes without compromising oncologic safety. In this narrative review, we tried to present the current perspectives and recent advancements in surgical techniques regarding continence preservation. The comprehensive comparison of various techniques has been significantly hampered by the lack of a standardized method for reporting results and the scarcity of RCTs. As our understanding of the complex periprostatic anatomy expands, it becomes obvious that the surgeon's experience is of utmost importance to decide the optimal surgical approach. Therefore, attention should be focused on conducting randomized trials, which are essential when comparing novel techniques and can assist surgeons on optimizing their outcomes.

## Author contributions

SK: Conceptualization, Data curation, Formal Analysis, Methodology, Writing – original draft. PJ: Methodology, Supervision, Writing – review & editing. AT: Conceptualization, Methodology, Supervision, Writing – review & editing. ZT: Conceptualization, Methodology, Supervision, Writing – review & editing. OA: Data curation, Methodology, Writing – review & editing. TB: Methodology, Writing – review & editing. FE: Data curation, Methodology, Supervision, Writing – review & editing. ST: Conceptualization, Methodology, Supervision, Writing – review & editing. IM: Data curation, Supervision, Writing – review & editing. AS: Conceptualization, Data curation, Supervision, Writing – review & editing. IV: Conceptualization, Project administration, Supervision, Writing – review & editing. BS: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. LT: Conceptualization, Data curation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Impact of multiparametric magnetic resonance imaging targeted biopsy on functional outcomes in patients following robot-assisted laparoscopic radical prostatectomy

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**Introduction:** Multiparametric magnetic resonance imaging guided prostate biopsy (mpMRI PBx) leads to a higher rate of successful nerve-sparing in robot-assisted laparoscopic prostatectomy (ns-RALP) for prostate cancer (PCa). This study aimed to evaluate the impact of mpMRI PBx compared to standard ultrasound-guided PBx on functional outcomes focusing on erectile function in patients following ns-RALP.

**Material and methods:** All RALPs performed between 01/2016 and 06/2021 were retrospectively stratified according to (attempted) ns vs. non ns RALPs and were then categorized based on the PBx technique (mpMRI PBx vs. standard PBx). We compared RALP outcomes such as pathological tumor stage, rates of secondary nerve resection (SNR) and positive surgical margin status (PSM). Furthermore, we explored the association between PBx-technique and patient-reported outcomes assessed 12 months after RALP using the prospectively collected 26-item Expanded Prostate Cancer Index Composite (EPIC-26) questionnaire. Chi-square tests and logistic regression analysis were conducted.

**Results:** A total of 849 RALPs included 517 (61%) procedures with (attempted) ns. Among these, 37.5% were diagnosed via preoperative mpMRI PBx. Patients with a preoperative standard PBx had a 57% higher association of PSM ($p = 0.030$) compared to patients with mpMRI PBx and a 24% higher risk of erectile dysfunction (ED) 12 months post RALP ($p = 0.025$). When ns was attempted, we observed a significantly higher rate of SNR in patients who underwent a standard PBx compared to those who received a mpMRI PBx (50.8% vs. 26.7%, $p < 0.001$) prior RALP. In comparison, upgrading occurred more often in the standard PBx group (50% vs. 40% mpMRI PBx, $p = 0.008$).

**Conclusion:** The combination of mpMRI PBx for PCa diagnosis followed by ns-RALP resulted in significantly fewer cases of SNR, better oncological outcomes and reduced incidence of ED 1 year after surgery. This included fewer PSM and a lower rate of postoperative tumor upgrading.

KEYWORDS

prostate cancer, localized, mpMRI-guided prostate biopsy, frozen section, nerve-sparing (NeuroSAFE), secondary resection, robot-assisted laparoscopic radical prostatectomy (RALP), EPIC 26

## Introduction

Preservation of neurovascular bundle during nerve-sparing open and robot-assisted laparoscopic radical prostatectomy (ns-RALP) for prostate cancer (PCa) is proven to be associated with a better erectile function and a higher rate of urinary continence following surgery (1–3). Several techniques for nerve-sparing approaches have been developed and the "best" way is still to be found. Nevertheless, NeuroSAFE frozen section, firstly described by Schlomm et al. (4), results in multiple advantages such as less positive surgical margins (PSM) (4, 5) (and higher rates of successful nerve-sparing (4) without affecting oncological outcomes (6).

National and international guidelines advocate for the use of multiparametric magnetic resonance imaging (mpMRI) of the prostate prior to prostate biopsy (PBx) (7–10). The use of mpMRI targeted PBx has relevantly improved the detection of clinically significant PCa defined as International Society of Urological Pathology (ISUP) grade ≥2 (Gleason grade ≥7a) compared to standard ultrasound guided PBx (11, 12). We previously showed, that mpMRI PBx prior RALP was further associated with a higher rate of successful ns and less secondary nerve resection (SNR) compared to standard PBx (13).

Our finding suggested that preoperative imaging and biopsy technique might also affect functional outcomes (13). We hypothesized that patients could experience improved preservation of erectile function if they receive mpMRI PBx before undergoing RALP. Given the increasing importance of patient reported outcome measurements (PROMs) in combination with clinical parameters, erectile function is best measured using a self-reported questionnaire such as the "26-item Expanded Prostate Cancer Index Composite (EPIC 26)" (14, 15).

The aim of this study was to evaluate the potential benefit of mpMRI PBx over standard PBx on erectile function 12 months after RALP.

## Materials and methods

### Study population

Based on an institutional ethics board approval, our institution prospectively collects data of all patients with PCa who undergo RALP. The current study includes all consenting patients, who underwent RALP between January 2016 and June 2021. We analyzed a range of clinical, perioperative, and oncological data, including age, initial prostate specific antigen value at diagnosis (iPSA), result of digital rectal examination (DRE), initial Gleason score/ISUP 2014 grade, PBx technique, the success/failure of ns and rate of SNR, operation time (measured from urinary bladder catheter placement to last skin stitch). The study was approved by the local Ethics Committee of the University Medical Center Göttingen.

### Prostate biopsy techniques

Patients included in the study had undergone either systematic transrectal ultrasound-guided "standard" PBx or perineal systematic as well as targeted mpMRI PBx. PBx was typically performed by the treating outpatient urologist, while mpMRI PBx was mainly conducted at our institution. Patients undergoing PBx did not receive mpMRI prior to biopsy. The PBx procedure involved taking 10–12 biopsy cores of the prostate using transrectal ultrasound. In our clinic, we no longer perform standard transrectal systematic biopsies, like outpatient urologists do. Therefore, 100% of the patients in the standard PBx group were treated there. In contrast, all patients who underwent mpMRI PBx received a standardized mpMRI scan using the Prostate Imaging Reporting and Data System (PI-RADS) version 2.0. All mpMRI reports were interpreted by specialized and trained radiologists. Using the PI-RADS 2.0 classification, all PIRADS ≥3 lesions were targeted with 4–5 biopsies per lesion, in addition to a systematic biopsy taking between 10 and 20 cores. MpMRI PBx was performed perineally using Biopsee© (Fa. MedCom, Darmstadt, Germany) (16).

### Robot-assisted laparoscopic radical prostatectomy (RALP) and NeuroSAFE

A transabdominal RALP with pelvic lymph node dissection (LAD) was performed in all patients using either the Da Vinci System Si© or Da Vinci System Xi© (Intuitive Surgical, Sunnyvale, CA, USA) (17). The surgical techniques, including the preservation and reconstruction of the pelvic floor, were standardized in order to ensure consistency and comparability across patients (18). In specific circumstances, such as when younger patients expressed a strong preference for a nerve-sparing approach despite having a high-risk oncological context, a personalized treatment pathway was followed and a ns-RALP was performed.

Preservation of the neurovascular bundle was carried out whenever it was oncologically feasible according to the guidelines (≤cT2) and intraoperative findings, and the patient expressed a preference for it (9). The patient's request for nerve preservation was recorded during a preoperative discussion. For oncological safety we performed a frozen section of the entire dorsolateral part of the gland surfacing the neurovascular bundle (from urethra to the bladder neck) during RALP (NeuroSAFE). When there was a cancer-positive area of the surgical margin (iopPSM), the corresponding bundle was fully resected. Intra-fascial NS approach was performed in all (attempted) ns RALPs as described by Budäus et al. for the open approach (19).

### Oncological outcomes

We evaluated postoperative cancer-related outcomes such as the postoperative Gleason score/ISUP 2014 grade and PSM based on the final pathology sample, potential oncological upgrading of the tumor stage, and nodal stage as per the LAD specimen.

## Patient reported outcomes

Patients were asked to answer the questions of the fifth version of the EPIC-26 just before and 12 months after undergoing RALP. The EPIC-26 questionnaire consists of five domains: urinary incontinence, urinary irritative/obstructive symptoms, hormonal function, gastrointestinal symptoms, and sexuality. All domains have a point range from 0 to 100, with less points indicating lower function. Scoring of the answers given by the patients was calculated according to standardized scoring instructions (20). Primary endpoint of this study was post-RALP Sexual Summary Score (SexSS) of the EPIC-26 ranging between 0% (worst) to 100% (best). ED was defined by the frequency of erections (EPIC-26 item 10: ≤"I had an erection less the half the time I wanted one").

## Statistical analysis

First, the total study population was divided into two groups based on whether they underwent (attempted) ns-RALP or not. Subsequently, patients who underwent ns-RALP were further split based on the biopsy technique (PBx vs. mpMRI PBx).

Continuous measures were summarized using means and standard deviations or medians and interquartile ranges, depending on the distribution of the data. Categorical data were presented as absolute numbers and percentages. Statistical analyses were conducted using either Student's *t*-tests or Mann Whitney *U* tests for continuous variables, depending on the data distribution. We used Chi-square for categorical variables. Chi-square and multivariable logistic regression analyses were used for prediction ED.

We also studied time trends and changes in the application of mpMRI PBx and NeuroSAFE technique. For both purposes, we used the Jonckheere-Terpstra test.

The significance level was chosen at $p < 0.05$. All analyses were performed using Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, version 28).

# Results

## Patients' characteristics of the total cohort and stratified according to PBX technique

Our study included a total of 849 patients who underwent RALP for PCa. The mean age of the total cohort was 66 years. 517 patients underwent (attempted) ns-RALP and 332 patients were scheduled for a non ns approach (Figure 1). iPSA value did not differ in both biopsy groups (12 vs. 12.5 ng/ml, $p = 0.35$).

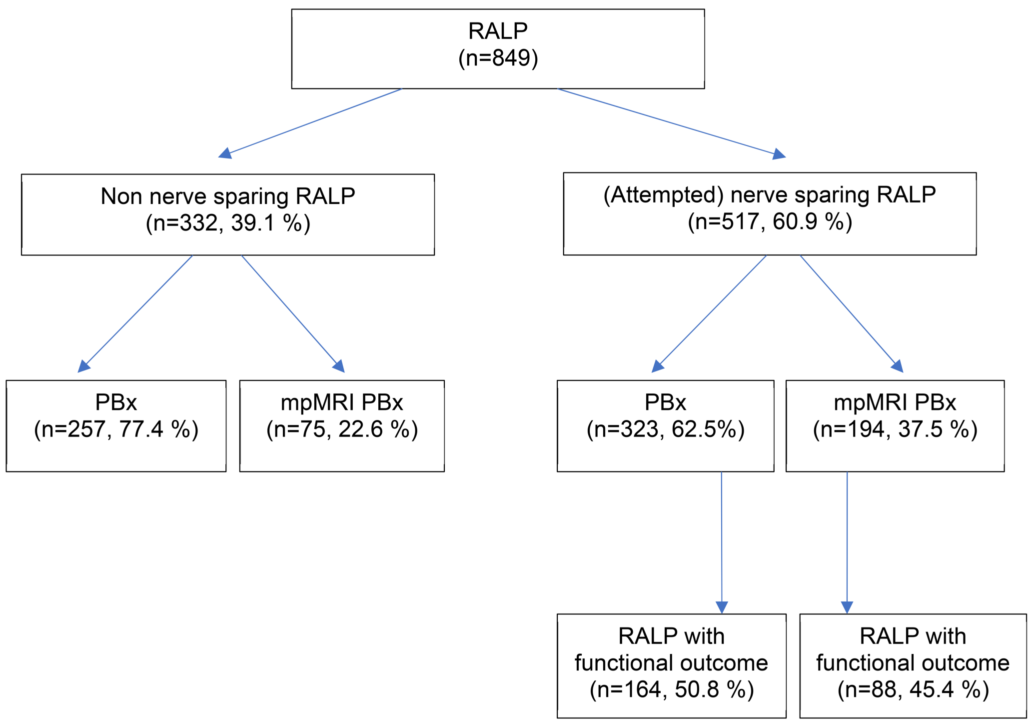


FIGURE 1
Study population. RALP, radical prostatectomy; PBx, ultrasound (US)-guided prostate biopsy, mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy.

Nevertheless, patients with a standard PBx had a higher rate of suspicious DRE (38% vs. 23%, $p < 0.001$). The (attempted) ns-RALP subgroup had a higher proportion of patients who underwent preoperative mpMRI PBx (37.5%) compared to the non-ns-RALP group (22.6%, $p < 0.001$) (**Figure 1**). 72% (194/269) of the patients diagnosed by mpMRI PBx and 55% (323/580) of those diagnosed by standard PBx received an (attempted) ns-RALP (**Table 1**).

Among patients who underwent (attempted) ns- RALP, 95% were diagnosed with ISUP grade 1–3, in contrast to 63% in the non ns-RALP subgroup. Overall, the (attempted) ns-RALP patients had a lower mean iPSA (8.4 vs. 17 ng/ml, $p < 0.001$) (**Table 1**).

## Clinical and oncological outcomes

Patients with an (attempted) ns- RALP with a preoperative mpMRI PBx experienced less often SNR than patients with a PBx (26.7% vs. 50.8%, $p < 0.001$) (**Table 2**).

Patients with a preoperative standard PBx had a 57% higher risk of PSM ($p = 0.030$) compared to patients with mpMRI PBx (**Table 3**).

Our analysis revealed a clear trend over the years (2016–2021) indicating a significant increase in nerve preservation among the patients we operated on ($p < 0.018$, **Figure 2**). Additionally, from 2018 onward, there was a clear trend towards an increase in mpMRI PBx use prior to surgery ($p < 0.001$, **Figure 3**).

## Functional outcomes

Out of the total of 513 functional evaluations conducted using the EPIC 26 questionnaire, 252 patients after (attempted) ns-RALP were available for analysis of the functional outcomes, including both preoperative and 12-month postoperative assessments. **Table 4** shows results of univariate analysis comparing PCa-patients diagnosed with either mpMRI PBx or standard PBx in regard of their functional characteristics. In our univariate analysis none of the parameter of EPIC 26 were significant.

**TABLE 1** Preoperative clinical and oncological patient characteristics of the total study cohort ($n = 849$) and the (attempted) nerve sparing RALP group ($n = 517$) stratified according to biopsy technique.

| | Total study cohort ($n = 849$) | | | (Attempted) nerve sparing RALP group ($n = 517$) | | |
|---|---|---|---|---|---|---|
| | PBx ($n = 580$) | mpMRI PBx ($n = 269$) | *p*-value | PBx ($n = 323$) | mpMRI PBx ($n = 194$) | *p*-value |
| Mean Age [years] (±standard deviation) | 66 (±6.8) | 66.9 (±6.8) | 0.056 | 64 (±6.7) | 66.2 (±6.4) | <0.001 |
| Mean prostate size [ml] (±standard deviation) | 44.4 (±21.6) | 50.7 (±26.6) | <0.001 | 44 (±20) | 51.5 (±27.5) | <0.001 |
| Preoperative Gleason/ISUP grade *n* (%) | | | 0.006 | | | 0.879 |
| 6/1 | 130 (22.4) | 66 (24.5) | | 105 (32.5) | 58 (30) | |
| 7a/2 | 216 (37.3) | 132 (49.1) | | 156 (48.3) | 101 (52.1) | |
| 7b/3 | 116 (20) | 41 (15.2) | | 46 (14.2) | 24 (12.4) | |
| 8/4 | 83 (14.3) | 20 (7.4) | | 14 (4.3) | 10 (5.2) | |
| 9/5 | 32 (5.5) | 10 (3.7) | | 2 (0.6) | 1 (0.5) | |
| 10/5 | 3 (0.5) | 0 | | 0 | 0 | |
| Mean initial PSA [ng/ml] (±standard deviation) | 12.04 (±16.2) | 12.5 (±18.2) | 0.35 | 7.7 (±4.9) | 9.5 (±5.7) | 0.004 |
| Suspicious DRE (%) | 221 (38.1) | 63 (23.4) | <0.001 | 69 (21.4) | 38 (19.6) | 0.655 |

RALP, radical prostatectomy; PBx, ultrasound-guided prostate biopsy; mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy.

**TABLE 2** Postoperative oncological patient characteristics of the total study cohort ($n = 849$) and the (attempted) nerve sparing RALP group ($n = 517$) stratified according to biopsy.

| | Total study cohort ($n = 849$) | | | (Attempted) nerve sparing RALP group ($n = 517$) | | |
|---|---|---|---|---|---|---|
| | PBx ($n = 580$) | mpMRI PBx ($n = 269$) | *p*-value | PBx ($n = 323$) | mpMRI PBx ($n = 194$) | *p*-value |
| Postoperative Gleason/ISUP grade *n* (%) | | | <0.001 | | | 0.05 |
| 6/1 | 58 (10) | 28 (10.4) | | 49 (15.2) | 27 (13.9) | |
| 7a/2 | 226 (40) | 143 (53.2) | | 163 (50.4) | 113 (58.2) | |
| 7b/3 | 151 (26) | 67 (24.9) | | 78 (24.1) | 45 (23.2) | |
| 8/4 | 68 (11.7) | 17 (6.3) | | 15 (4.6) | 7 (3.6) | |
| 9/5 | 75 (12.9) | 13 (4.8) | | 18 (5.6) | 2 (1) | |
| Nodal positive (%) | 41 (7.1) | 7 (2.6) | 0.01 | 7 (2.2) | 2 (1) | 0.494 |
| Positive surgical margin (%) | 136 (23.4) | 43 (16) | 0.014 | 52 (16.1) | 27 (13.9) | 0.53 |
| Secondary nerve resection (%) | 164 (28.3) | 53 (19.7) | 0.009 | 164 (50.8) | 52 (26.7) | <0.001 |
| Upgrading (%) | 288 (49.7) | 107 (39.8) | 0.008 | 153 (47.4) | 75 (38.7) | 0.05 |
| Surgery time (±standard deviation) | 3 h 14 min (±48 min) | 3 h 27 min (±51 min) | <0.001 | 3 h 26 min (±42 min) | 3 h 37 min (±45 min) | 0.005 |

RALP, radical prostatectomy; PBx, ultrasound (US)-guided prostate biopsy; mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy.

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TABLE 3 Multivariable analysis of predictors for positive surgical margin in the final RALP specimen ($n = 849$).

| | *p*-value | odds ratio |
|---|---|---|
| Age | 0.607 | 1.007 |
| iPSA | **<0.001** | 1.037 |
| mpMRI PBx | **0.030** | 0.651 |

mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy; iPSA, initial PSA at diagnosis.
Bold values are statistically significant.

In the multivariable analysis mpMR PBx was a significant negative predictor for ED. ED was defined by the frequency of erections (EPIC-26 item 10: ≤"I had an erection less than half the time I wanted one"). Patients with mpMRI PBx had a 24% higher risk of erectile dysfunction (ED) 12 months post RALP ($p = 0.025$) (Table 5).

## Discussion

Even though there is a trend towards mpMRI PBx prior to surgery, as also observed in the current study, standard PBx is still the current standard of care in Germany (10, 21). The German Institute for Quality and Efficiency in Health Care (IQWiG) stated no evidence for the standardized use of an mpMRI PBx contrasting current guidelines (9, 10, 22). It's disheartening because, besides the established oncological advantage (21, 23), we had earlier demonstrated that a successful ns-RALP is predictably associated with an mpMRI-PBx ($p < 0.001$) (13). In the examined population SNR of neurovascular bundles occurred in 26% when PCa was diagnosed via mpMRI-PBx and in 56% for standard PBx ($p < 0.001$). A trend towards postoperative upgrading of the tumor after standard PBx suggests that standard PBx results sometimes underestimate PCa aggressiveness.

In the context of higher rates of successful ns RALPS in combination with prior mpMRI PBx (13), we hypothesized that patients in this setting could consequently experience improved preservation of erectile function. EPIC-26 questionnaire with a 1-year follow up was used to show the possible benefit of mpMRI PBx in (attempted) ns RALPs on functional outcomes. Concerning erectile function status, EPIC-26 seems to have more descriptive validity for not sexually active men compared to other instruments (24), especially for the difficult and interindividual assessment of ED (25). It is crucial to consider the preoperative erectile function for an accurate assessment of sexual function (25). Salonia et al. postulated that validated questionnaires with defined cut-offs, including the preoperative erectile function status, should be routinely used to enhance post-RALP satisfaction (25). According to the van der Slot findings (26), implementing the NeuroSAFE technique resulted in a continence rate of 92% at the 1-year mark and 94% at the 2-year mark among patients. Additionally, 44% of the men achieved a favorable or moderate score for erectile function at both, 1 and 2 years, following the surgery. In our multivariate

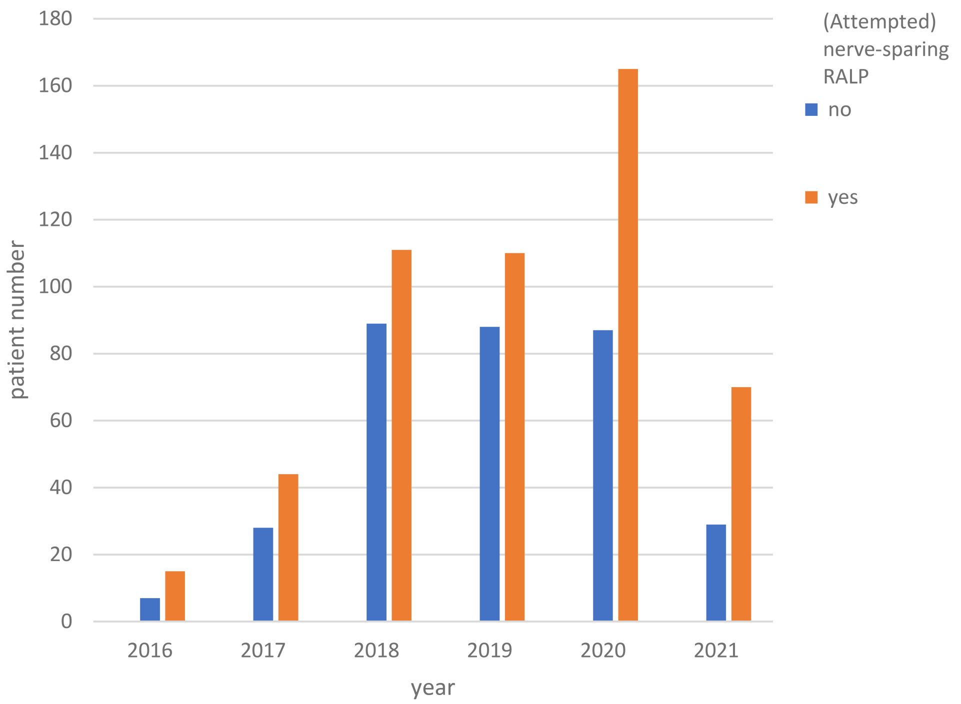


FIGURE 2
Time trend of nerve sparing RALP over the years ($p < 0.018$). RALP, radical prostatectomy.

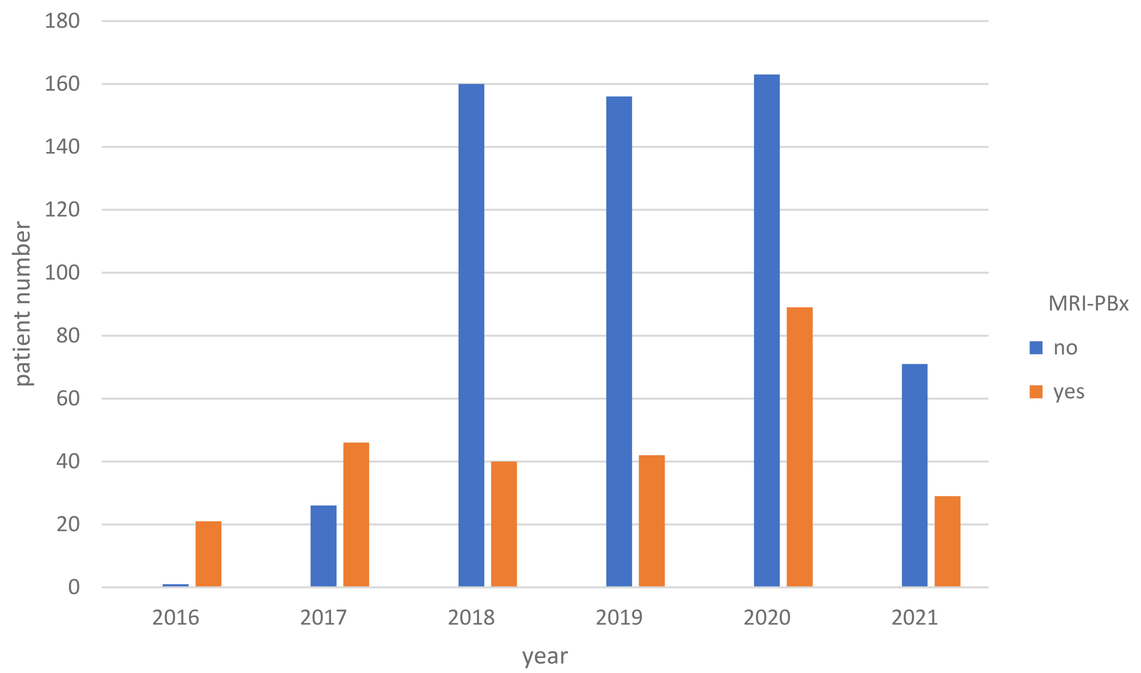


FIGURE 3
The distribution of preoperative mpMRI PX over the years ($p < 0.001$). mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy.

**TABLE 4** Functional outcomes according to the biopsy technique [subgroup with (attempted) nerve sparing RALP, *n* = 252] using EPIC 26 questionnaire.

| | Total cohort (*n* = 252) | PBx (*n* = 164) | mpMRI PBx (*n* = 88) | *p*-value |
|---|---|---|---|---|
| Difference in erectile function (pre to postoperative) (±standard deviation) | −30.3 (±26.7) | −32.7 (±26.6) | −25.9 (±26.6) | 0.094 |
| Difference incontinent complaints (pre to postoperative) (±standard deviation) | −16.6 (±27) | −18.2 (±27.3) | −13.8 (±26.5) | 0.23 |
| Difference in irritating complaints (pre to postoperative) (±standard deviation) | 2.4 (±14.7) | 2.2 (±15.9) | 2.7 (±12) | 0.8 |
| Difference in hormonal complaints (pre to postoperative) (±standard deviation) | 6.9 (±22.4) | 7.3 (±22.6) | 6.3 (±22.1) | 0.433 |
| Difference in gastroenterological complaints (pre to postoperative) (±standard deviation) | −3 (±24) | −7.7 (±24.4) | 0.5 (±15.1) | 0.132 |
| Manifest erectile function (%) | 72 (28.6) | 50 (30.5) | 22 (25) | 0.229 |

PBx, ultrasound-guided prostate biopsy; mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy.

**TABLE 5** Multivariable analysis of predictors for ED among patients with (attempted) nerve sparing RALP (*n* = 252).

| | *p*-value | odds ratio |
|---|---|---|
| mpMRI PBx | **0.025** | 0.464 |
| Suspicious DRE | 0.789 | 1.105 |
| Age | **<0.001** | 1.119 |
| iPSA | 0.263 | 1.028 |

mpMRI PBx, mpMRI (multiparametric magnetic resonance imaging) targeted prostate biopsy; iPSA, initial PSA at diagnosis; DRE, digital rectal examination.
Bold values are statistically significant.

analyses mpMRI PBX was found to be a predictor for a better erectile function 1 year following surgery. We found an almost 25% higher risk of suffering ED when PCa was diagnosed via standard PBx compared to patients with mpMRI PBx ($p = 0.025$).

We further observed less rates of SNR in the mpMRI PBx group compared to the standard PBx group (26.7% vs. 50.8%, $p < 0.001$). A discussion regarding the potential presence of a selection bias is necessary, taking into account the possibility of a more precise characterization of the carcinoma with mpMRI PBx compared to a standard PBx. Apart from iPSA the preoperative oncological patient characteristics for ns attempts did not differ from each other between the two groups. There were no differences in the preoperative histological- and clinical findings between the standard PBx and the mpMRI PBx population. However, the percentage of (attempted) nerve sparing out of all mpMRI PBx was 72% compared to 56% for standard PBx.

Successful ns-RALPs without SNR could be performed in 73% of the mpMRI PBx group and in 49% of the standard PBx group.

Interestingly, even though preoperative patient characteristcs did not differ between the two groups and fewer intraoperative SNR were needed in the mpMRI PBx group, a higher rate of final positive surgical margins (posSM) can be observed in the standard PBx group.

In our multivariate analyses, the risk of a PSM was more than twice as high when PCa was diagnosed via standard PBx compared to mpMRI PBx ($p = 0.03$). Also upgrading of the tumor was observed significantly more often in the standard PBx group. This fact, in addition to the lower SNR rate for mpMRI PBx in patients with (attempted) ns-RALPs suggests, that mpMRI PBx provides more, and correct information of the carcinoma and it seems that surgeons may be able to characterize the prostate and the carcinoma within the gland in a more precise way.

In our institution ns is standardly performed intrafascially. In a recently published review intrafascial ns showed advantages for urinary incontinence and EF compared to interfascial ns (2).

There are multiple different techniques to perform intraoperative frozen sections. Schlomm et al. firstly described the NeuroSAFE technique in 2012 (4). Beyer et al. transferred this frozen section technique into the RALP era (27). In our (attempted) ns RALPs we used NeuroSAFE to provide best oncological safety, since the "NeuroSAFE PROOF feasibility trial" states that no PSM seems to be missed in the NeuroSAFE intraoperative frozen section (5). Whenever an PSM was found intraoperatively we performed a full SNR of the whole neurovascular tissue on the adjacent side including the rectolateral half of the Denonvilliers fascia. Up till now SNR techniques are heterogenous. However, several studies confirm the usage of NeuroSAFE (4, 27–29).

In conclusion, the NeuroSAFE ns RALP procedure, even with the potential requirement for a full SNR does not appear to compromise the level of oncological safety.

To summarize our findings, we saw more ns attempts when mpMRI PBx diagnosed PCa with less SNR, a better functional outcome and less upgrading of the carcinoma postoperatively but with comparable preoperative conditions to standard PBx diagnosing PCa. We attribute the better erectile function to a lower rate of secondary resections of the neurovascular bundles and a better understanding of tumor spread in the gland. Therefore, a better functional result can be achieved by the surgeon. Although there was no selection bias towards less ns attempts in the mpMRI PBx group these findings suggest, that the oncological information combined with the imaging and knowledge of the intraprostatic distribution of carcinoma-lesions leads to a better understanding of the gland itself. This issue, however, remains speculative for our results but confirm existing studies (13, 23).

Finally, we observed a trend towards the usage of mpMRI-PBx prior to RALP ($p = 0.001$). While mpMRI PBx isn't currently a standard care procedure and comes with higher costs compared to standard PBx, studies have demonstrated its cost-effectiveness for the healthcare system. This is primarily due to the prevention of delayed diagnosis, understaging, biopsy-related complications, and unneeded repeat biopsies (30, 31).

Simultaneously to the increased usage of mpMRI-PBx we also saw a trend towards a higher rate of ns RALPs ($p < 0.018$), which could be explained by the increased usage of mpMRI-PBx. Another reason could be that the surgeons' experience increased over the years, and thus the proportion of nerve sparing RALPS did as well. But, at our clinic, during this period, there were 4 experienced surgeons (more than 100 surgeries) who performed the da Vinci surgeries. Only 1 surgeon was on his learning curve. Therefore, this effect is unlikely in our analysis.

This study completes our previously findings by adding follow-up data on erectile function (13). The biggest advantage of this study is the combination of functional and oncological data. The main limitations include the retrospective analysis of the prospectively collected data. However, prospective patient randomization would be largely unfeasible due to specific histological characteristics and patients' preferences. As such, we do not see the lack of randomization as a detrimental element of this study. However, we lack information about individual decision-making processes, such as whether ns was attempted or not. The next phase should involve assessing the impact of MRI on the surgical decision. Another limitation of our study was that the standard biopsy was performed by the outpatient urologist. Therefore, standardized execution is not guaranteed. However, this fact reflects the current care landscape in many parts of Germany.

## Conclusion

The combination of mpMRI PBx for PCa diagnosis followed by ns-RALP resulted in significantly fewer cases of SNR, better oncological outcomes and reduced incidence of ED 1 year after surgery. This included fewer PSM and a lower rate of postoperative tumor upgrading. Especially younger patients may potentially benefit from undergoing mpMRI PBx prior RALP. This approach not only contributes to improved oncological outcomes but also to the preservation of nerves to maintain erectile function.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving humans were approved by Ethikkommission der Universitätsmedizin Göttingen Von-Siebold-Str.3 37075 Göttingen. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

## Author contributions

CL: Conceptualization, Data curation, Formal Analysis, Investigation, Validation, Writing – original draft, Writing – review and editing. AU: Formal Analysis, Supervision, Writing – review and editing. FB: Writing – review and editing. MM: Writing – review and editing. LT: Writing – review and editing. ML: Writing – review and editing. MR: Conceptualization, Data curation, Formal Analysis, Investigation, Validation, Writing – original draft, Writing – review and editing.

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## Publisher's note



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# Minimally invasive transvaginal single-port laparoscopic vesicovaginal fistula repair: a case report and the point of this technique

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The optimal surgical method of vesicovaginal fistula (VVF) remains uncertain. Minimally invasive surgical approaches have become highly popular in line with technological advancements, namely, laparoscopic, robotic, and transvaginal techniques. However, these techniques still require invasiveness. This is the first case report that described a novel "zero-incision" technique for natural orifice transvaginal single-port laparoscopy used to repair a recurrent and high-position VVF. The patient underwent transvaginal single-port laparoscopic repair of a VVF. Methylene blue was used to locate the VVF, and a needle electrode was used to thoroughly remove the scar tissue of the VVF. In addition, this technique for transvaginal single-port laparoscopy provides more working space to expose and repair fistulas conveniently and adequately. One year after surgery, the patient remained asymptomatic and had no fistula recurrence. Minimally invasive transvaginal single-port laparoscopy provides a clear surgical field, is safe and feasible. This novel technique has promising as an additional personalized treatment option for VVF repair.

KEYWORDS
transvaginal, single-port laparoscopy, vesicovaginal fistula, repair, case report

## Introduction

A vesicovaginal fistula (VVF) is an abnormal anatomical connection between the vagina and bladder that causes continuous and involuntary urinary leakage from the vagina and has a serious impact on patients' quality of life. The etiology of VVF varies, and the socioeconomic status of the country affects its incidence. Obstetric trauma resulting in a VVF is more commonly found in developing countries, whereas iatrogenic injuries during gynecological surgeries, such as hysterectomy, are the primary causes in developed countries.

Management options for VVF include both conservative and surgical approaches, although there is currently no consensus on the optimal treatment. The choice of treatment depends on the disease characteristics and the surgeon's preference. Conservative treatments may be considered the initial approach for small (<10 mm), clean, nonmalignant fistulas, with a reported success rate of 5%–11% (1).

Numerous surgical techniques have been described for repairing VVFs, such as laparotomy, transvaginal laparoscopy, robot-assisted surgery, and other minimally invasive techniques. Minimally invasive approaches, including a hybrid technique utilizing cystoscopy and intravesical treatment, have shown promising outcomes (2). Nonetheless, these techniques still involve some degree of invasiveness. In this report, we present a case of iatrogenic VVF that was repaired via a novel "zero-incision" technique called natural orifice transvaginal endoscopic (NOTE). This approach involves advancing a single-port laparoscopic trocar through the vagina, which is a natural orifice, to repair the fistula tract. This technique is potentially less invasive for VVF repair.

## Case presentation

A 53-year-old female patient presented to our hospital complaining of continuous urine leakage from the vagina as a result of an abdominal hysterectomy that was performed at a local hospital due to cervical cancer (the patients did not undergo a radiotherapy) two years prior. Urine leakage from the vagina occurred in perioperative period and the VVF was diagnosed at that time, the patient needed two pads one day. Half a year later, she underwent an open abdominal transvesical repair of the fistula (the VVF was located at the apex of the vagina, a conventional transvaginal repair would likely fail) at another medical center. However, urinary leakage persisted following surgery and the patient still need one pad one day. There were no other chronic comorbidities for the patient. Due to the high location of the VVF, it could be challenging to adequately expose and suture the fistula correctly through a conventional transvaginal approach. Attempting a transabdominal or laparoscopic approach would also be problematic due to extensive adhesions and anatomical distortion. Considering these challenges, a novel technique called transvaginal single-port laparoscopic VVF repair was deemed appropriate. The patient was fully informed about this new approach and provided written consent for the surgery and potential publication of the case.

## Surgical procedure

After general anesthesia, the patient was placed in the lithotomy position. A 22 F cystoscope was used to begin the procedure in the bladder. The bilateral ureteral orifices were seen clearly, and a 6 F ureteric catheter was inserted into the ureter. However, the fistula opening was not found. A single-port laparoscope was introduced into the vagina, and the vagina was expanded by insufflation with CO2 at 6–8 mmHg pressure (Figure 1A). The laparoscope showed the closed apical vagina but no fistula. Methylene blue solution that was injected into the bladder through a Foley catheter immediately gushed from the apex of the vagina, thereby revealing a 4 mm fistula. After removal of the single-port laparoscope, a 20 F Foley catheter was inserted into the vagina, and the balloon was filled with 60 ml of

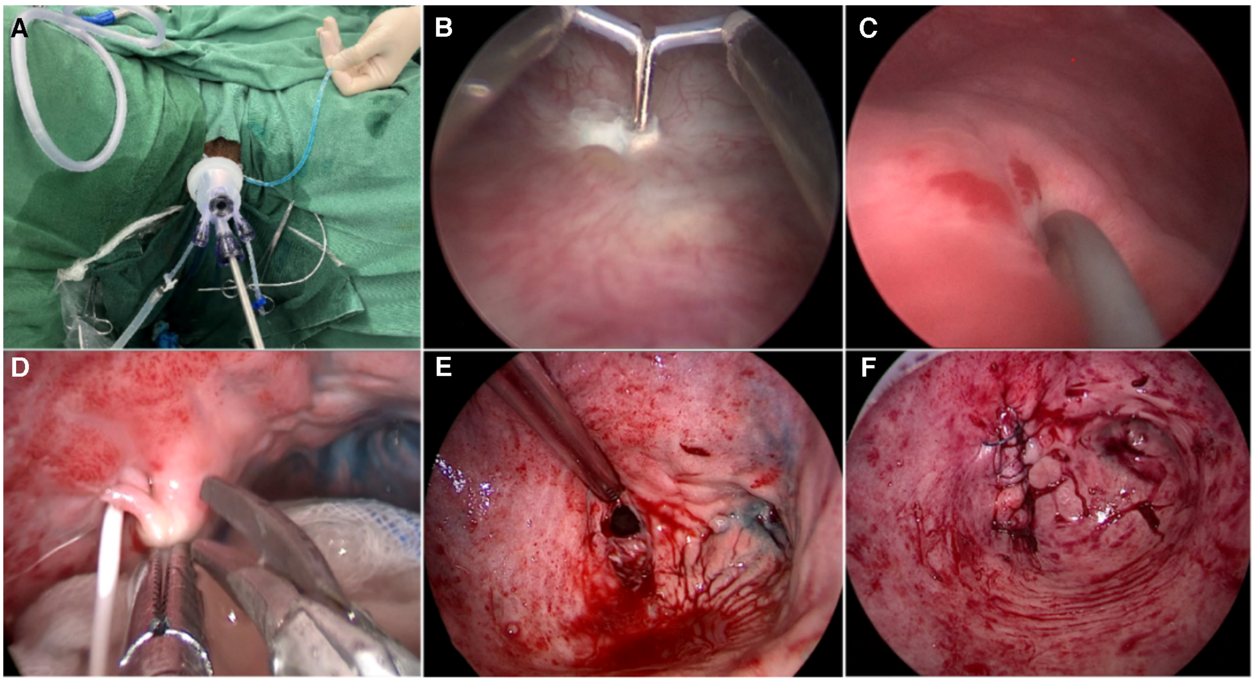


FIGURE 1
Surgical procedure of transvaginal single-port laparoscopic vesicovaginal fistula repair. (A) A single-port laparoscope was introduced into the vagina, and the vagina was expanded by insufflation with CO2 at a pressure of 6–8 mmHg. (B) A needle electrode was used to make a 0.5 cm circumferential incision to thoroughly remove scar tissue in the bladder around the fistula. (C) A ureteric catheter was passed under vision through the VVF from the bladder to the vagina. (D) Excision of 1-cm of the mucosa and muscle surrounding the vaginal scar tissue and the fistula with scissors. (E) The VVF tract was similar to a trumpet. (F) Successive single-layer closure of vesical and vaginal fistulas with 3-0 V-Loc barbed sutures under transvaginal single-port laparoscopic vision.

saline solution. Gauze soaked with iodophor was placed in the vagina. Methylene blue solution was injected through the Foley catheter, and the cystoscope showed methylene blue gushing from the right side of the bladder trigone region, the fistula was 3 cm away from the right ureteral orifice. Then, the scar tissue around the fistula was removed by making a 0.5-cm incision using a needle electrode (Figure 1B). A ureteric catheter was passed, under direct vision, from the bladder to the vagina through the VVF (Figure 1C). The single-port laparoscope was reintroduced into the vagina to allow mucosal and muscular excision of 1-cm vaginal scar tissues surrounding the fistula using scissors (Figure 1D). The fistula tract was shaped like a trumpet (Figure 1E). Finally, single-layer closure of vesical and vaginal fistulas was performed using 3–0 V-Loc barbed sutures under transvaginal single-port laparoscopic guidance (Figure 1F). We injected diluted methylene blue solution to check for fluid leakage from the anterior wall of the vagina. The vagina was filled with iodophor yarn strips, and the surgery was completed, the whole operation took two hours. There was minimal bleeding and no intra or postoperative complications. The patient was catheterized for two weeks and maintained antibiotic therapy for six days and hospitalized for six days. Figure 2 illustrates the schematic diagram of transvaginal single-port laparoscopic vesicovaginal fistula repair and highlights the key points of the technique. The patient remained asymptomatic with no recurrence of the VVF after a half year.

## Discussion

Vesicovaginal fistula is the most common type of genitourinary fistula in females and can have significant physical and psychological impacts. Diagnosing and treating VVF requires caution due to its iatrogenic causes, and a definitive diagnosis typically relies on standardized and convincing evidence. Imaging methods such as intravenous pyelography or computed tomography urography can confirm the diagnosis. Cystoscopy after methylene blue injection can provide further information about the location, size, and number of fistulas. When planning the treatment for VVF, meticulous care is necessary, especially when considering surgical intervention. A well-designed surgical plan is crucial to ensure the success of the operation, as the local conditions at the operative site

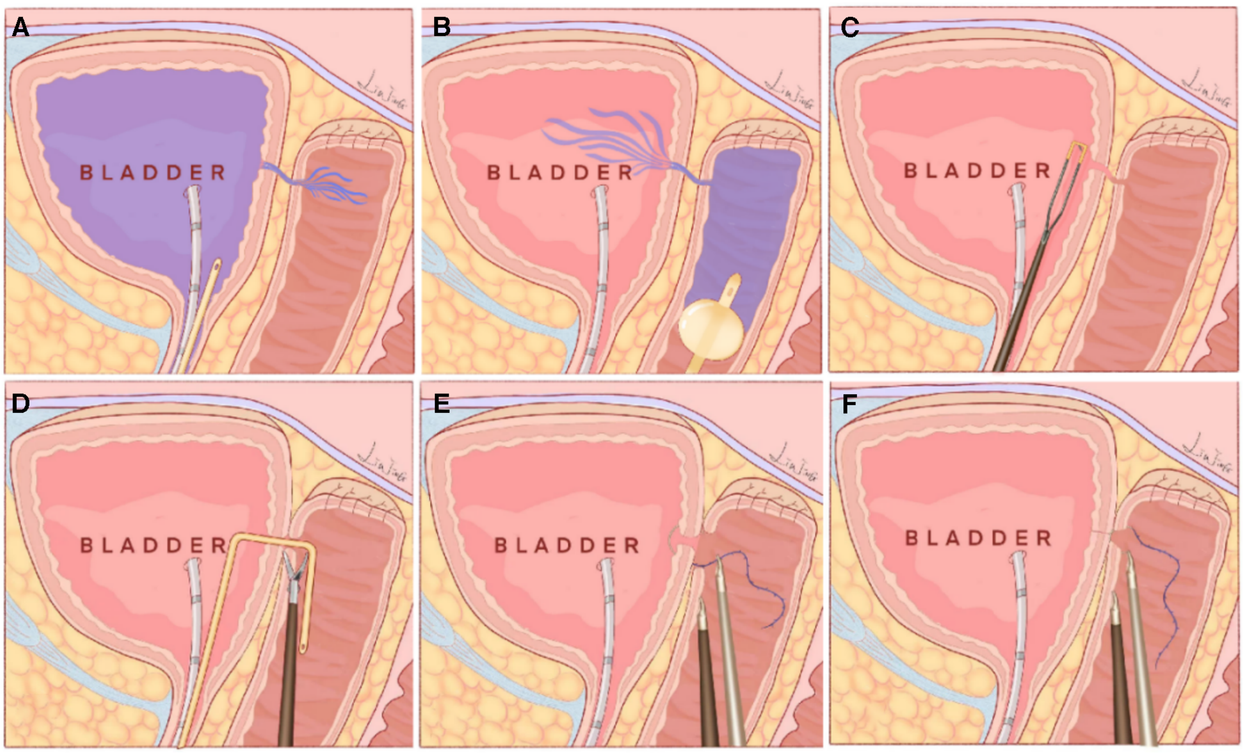


FIGURE 2
Schematic diagram of transvaginal single-port laparoscopic vesicovaginal fistula repair, which shows the innovations of this technique. (A) A 20 F Foley catheter was inserted into the bladder, 200 ml methylene blue solution was injected and immediately gushed from the apex of the vagina, thereby showing the fistula opening in the vagina. (B) A 20 F Foley catheter was inserted into the vagina, and the balloon was filled with 60 ml of saline solution. Then, 150 ml of methylene blue solution was injected into the vagina, and the cystoscope showed methylene blue gushing from the fistula opening in the bladder. (C) A needle electrode was used to make a circumferential incision to thoroughly remove scar tissue in the bladder around the fistula. (D) A ureteric catheter was passed under vision through the VVF from the bladder to the vagina. The single-port laparoscope was introduced into the vagina again. The scar tissue surrounding the fistula in the vagina was removed using scissors. (E) The fistula opening in the bladder was closed using 3-0 V-Loc barbed suture under transvaginal single-port laparoscopic vision. (F) The fistula opening in the vagina was sutured using a 3-0 V-Loc barbed suture under transvaginal single-port laparoscopic vision.

are often most favorable during the initial repair, thus maximizing the chances of a successful outcome. If the first repair fails, subsequent treatment attempts may become more challenging. However, there is currently no standardized protocol determining the optimal surgical route and timing for VVF treatment. The choice of surgical approach depends on various factors, including the location, size, number of fistulas, vaginal conditions, surgeon's expertise, and patient preferences.

The traditional transvaginal approach is the most commonly used surgical method for repairing VVF. It has several advantages, including a shorter surgical time, less intraoperative bleeding, a shorter hospital stay, faster postoperative recovery, and high success rates. It is a minimally invasive procedure that can be repeated if needed, regardless of the timing of recurrence or repeat repair (3). However, there are some limitations to this approach. The transvaginal technique may be associated with an increased risk of vaginal shortening. It can be challenging to adequately expose and repair high-position VVFs, as well as complex and recurrent VVFs. Suturing these fistulas correctly can also pose difficulties. In such cases, a conventional transabdominal repair is often recommended (4). The transabdominal approach creates more space for meticulous preparation of the bladder and vaginal wall. It facilitates the identification of scar tissue and fistulas, thereby allowing for complete excision of inflamed tissues and ensuring proper mobilization of the bladder wall. The abdominal approach creates a secure foundation for tension-free closure of the bladder. Although studies have reported similar success rates between transabdominal and transvaginal surgeries, the former is more invasive and requires a longer hospital stay. Additionally, it has a higher risk of complications (4).

In recent years, minimally invasive techniques such as laparoscopic and robotic repair, were first reported in 1994 and 2005, respectively (5, 6), and have emerged as promising techniques for the management of VVFs because of their safety, feasibility, and effectiveness in various studies. Compared to open surgery, laparoscopic repair is associated with a lower morbidity rate and comparable success rates (7). A systematic review conducted by Miklos et al. focused on laparoscopic and robot-assisted VVF repair (7). The review demonstrated an overall success rate of 80%–100% for laparoscopic repair, with follow-up periods ranging from 1 to 74 months. The results suggest that laparoscopic repair is a reliable and successful treatment option for VVFs. Robot-assisted repair is particularly promising for high supratrigonal fistulas. It offers optimal exposure to the fistula area, allowing for wide excision of the fistula tissue. Robot-assisted repair has shown good success rates and lower morbidity rates in these cases. However, it is important to note that laparoscopic repair can be challenging due to the tricky preparation of previously damaged tissue and the suturing process. These difficulties need to be carefully addressed to ensure successful outcomes. Additionally, the robotic approach is associated with higher costs, which may limit its accessibility in some health care settings.

The laparoscopic approach, despite its advantages, is still considered invasive due to the requirement for several incisions. Studies have shown that nearly three-quarters of VVFs can be repaired vaginally, with a success rate that is comparable to that of transabdominal path repair and no significant differences (8). Transvaginal repair offers several benefits, including being more cost-effective than transabdominal repair. Thus, transvaginal repair is currently becoming increasingly valued and favored (3). A novel technique in which the advantages of both laparoscopic and transvaginal approaches were combined has been developed. This technique, a minimally invasive operation, involves the insertion of a single-port laparoscope through the vagina and thus allows adequate exposure of the VVF. This innovative approach incorporates the principles of natural orifice transluminal endoscopic surgery, which was first proposed by Mack in 2001 and has been applied in various urologic and gynecologic procedures (9). Galan et al. demonstrated the effectiveness and benefits of natural orifice transurethral endoscopic VVF treatment through their own case reports (10). It is believed that the transvaginal endoscopic method is superior to the transurethral route for treating VVFs, maybe especially for complex and recurrent cases. This technique has several advantages. First, use of a Foley catheter to find the fistula opening in the bladder (11): by using a Foley catheter, the fistula opening in the bladder can be precisely located, thus aiding in the identification and treatment of the VVF. Second, scar tissue removal with a needle electrode: the transvaginal endoscopic method with a needle electrode allows thorough removal of scar tissue in the bladder, ensuring optimal closure and healing of the VVF. Third, a larger working space and more convenience: this technique creates more room for maneuverability and better access to adequately expose the fistula, remove scar tissue in the vagina, and suture the fistula in layers using a transvaginal single-port laparoscope. Other advantages of the natural orifice transvaginal endoscopic technique include no incision and better visualization. Overall, the transvaginal single-port laparoscopic approach has the potential as an additional personalized treatment option for selected VVF repair.

## Strengths and limitations

The transvaginal single-port laparoscopic technique proposed in this study effectively meets the requirements for successful VVF repair. It provides adequate exposure, good anatomical assessment, allows precise dissection, tension-free suturing, proper postoperative bladder drainage, and provides sufficient blood supply for tissue healing. This technique is valuable in VVF treatment because of its ability to address these crucial aspects. To the best of our knowledge, this study includes the first reported transvaginal single-port laparoscopic repair of VVF and highlights the key advantages of this technique. These include the use of a Foley catheter to locate the fistula opening in the bladder, thorough removal of scar tissue using a needle electrode, and establishment of a larger working space for convenient and optimal exposure, scar tissue removal, and suturing using a transvaginal single-port laparoscope. However, additional multicenter studies with larger patient populations are needed to evaluate the effectiveness of this technique and to establish recommendations for its use.

## Conclusion

In conclusion, minimally invasive transvaginal single-port laparoscopic repair of VVFs has several advantages. The procedure has shown promising outcomes and is considered a safe option for VVF repair.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving humans were approved by Institutional Review Board of the Second Affiliated Hospital of Nanchang University. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin due to the retrospective observational nature of this case report.

## Author contributions

JH: Conceptualization, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing. YC: Data curation, Investigation, Writing – original draft, Writing – review & editing. BW: Data curation, Formal Analysis, Writing – review & editing. HC: Data curation, Formal Analysis, Writing – review & editing. XX: Data curation, Formal Analysis, Writing – review & editing. TZ: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Validation, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Current status of the adjustable transobturator male system (ATOMS™) for male stress urinary incontinence

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Male stress urinary incontinence is a debilitating condition, which can occur after prostate surgery. In persistent cases, surgery is indicated and a number of options are available. This includes one of the male slings, Adjustable transobturator male system (ATOMS™, A.M.I, Austria). There are now an increasing number of studies published. This review provides an overview of the current status of this implant device including technical considerations, surgical outcomes and potential advantages and disadvantages compared to alternatives such as the artificial urinary sphincter.

KEYWORDS
adjustable transobturator male system, artificial urinary sphincter, male stress urinary incontinence, post prostatectomy incontinence, ATOMS system

## Introduction

Male stress urinary incontinence (SUI) is one of the major long term adverse effects that can occur following prostate surgery and in particular, radical prostatectomy (RP). According to a recent analysis of the SEER (Surveillance, Epidemiology and End Results) database, 6% of patients who have undergone RP, will later go on to have incontinence surgery (1). Risk factors include larger prostate size, membranous urethral length and age (2, 3). The resulting impact on a patient´s quality of life can be considerable. As for many other patient groups who suffer UI, it can lead to embarrassment and deep restrictions upon a persońs activities of daily living (4). This sense of embarrassment can lead to delays in seeking formal treatment (5). Once the indications for incontinence surgery have been fulfilled, a range of potential surgeries are available. Local expertise, surgeon preference and availability impact the range of options a patient will be offered. Other elements to consider include the symptom severity, manual dexterity as well as previous radiotherapy (6). While use of bulking agents is the least invasive option, success rates are low and it is no longer recommended by the European Association of Urology guidelines (7). Rather, implantable devices form the mainstay of surgery for male SUI. This treatment can be broadly categorised into two groups: the artificial urinary sphincter (AUS) and male slings. The latter can be further divided into devices that are referred to as adjustable and those that are fixed. Regarding the former, several different such slings are available including ATOMS™ (A.M.I, Austria). First described in a cadaveric setting in 2005, it was developed and in use for clinical purposes since 2008 (8, 9). Since then, a gradual increase in original studies have been published reporting outcomes associated with the device including for patients with a broader selection criteria. It is usually compared against the AMS 800™, which since it has been commercially available since 1983, is the intervention for which most evidence is available and as a result, it has long been the reference treatment (10). However, the advances recorded with use of ATOMS™ have generated debate in terms of the role it should play for male SUI post prostate surgery including when and if it can be a preferred choice over the AMS 800™.

Our aim was to review the available literature and provide an update on its current status including technical considerations, surgical outcomes and the guideline perspectives.

## Methods

A comprehensive but non-systematic search of the literature was performed to identify studies on ATOMS™ that were available over the past 15 years since it was first described. Only those published in the English language were considered. Bibliographic databases used included Medline and Google Scholar. The following key topics were identified: Technical considerations, Short term outcomes, Long term outcomes, Complication burden, Re-do surgery, Previous radiotherapy, ATOMs for severe male SUI, Advantages/disadvantages, Recommendations from international guidelines, Challenges and Future directions.

## History and technical considerations

The initial clinical experiences to be published appeared a few years after its development. The Austrian study by Seweryn et al., which included 38 patients since 2009 was among the first (11). The authors reported continence success (defined as maximum one pad per 24 hours) at 60.5%. Since that report, the device has undergone modifications, most notably in 2013 with a silicone rather than titanium port cover and after 2014, this could be placed in the scrotum with the port pre-attached. This element along with its mesh arms and silicone cushion form key characteristics that distinguish it from adjustable male sling alternatives such as the Remeex system (Neomedic, Spain), consisting of a suprapubic pressure adjusting device ("varitensor") connected via two traction threads to a suburethral prosthesis made of polypropylene and the Argus sling (Promedon, Argentina) (6, 12). The latter features a silicone cushion pad to compress the bulbar urethra, cone shaped columns on either side and "washers" to secure tension (13).

The switch to a silicone covered port was driven by early reports of device explantation as a result of reported titanium intolerance (14). The transition away from the inguinal port placement has reduced the total number of incisions required from two down to only one. The 3rd generation port is also smaller. In a multi-centre study from Germany and Spain, port related complications were 19.2% with the first device but 6.5% with the 3rd generation model (15).

In a recent series by Giammò et al., the mean operative time was 51 min, and most studies report similar results that total operative times under 60 min (16). Hospital discharge is usually planned for within 24 h and adjustments can be made to the port in the outpatient setting. In a recent systematic review, the mean number of fillings required was 2.4 (17).

## Symptom improvement

In a 2019 meta-analysis of pooled data from 1,393 patients (20 studies), 90% were found to have symptom improvement at follow up (18). Sample sizes of the included studies ranged from 13 to 287 patients. Seven of the included studies reported patient satisfaction and rates ranged from 61.8% to 100%. Interestingly, in the study with a satisfaction rate of 61.8%, 39% of the sample had undergone previous radiotherapy and the explantation rate was 31.5% (19). In contrast, in the study recording 100% satisfaction, only 7.7% had received previous radiotherapy and the explantation rate was zero (20). More research is needed to determine what affects long term patient satisfaction.

Pooling data on dryness rates is difficult given the varying definitions for this parameter. In a retrospective study of 155 patients by Angulo et al. published in 2020, which had a mean follow up of 60 months, 72.1% achieved a dry status as defined by no pads or one security pad (21). Friedl et al. reported on the impact of ATOMS™ on sexual function (22). Erectile function scores were improved at six months follow up and 38% of the sample started to have intercourse again after having stopped previously. Dual implantation of penile prosthesis and ATOMS™ has been reported. To date, only data on simultaneous AUS placement at the time of surgical repair of refractory bladder neck contracture has been reported (23–25).

## Complications

Muhlstadt et al. reported the overall complication rate to be 27.3% in their series of 187 patients. The authors found previous radiotherapy as well as previous urethral surgery to be significant predictors of a post operative complication (15). The learning curve associated with ATOMS was also studied and found the rate of complication to fall from 44% to 21.1% after 25 cases were performed. Angulo et al. reported an explantation rate of 8.5% in their multi-centre study of 902 patients (26). The two commonest indications for removal were persistent incontinence and port erosion. Explantation rates do vary, with reports of as high as 19% previously recorded (27). Possible reasons for such wide variations include different follow up lengths and the proportion of patients with radiotherapy. Giammo et al. reported the survival of the ATOMS™ device to be 97% at 12 months and 89.9% at 60 months (28). As with all prosthetic devices, infection can be a major complication and rates between 2.7%–6.2% have been reported (8). Predictive nomograms have become increasingly popular across many areas of urology and tools are now available in the setting of ATOMS™ (29, 30). This includes the tool developed by Dorado et al., which serves to predict risk of failure (30). Variables included in that tool are Male Stress Incontinence Grading Scale (MSIGS), 24-h pad test and history of radiotherapy.

## Guidelines perspective

While ATOMS™ surgery is covered in the latest EAU guideline, no formal recommendations regarding any of the adjustable male slings are given as the panel determined the current body of literature to be still lacking (31). Fixed male slings do however receive a recommendation. Here it is stressed that the role of such fixed devices should be limited to the setting of men with mild to moderate incontinence. Again however, it is underscored that the evidence is also limited for this intervention type. The American Urological Association guidelines do not make any specific comment regarding the ATOMS™ device (2). Male slings as a group are discussed with a similar recommendation that they are avoided in the setting of severe incontinence. These positions shared by the EAU and AUA guidelines are very similar to those from the Urological Society of India, Canadian Urological Association (CUA) and the International Consultation on Incontinence (ICI) (32–34). Of note, some of these guidelines are not updated yearly. The CUA document was disseminated in 2012, which was before the last generation of ATOMS™ was released and there have been multiple original studies published since then (32). Bhatt et al. evaluated all five of these guidelines on the topic of post prostatectomy incontinence using the Appraisal of Guidelines for Resarch and Evaluation II (AGREE II) tool on domains such as scope, clarity and applicability (35). The authors concluded the AUA guidelines to score highest.

## Advantages and disadvantages compared to AUS

There are several advantages that can be found with the ATOMS™ device. Firstly, and in contrast to fixed slings such as the AdVance™ and the AUS, adjustments can be made without the need to return to surgery and the scrotal port placement allows for ease of access when doing so. Also, if there is a complication that is localised to the port only, the port can be removed in isolation. While this means that further adjustments cannot be made, it avoids the complete explantation of the device. ATOMS™ is also associated with a shorter operative time compared to AUS. In a propensity-score-matched analysis comparing the two devices, the mean operative time associated with ATOMS™ was significantly shorter (56 vs. 100 min, $p < 0.001$) (36). In contrast to AUS where satisfactory manual dexterity and cognition is required, patients are not required to manipulate the ATOMS™ device themselves. While simpler methods for activation of the AMS 800 have been proposed, these are not yet in clinical use. Even if patients have normal cognition and dexterity at the time of surgery, if they later suffer an acute medical event such as a stroke that impairs their upper motor function and/or their cognitive status, this can pose obvious problems for those with an AUS *in situ*. From a practical perspective, patients with AUS also require greater caution when performing a subsequent cystoscopy as well as the need for a urologist to attend the operating theatre to deactivate the AUS device if undergoing surgery by another specialty when catheterization is being performed. From an anatomical perspective, the non-circumferential design reduces the risk of urethral atrophy and erosion. Infection rates are also lower when compared to AUS as well as Argus and Remeex. There is a potential cost advantage too, with Constable et al. reporting costs associated with ATOMS™ procedure to be £6,000 compared to £9,000 with the AUS (37).

However, as raised by international guidelines, the levels of evidence supporting the role of ATOMS™ is more limited compared to AUS. This is perhaps the biggest disadvantage. How these abovementioned advantages translate overall is thus yet to be fully determined.

While the body of original studies for ATOMS™ does exceed 20, many are single centre and retrospective in nature and to date, there have been no randomised studies, which have placed ATOMS™ head-to-head against AUS. The MASTER trial did compare male slings with AUS but most of the slings included in that non inferiority trial were the fixed type and a full breakdown is not given (38). The authors found no differences in SUI burdens at follow up. However, secondary outcomes such as complication rates did favour AUS. The proposed advantages of the AUS are its feasibility in patients with previous radiotherapy and those with severe SUI.

## Challenges

Beyond the abovementioned lack of studies in comparison to other incontinence devices, other challenges exist. For example, the lack of standardised reporting as well as lack of consensus regarding reporting of SUI. Some author groups prefer to use pad count while others choose pad weight. Furthermore, for each one of these, consensus is lacking regarding how to how to grade severity. This makes comparisons between studies more difficult. Another area that appears to lack standardisation is reporting of port removal/total explantation. For example, some groups report this as a complication but others consider it a late treatment failure. Unless a reader studies the results very carefully and is aware of this, one can easily misinterpret the complication burdens across different studies.

Heterogeneity in other forms is also common among studies. For example, populations with both RP and benign prostate surgery patients and some having had radiotherapy. Furthermore, radiotherapy type (e.g., adjuvant vs. salvage) is not routinely specified in these studies. Studies reporting their experiences with ATOMS™ over several years will usually include patients have had different generations of ATOMS™ devices. This can introduce further bias.

## Conclusions

With over a decade of published results associated with ATOMS™ now available, this adjustable sling device has positioned itself as an effective surgical option. It offers strengths that can complement the longer established AUS. Further studies will allow for optimal selection criteria to be further defined and its recommended role in international guidelines to be delineated. This includes the role of ATOMS™ in the setting of previous radiation as well as severe incontinence.

## Author contributions

PJ-J: Conceptualization, Data curation, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing. IR: Writing – original draft, Writing – review & editing. LT: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. KH: Conceptualization, Supervision, Writing – original draft, Writing – review & editing. CM: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. FE: Methodology, Writing – original draft, Writing – review & editing. BS: Supervision, Writing – original draft, Writing – review & editing. CB: Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing.

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# Patient experiences and perceptions of kidney stone surgery: what lessons can be learned from TikTok?

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**Introduction:** The aim of this study was to perform an evaluation of patient experiences and perceptions regarding kidney stone surgery on the social media platform TikTok. An increasing number of the public use social media (SoMe) as a platform to share their views regarding their experiences related to surgical treatment.

**Methods:** Using the hashtag #kidneystonesurgery, the 100 most recent video posts as of 01.01.2024 on TikTok were included. As well as demographic data such as gender and location, thematic content was also collected. To achieve this, a previously published framework was used and adapted for application in the setting of kidney stone surgery. This was piloted on 20 sample videos to assess its feasibility before revision and establishment of the final framework. This included the following key areas: Pain, Complications, Anxiety, Recovery, Return to work, Finances, Treatment delays, Diet and Prevention and stent complaints.

**Results:** The majority of posts (95%) were from North America, 80% by females and the mean number of video views was 92,826 (range: 261–2,000,000). 76% of the videos discussed ureteroscopy (URS). 49% were filmed at the hospital, which was named in 9% of the videos. Top three topics discussed were: Recovery (65%), pain (62%) and stents (55%). This was followed by anxiety (39%) and complications (24%). 12% of these videos uploaded by lay people included basic medical information that was wholly incorrect. More than half of the posts (51%) were negative in tone. Treatment delays (5%) and a lack of sufficient preoperative information (4%) were also raised, that appeared to contribute to the negative reports. However, the main cause for negative tone owed to the 80% of the patients ($n = 44$) who discussed stents that focused their video on the pain suffered from the post operative stent.

**Conclusion:** There is a high level of usership and engagement on TikTok on the subject of kidney stone surgery. The proportion of negative videos is high and much of this is related to the bothersome stent symptoms and complications. This could easily lead to misperceptions among potential patients about the true burden of such adverse events.

KEYWORDS

urolithiasis, ureteroscopy, TikTok, social media, shockwave lithotripsy

## Introduction

With an increasing prevalence of kidney stone disease (KSD) worldwide, the volume of surgeries performed has increased accordingly (1, 2). Traditional outcome measures of interest have been largely focused on objective parameters such as stone free rate and complications. However, in the recent era, patient experience and the impact on quality of life related to surgery has been appreciated more (3–5). Research across a number of surgical fields has highlighted how patients use social media (SoMe) as a platform to share their views regarding their experiences related to surgical treatment (6, 7). At the same time, patients awaiting surgery often wish to hear first-hand, the experiences of others and SoMe can allow for this. In a survey of patients undergoing maxillofacial surgery, it was found that SoMe can influence decision to undergo surgery as well as by which medical provider (8).

While there are a number of SoMe platforms available, TikTok, which has over one billion active users per month, is one which allows for users to make extended videos (maximum 10 min) (9). These are often in a talking heads style where users discuss a topic, and in this way, it lends itself to recounting their own treatment and experiences as a patient. While SoMe findings related to patient experience has been studied in a number of other surgical fields, there is a very limited amount related to the management of KSD. An increasing proportion of the lay community use the internet and SoMe to learn more about their health-related problems (10). This has only been further augmented as a result of the Covid-19 pandemic.

Our aim was to perform an evaluation of patient experiences, perceptions and lessons learnt from kidney stone surgery on TikTok.

TABLE 1 Summary of demographics.

| | |
|---|---|
| Mean number of views (range) | 92,826 (261–2,000,000) |
| Mean number of likes (range) | 7,669 (2–208,200) |
| Mean number of comments (range) | 113 (0–2,366) |
| Mean number of times video set as a favourite (range) | 249 (0–8,599) |
| **Country of video origin** | |
| North America | 95% |
| Asia | 3% |
| Europe | 2% |
| **Gender** | |
| Male | 20% |
| Female | 80% |
| **Setting** | |
| Elective surgery | 64% |
| Emergency surgery | 14% |
| Unknown | 22% |
| **Surgery type** | |
| URS | 76% |
| PCNL | 3% |
| SWL | 2% |
| Unknown | 19% |
| **Timing** | |
| Before surgery | 20% |
| After surgery | 64% |
| Before and after surgery | 16% |
| Filmed at hospital | 49% |
| Hospital named | 9% |

URS, ureteroscopy; PCNL, percutaneous nephrolithotomy; SWL, shockwave lithotripsy.

## Materials and methods

After creating an anonymous account, a search was performed on the SoMe platform TikTok using the hashtag #kidneystonesurgery. The 100 most recent video posts as of 01.01.2024 were included. Videos considered eligible were those in the English language, uploaded by self-identifying patients, and videos deemed to be made for the purposes of humour e.g., comedy sketches were excluded. Given that all data was freely available in the public domain, it was determined that ethical approval was not required. Content uploaded from minors was excluded. As well as demographic data such as gender and location, thematic content was also collected. To achieve this, a previously published framework was used and adapted for application in the setting of kidney stone surgery (6). This was piloted on 20 sample videos to assess its feasibility before revision and establishment of the final framework. To this end, data was collected on the following key areas: (1) Pain (2) Complications (3) Anxiety (4) Recovery (5) Return to work (6) Finances (7) Treatment delays (8) Diet and Prevention (9) Stent (10) Gratitude to healthcare workers and (11) Activities of daily life (ADLs). Supplementary data was also collected in the form of where filming occurred, and timing in relation to surgery among other characteristics. It was also noted if the user stated any basic medical facts, which were completely incorrect.

## Results

Of the 100 videos evaluated, 95% of posts were uploaded from North America and 80% by females. The mean number of video views was 92,826 (range: 261–2,000,000) while the mean number of likes and comments was 7,669 (range: 2–208,200) and 113 (range: 0–2,366), respectively (Table 1). Elective surgery was the most common setting (64%). 76% of the videos discussed ureteroscopy (URS) and most were captured after the surgery had been performed. 49% were filmed at the hospital, which was specifically named in 9% of the videos. 10% showed the viewers their removed stent and 2% showed their own radiographic images.

The top three topics discussed were: Recovery (65%), pain (62%) and stents (55%). This was followed by anxiety (39%) complications (24%) and ADLs (22%) (Table 2). All the complications involved readmission to the emergency department. 12% of these videos uploaded by lay people included basic medical information that was wholly incorrect. These covered how the surgery was performed, potential complications and evidence supporting natural remedies. None of the videos discussed surgical technology. Discussion of stone diet (5%) and finances (3%) were relatively low. 5% of the patients reported that the clinician had told them about being completely stone free on leaving the hospital.

TABLE 2 Summary of content analysis.

| Domains covered | |
|---|---|
| Recovery | 65% |
| Pain | 62% |
| Stent | 55% |
| Anxiety | 39% |
| Complications | 24% |
| Activities of daily life | 22% |
| Disease recurrence | 14% |
| Need for multiple surgeries | 24% |
| Incorrect basic medical information: | 12% |
| Return to work | 7% |
| Diet and stone prevention | 5% |
| Treatment delays | 5% |
| Lack of sufficient pre-operative information | 4% |
| Gratitude to healthcare providers | 4% |
| Financial costs | 3% |
| Technology in stone surgery | Zero |
| **Tone** | |
| Positive | 22% |
| Neutral | 37% |
| Negative | 51% |

More than half of the posts (51%) were negative in tone. Treatment delays (5%) and a lack of sufficient preoperative information (4%) were also raised, that appeared to contribute to the negative reports. However, the main cause for negative tone owed to the 80% of the patients ($n = 44$) who discussed stents that focused their video on the pain suffered from the post operative stent.

## Discussion

This study highlights that patients do use SoMe platforms such as TikTok to communicate their patient experiences related to kidney stone surgery. As also seen by the volume of comments, patients also use this as a vehicle to communicate with other patients regarding all areas of the treatment pathway. The findings also serve as a reminder to clinicians that patients may well film while at the hospital, both during elective and emergency admissions, as well as potentially name the medical provider publicly. The representation of complications related to kidney stone surgery could easily give an impression to a lay person that the true complication burden is much higher than what is formally reported in studies. Doctors should therefore counsel patients that patient experiences on social media should be taken with caution. This is highly relevant given the findings of Kunitsky et al. where it was found that 51% of respondents in a survey answered that they use a combination of Reddit, Facebook and/or YouTube to gain medical information (11). Stents are well recognised to be associated with negative quality of life in some patients (12). This study confirms this as an issue and supports the supposition that pain related to indwelling stent is an issue that surgeons should proactively take up with patients pre-operatively. Videos uploaded on the topic of kidney stones also originate from health care professionals. In a recent study by Diaz et al, which evaluated the educational content of such videos, the overall scores were quite low (13). More attention towards creating educational content at the appropriate level is needed. Yilmaz et al. assessed similar YouTube content that focused on miniaturised PCNL and found that these seemed to be aimed at other medical professionals than patients (14). Moving away from SoMe, the readability of educational materials found online have also been found to be substandard (15). Assessment of the online education content produced by the European Association of Urology (EAU) has also been recently performed (16). This study found that while the readability of this web-based content is superior to the abovementioned sources, further simplification is much needed. In recent times, there has been an increased demand by some journals for scientific manuscripts to also include a patient summary. While the possible merits of this are clear, a recent analysis of 266 articles by Ganjavi et al. found these also to be too difficult to the lay community to read (17). Such are the advances that have taken place, much attention is given by urologists on SoMe to new technologies such as novel laser platforms (e.g., Thulium fiber laser) and new accessories (e.g., suction access sheaths) (18, 19). It is interesting but perhaps not surprising that none of this was ever mentioned by patients. There are many areas that health care professionals need to stay up to date on such as artificial intelligence and new simulation methods, staying up to date with social media and its impact on health care is yet another new field (20).

This study does have certain limitations. Only 100 videos were sampled and these were the most recent videos captured. Inclusion of older videos may have provided a better impression of overall viewership and engagement. Sampling of more videos would have allowed for the findings to be more generalisable. This study only evaluated videos in the English language and may therefore misrepresent findings on a worldwide level. Different surgical interventions were also not differentiated in the analysis. However, the merits of this novel study include that it assesses the patient perspective as opposed to the content posted by health care professionals (13). Given the relative low volume of research focused on quality of life compared to those evaluating objective outcomes, studies such as this one that offer a new means to gauge patient experiences are arguably welcomed (3). More prospective studies of a qualitative nature are needed to explore patient experiences and perceptions of kidney stone surgery. This would allow the domains highlighted in this study to be explored more substantially.

## Conclusion

There appears a high level of usership and engagement on TikTok on the subject of kidney stone surgery. Much of this is filmed by patients while physically being at the hospital site. In this way, it is being used as a platform to share and communicate experiences among patients. The proportion of negative videos is quite high and much of this is related to the bothersome stent symptoms and complications. This could easily lead to misperceptions among potential patients about the true burden of such adverse events. This supports the need for comprehensive pre-operative counselling.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors upon reasonable request.

## Author contributions

PJ: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. LT: Conceptualization, Resources, Visualization, Writing – original draft, Writing – review & editing. CB: Conceptualization, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. IR: Conceptualization, Resources, Writing – original draft, Writing – review & editing. BS: Conceptualization, Investigation, Resources, Supervision, Writing – original draft, Writing – review & editing.

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## Conflict of interest

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# A retrospective study of paraganglioma of the urinary bladder and literature review

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**Objective:** To review and summarize the characteristics and therapy of paraganglioma of the urinary bladder (PUB).
**Method:** Patients who underwent the operation in Peking Union Medical College Hospital between January 2012 and December 2021 were reviewed for this retrospective study.
**Results:** A total of 29 patients, comprising 9 (31%) men and 20 (69%) women, were included. The main manifestations were hypertension, palpitation, and micturition syncope. Eight patients had an increased 24-h urinary catecholamine, and seven of them had increased norepinephrine. Normetanephrine in seven patients was increased. Six of 18 metaiodobenzylguanidine and 8 of 22 octreotide scans were positive. In total, 15 cases underwent laparoscopic partial cystectomy and 14 underwent transurethral resection of bladder tumor. In all patients, the immunohistochemical index of Melan-A, AE1/AE3, and α-inhibin were negative, and chromogranin A, S-100, and succinate dehydrogenase were positive. The Ki-67 of 28/29 cases was under 5%, and 1 case with a Ki-67 of 20% was diagnosed with malignant PUB. A total of 27 patients had a regular follow-up, 2 patients were lost during the follow-up, 3 patients had a recurrence, and 1 of these patients died within 1 year of surgery. The symptoms all disappeared or were relieved after the surgery.
**Conclusion:** The transurethral surgery approach fits PUB tumors with a size <3 cm or that protrudes into the bladder and can significantly reduce the postoperative hospital stay. Early detection and treatment are effective, and regular review is necessary after the surgery.

KEYWORDS

paraganglioma of the urinary bladder, diagnosis, transurethral resection of bladder tumor, cystectomy, prognosis

## 1 Background

Paraganglioma of the urinary bladder (PUB) is a rare tumor that was first reported by Zimmerman et al. in 1953 (1). Like all the other paragangliomas, PUB derives from chromaffin cells of the sympathetic nervous system. However, it only constitutes 0.06% of urinary tumors and approximately 6%–9.8% of paragangliomas (2, 3). The tumors can be functional or non-functional; the clinical manifestation of the functional tumor mainly includes micturition syncope, hypertension, headache, and palpitation, which are caused by extensively increased endogenous catecholamine (CA) secretions. Due to their rarity and the variable nature of their symptoms, PUBs are commonly misdiagnosed and mistreated. Treatment options generally include transurethral resection or partial or radical cystectomy. We reviewed the clinical and pathological characteristics of all patients diagnosed with PUB in our hospital over the past 10 years and compared postoperative hospitalization and follow-up with different surgical approaches. This will improve our understanding of PUB and help to give the patients a safer and more effective treatment method.

# 2 Methods

We reviewed patients who were diagnosed with PUB and underwent surgery in our hospital between January 2012 and December 2021. The patients' general information, laboratory and radiology examinations, surgery, pathology, and follow-ups were collected. All PUB tumors were defined as functional when urine or plasma fractionated CAs or fractionated or total metanephrines (MN) were elevated above the upper limit of respective reference ranges. Length of stay exceeding the 75th percentile of the total length of stay was defined as an extended length of stay (4). High-performance liquid chromatography with electrochemical detection determined 24-h urinary CA levels in all patients. In addition, normetanephrine (NMN) and MN were detected in blood samples utilizing the same method for patients from 2019 onward, which helped us to save diagnostic time and improve accuracy. The operative method of PUB was diverse. According to our experience, when the tumor diameter is ≤3 cm, a transurethral resection of bladder tumor (TURBT) can be selected, which can ensure the *en bloc* resection of the tumor and complete removal from the urethra to avoid implantation and metastasis. All tumors were completely resected. All surgical specimens were diagnosed by urologic pathologists. Tumor markers for paragangliomas of the bladder, including CD56, NSE, chromogranin A (CgA), Syn vimentin, succinate dehydrogenase (SDHB), Von Hippel–Lindau (VHL), PGP9.5, and S-100 protein, were detected using immunohistochemical techniques. Tumor size was determined based on the largest diameter of the PUB on histopathology. To assess the effectiveness of PUB treatment, a long-term follow-up was carried out by reviewing patients in the outpatient clinic or by telephone interviews at intervals of approximately 3–6 months. The follow-up period is calculated from the date of surgery to the date of the last follow-up or death. SPSS version 26.0 software was used for data processing and analysis. In this study, measurement data that did not obey normal distribution were expressed as median (M) and quartiles (P25–P75), and the Mann–Whitney *U* test was used for comparison between groups. Count data were expressed by frequency or composition ratio, and the chi-square test was used for comparison between groups. $P < 0.05$ was considered statistically significant.

# 3 Results

## 3.1 Patient demographics

In this study, 29 cases of PUB were diagnosed, accounting for 5.7% (29/508) of patients with all paragangliomas treated in our hospital during the same period. Baseline characteristics, diagnostic findings, operation methods, results, and postoperative follow-up for each patient can be found in Table 1. The mean age of the patients with PUB was 48 years (range 28–68), and these included 9 (31%) men and 20 (69%) women. Of the 29 cases, 11 (37.9%) were functional and 18 (62.1%) were non-functional. Patients with PUB presented with strong headache (44.9%), palpitation (62.1%), weakness (20.7%), and increasing blood pressure after urination (41.4%). Two patients (6.9%) detected the tumor coincidentally, without any symptoms. One patient with a history of hypertension for more than 10 years had postoperative symptom relief and his blood pressure remained at normal levels during the long-term follow-up. Among the 20 patients who underwent SDHB gene screening for paraganglioma genetic syndrome, four patients were identified as SDHB-positive (SDHB+), one patient was classified as SDHB-indeterminate (SDHB±), and the remaining patients tested negative for SDHB (SDHB–). All patients experienced complete symptom relief after surgery, with a recurrence rate of 20% observed in SDHB+ or SDHB± patients, while no recurrences were observed in those who tested negative for SDHB.

## 3.2 Treatment

The traditional methods of B-ultrasound and contrast-enhanced enhanced computed tomography (CT) were taken preoperatively to assess the location and the statement of invasion of the tumor (Figures 1, 2). PUB performs an obvious enhancement because of the rich blood supplement. The mean size of the largest tumor diameter was 2.57 cm. In total, 18 patients underwent metaiodobenzylguanidine (MIBG) imaging and 6 (33.3%) patients had positive results. A total of 22 patients underwent octreotide imaging, and 8 (36.3%) patients had positive results. MIBG and octreotide imaging were both positive in two patients. Notably, two patients had positive MIBG imaging results but negative octreotide imaging results, and one patient had negative MIBG imaging results but positive octreotide imaging results. Three patients underwent 68GA PET-CT for suspected metastases and all had positive results. The locations of the PUBs included the right wall (9 cases, 31.0%), right posterior wall (1 case, 3.4%), right anterior wall (1 case, 3.4%), left wall (1 case, 3.4%), left posterior wall (4 cases, 13.8%), posterior wall (4 cases, 13.8%), and anterior wall (9 cases, 31.0%) (Figure 3).

All 29 patients underwent rigorous preoperative preparation using alpha blockers for 2–4 weeks. The preoperative evaluation of patients' supine blood pressure, heart rate, hematocrit (HCT), and other indicators suggested that surgery should be performed only after full preoperative preparation and that changes in blood pressure and heart rate should be strictly monitored during the operation. The results showed that the blood pressure and heart rate of all patients did not fluctuate significantly, and the hemodynamics were stable. All patients underwent surgery in our hospital, with 15 combined transurethral and laparoscopic partial cystectomies (Figure 4) and 14 TURBT. Among the patients who underwent a combined transurethral and

TABLE 1 Baseline characteristics, operation methods, results, diagnosis, and follow-up for each patient.

| Number | Gender | Age | Tumor size | Operation methods | Results | Diagnosis | Follow-up |
|---|---|---|---|---|---|---|---|
| 1 | M | 39 | 2.7 | Partial cystectomy | Asymptomatic | PUB | Recurrence |
| 2 | F | 49 | 0.9 | TURBT | Non-remission | PUB | Relief after 1 year |
| 3 | F | 50 | 4.7 | Partial cystectomy | Remission | PUB | Normal |
| 4 | F | 51 | 1.8 | TURBT | Remission | PUB | Normal |
| 5 | M | 34 | 2.7 | TURBT | Remission | PUB | Normal |
| 6 | F | 68 | 2.4 | Partial cystectomy | Remission | PUB | Normal |
| 7 | F | 44 | 1.1 | Partial cystectomy | Remission | PUB | Normal |
| 8 | F | 43 | 8.8 | Partial cystectomy | Remission | PUB | Recurrence |
| 9 | M | 51 | 3.2 | Partial cystectomy | Remission | PUB | Normal |
| 10 | F | 54 | 2.0 | TURBT | Remission | PUB | Normal |
| 11 | M | 50 | 1.5 | TURBT | Remission | PUB | Normal |
| 12 | F | 36 | 2.0 | Partial cystectomy | Remission | PUB | Normal |
| 13 | F | 61 | 1.5 | TURBT | Remission | PUB | Normal |
| 14 | F | 40 | 3.5 | Partial cystectomy | Remission | PUB | / |
| 15 | F | 46 | 1.4 | TURBT | Remission | PUB | Normal |
| 16 | F | 56 | 2.0 | Partial cystectomy | Remission | PUB | Normal |
| 17 | M | 49 | 6.5 | Partial cystectomy | Remission | PUB | Recurrence |
| 18 | F | 40 | 1.2 | Partial cystectomy | Remission | PUB | Normal |
| 19 | F | 50 | 1.7 | TURBT | Remission | PUB | Normal |
| 20 | M | 62 | 1.1 | TURBT | Remission | PUB | Normal |
| 21 | M | 28 | 2.9 | Partial cystectomy | Asymptomatic | PUB | Normal |
| 22 | F | 47 | 1.1 | TURBT | Remission | PUB | Normal |
| 23 | F | 28 | 3.0 | Partial cystectomy | Remission | PUB | Normal |
| 24 | M | 61 | 2.7 | TURBT | Remission | PUB | Normal |
| 25 | F | 48 | 2.0 | TURBT | Remission | PUB | Normal |
| 26 | F | 55 | 4.0 | Partial cystectomy | Remission | PUB | Normal |
| 27 | M | 56 | 2.7 | Partial cystectomy | Remission | PUB | Normal |
| 28 | F | 39 | 1.6 | TURBT | Remission | PUB | / |
| 29 | F | 47 | 1.8 | TURBT | Remission | PUB | Normal |

"/" indicates missing follow-up data.

FIGURE 1
The arterial phase enhanced CT scan of the patient whose PUB tumor was located in left posterior wall.

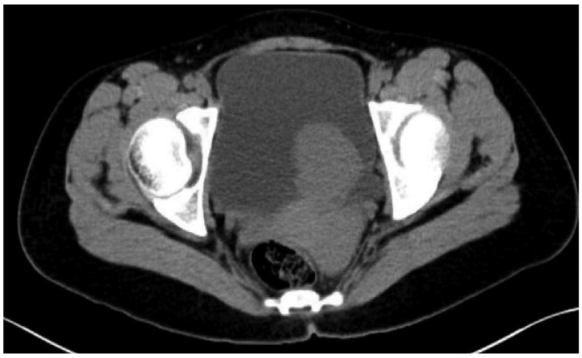

FIGURE 2
The unenhanced CT scan of the patient whose PUB tumor was located in left posterior wall.

laparoscopic partial cystectomy, the tumor size in eight cases was smaller than 3 cm; all patients who underwent a TURBT procedure had a tumor size smaller than 3 cm. The mean postoperative hospital stay was 7.7 days in the partial cystectomy group and 3.6 days in the TURBT group, with a significant difference in whether postoperative hospital stay was prolonged in the two groups ($p < 0.001$) and no difference in whether there was a recurrence after surgery ($p > 0.05$) (Table 2).

## 3.3 Pathology

The historical pathology results of the 29 patients were all paraganglioma of urinary bladder. The immunohistochemical index of Melan-A, AE1/AE3, and α-inhibin were negative, while CgA, S-100, and SDHB were positive. The Ki-67 index can determine the proliferative activity of the tumor.

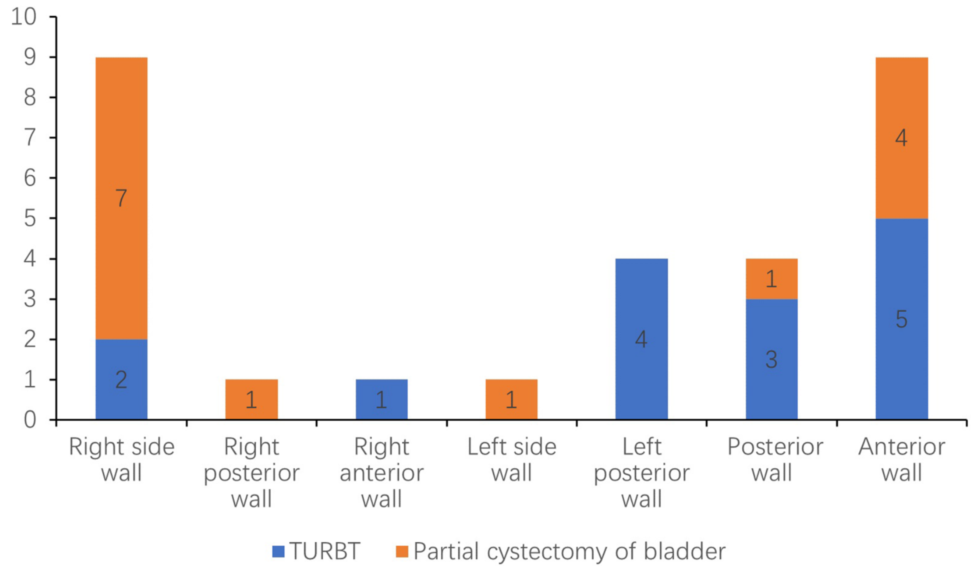


FIGURE 3
The distribution of different tumor locations of bladder and surgical approach.

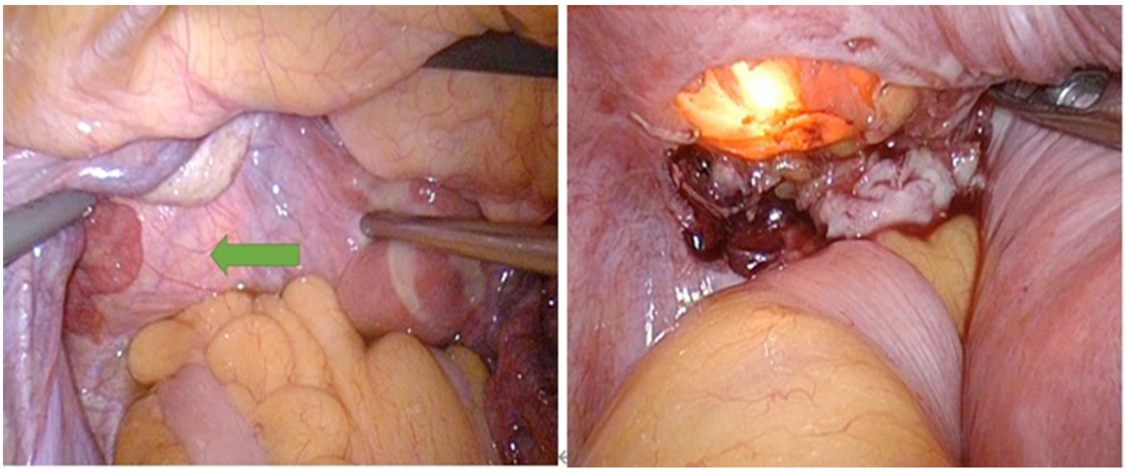

FIGURE 4
In a combined transurethral laparoscopic partial cystectomy, the transurethral approach helps the surgeon avoid damaging important anatomical structures.

**TABLE 2** Intergroup comparison of postoperative hospital stay by surgical approach.

| Index | | Partial cystectomy group | TURBT group | $Z/\chi^2$ | $P$ |
|---|---|---|---|---|---|
| Age | | 46 (39.55) | 50 (47.56) | −1.027 | 0.304 |
| Gender | Male | 5 (33.3%) | 4 (28.6%) | −0.272 | 0.785 |
| | Female | 10 (66.7%) | 10 (71.4%) | | |
| Postoperative hospital stay | | 7.7 (6.9) | 3.6 (3.5) | −4.232 | <0.001 |
| Prolonged postoperative hospital stay | Extension | 12 (80%) | 0 (0%) | 19.106 | <0.001 |
| | No extension | 3 (20%) | 14 (100%) | | |
| Postoperative recurrence | Recurrence | 3 (21.4%) | 0 (0%) | 1.340 | 0.247 |
| | No recurrence | 11 (78.6%) | 13(100%) | | |

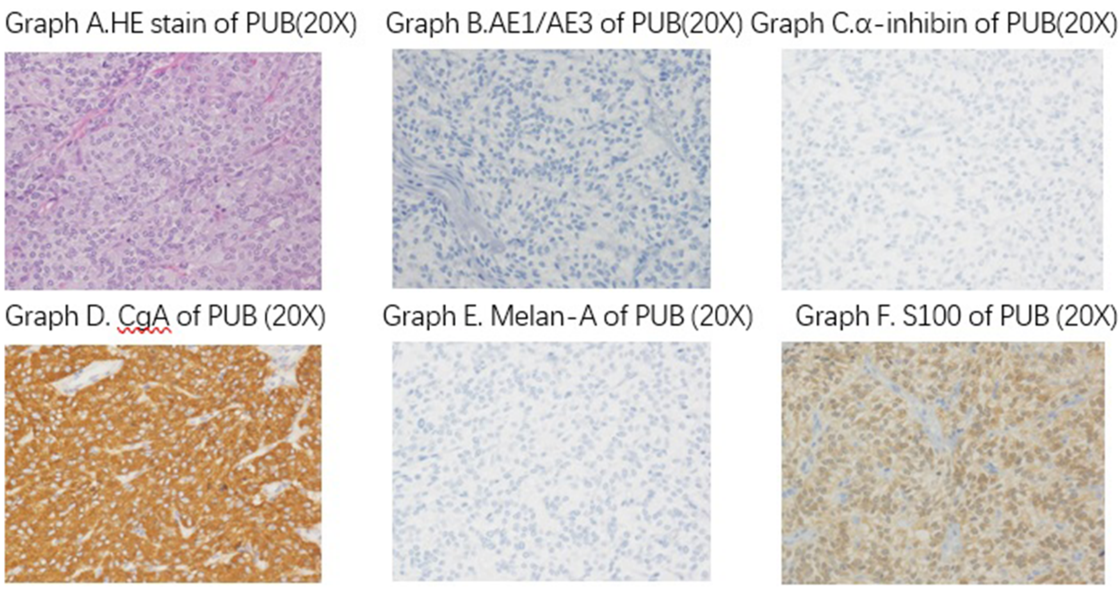


FIGURE 5
The pathology historical results of the 29 patients are all paraganglioma of urinary bladder. The immunohistochemical index of Melan-A, AE1/AE3, and α-inhibin are negative, while CgA, S-100, and SDHB are positive.

In our patients, the Ki-67 index of 28 cases was <5%. One patient, whose Ki-67 was 20%, was diagnosed with metastatic PUB, and the pathology results showed that the bladder muscle was invaded and an intravascular tumor thrombus had formed (Figure 5).

### 3.4 Follow-up and prognosis

Of the 29 cases, 2 (6.9%) were lost during the follow-up. The remaining 27 patients were reviewed regularly. One patient had a new mass in the left pelvis 9 months after surgery; metastases in the lumbosacral region, the right side of the chest, and the right side of the back were detected by MIBG and octreotide scanning. The patient died within 1 year after surgery. The patient with a recurrence 2 years after surgery showed intravesical metastases, right paracolonic parappendiceal metastases, multiple metastases in both lungs (the largest in the lower lobe of the left lung), and an elevated systolic blood pressure of >180 mmHg. We gave him alpha receptor blockers to control the blood pressure, and there was no progress with the recurred mass and multiple metastatic foci. One patient had a recurrence 5 years postoperatively, with two masses detected: one in the retroperitoneum and the other in front of the sacrum. Temozolomide was taken with side effects of weakness and nausea. The symptoms of headache, palpitation, and high blood pressure after urination in 26 patients disappeared after the surgery, and one patient experienced symptom relief within 1 year.

## 4 Discussion

A paraganglioma is a non-epithelial tumor that arises in a paraganglial location. Less than 10% of paragangliomas are found in the urinary bladder, and young people are more likely to develop PUB. PUBs arise more frequently in the trigone of the bladder, with a mean size of 3.9 cm (5). To the best of our knowledge, we have reported the largest number of patients with PUB in one center to date.

The detection and diagnosis of PUB in the early stage depend on the clinical manifestation of hypertension and radiology examination. Symptoms may include headache, paranesthesia, dyspnea, angina, hematuria, and lower urinary tract symptoms (6). Unfortunately, PUB is always misdiagnosed as bladder cancer, especially the non-functional tumors with no symptoms. According to our previous literature review, 61.6% of patients with PUB were misdiagnosed before pathologic diagnosis, and less than 30% were diagnosed preoperatively (7).

Due to the difficulties in diagnosing PUB, crucial laboratory examinations and imaging analyses are necessary before surgery. CAs, which are secreted by chromaffin cells, include dopamine, adrenaline, and norepinephrine, and are important indexes. The level of these indexes, either in blood or 24-h urinary samples, are increased in functional PUB, and these laboratory results can help us finish the etiology diagnosis before the operation. In our study, all three patients with non-functional PUB had a normal level of 24-h urine CA, NMN, and MN. Almost all abnormal laboratory indexes show increased NE and NMN in functional PUB tumors. This may suggest that increased NE and NMN are specific to PUB tumors.

Imaging analysis provides a localization diagnosis and improves the etiology diagnosis. Contrast-enhanced CT and magnetic resonance imaging (MRI) are two basic screening methods. PUB demonstrates a regular-shaped bladder tumor with obvious enhancement and hyperintensity on T2-weighted imaging (T2WI) (8). MIBG and octreotide imaging are used as important tools in the diagnosis of PUB; in some studies, MIBG imaging has shown a higher sensitivity and specificity and is superior to octreotide imaging, but the latter has a clear advantage in the detection of some metastatic lesions. In our study, three patients had recurrent postoperative metastases: one patient underwent MIBG imaging with positive results; one patient underwent octreotide imaging with positive results; and one patient had both scans, in which MIBG imaging was negative and octreotide imaging was positive. This is consistent with results in previous studies. For the patients who underwent both MIBG and octreotide imaging, one was negative on MIBG imaging but positive on octreotide imaging, and two were positive on MIBG imaging but negative on octreotide imaging. Overall, MIBG and octreotide scans each have their own advantages and are complementary, which need to be selected with the patient's characteristics in the clinic. In previous studies, fluorodeoxyglucose (FDG)-PET was found to be more sensitive than MIBG imaging (9), whereas Ga-68 DOTATATE PET/CT could detect metastatic PUBs (10). However, non-functional PUBs are difficult to detect preoperatively because of the lack of secreting CA and non-typical symptoms. A case of functional PUB was reported without any radiographic and laboratory tests (11). Musa et al. (12) recommended cystoscopy before surgery because PUBs have the cystoscopic feature of hypervascularization. However, the final diagnosis must be based on histopathology and immunohistopathology after tumor resection.

Surgery is the most important treatment for PUB. To date, two main surgical options, transurethral resection and combined transurethral and laparoscopic partial cystectomy, have been used. Most PUB tumors were functional and could be detected in the early stage; the tumor size was small, and transurethral resection was a safer and better surgical approach. Approximately one-fifth of patients were treated with the TURBT procedure alone (13). The combined transurethral and laparoscopic partial cystectomy should be used for tumors that invade the muscle layer of the bladder or go even deeper. Transurethral methods can help surgeons avoid injury of this important anatomical structure, such as the bilateral ureteral orifice. We can coagulate the vessel at the tumor base early and it may be beneficial to use short bursts to limit the fluctuations in blood pressure during the procedure (14). At present, laser resection and electro-excision are reported to treat PUB, with good results (15), while it is suggested that resection rarely leads to a high level of recurrence (16).

In this article, we compared the effects of both partial cystectomy and TURBT procedure on postoperative length of stay and postoperative recurrence. The results showed that the different surgical approaches did not have an effect on postoperative recurrence and that the TURBT procedure significantly reduced the postoperative length of hospital stay. Moreover, recent findings suggest that the TURBT procedure is feasible for tumors with a diameter <3 cm with adequate preoperative preparation (17). Therefore, we recommend the TURBT procedure for PUBs smaller than 3 cm, while for larger tumors, partial cystectomy or radical cystectomy can be chosen, depending on the PUB's invasion of the bladder wall. Pelvic lymph node dissection or biopsy is necessary if metastasis is suspected. However, due to limitations in our sample size, we were not able to compare the differences between the two surgical approaches separately when the tumor was smaller than 3 cm. Therefore, more studies are needed to confirm this conclusion. On the other hand, almost all paragangliomas have a whole regular membrane, and excision extension involving the muscularis of the bladder is the key point to respect the tumor completely, and complete excision of the membrane is most important to avoid or decrease the rate of recurrence.

Pathology is the gold standard for a definite diagnosis. A typical paraganglioma has neuroendocrine markers combined with neuroendocrine markers and negative mesenchymal and epithelial markers. CD56, NSE, CgA, Syn vimentin, SDHB, VHL, PGP9.5, and S-100 protein are in common use (18). In our study, a typical PUB tested negative for Melan-A, α-inhibin, and AE1/AE3, and positive for CgA, S-100, and SDHB. A Ki-67 index >5% indicates a high risk of metastasis. Genetic disorder is another factor in occurrence, and SDHB is the most common gene associated with the highest rate of metastasis (19).

## 5 Conclusion

PUB is a rare bladder tumor with gradually advanced appropriate methods of diagnosis and surgery approaches in recent years. The transurethral surgery approach fits for most PUB tumors with a size <3 cm or that protrudes into the bladder. Early detection and treatment are effective, and regular postoperative reviews are necessary.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving humans were approved by Ethics Review Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences. The studies were conducted in accordance with the local legislation and institutional requirements. The human samples used in this study were acquired from primarily isolated as part of our previous study for which ethical approval was obtained. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

## Author contributions

YZ: Writing – original draft, Investigation, Funding acquisition, Formal Analysis, Data curation. ZZ: Writing – original draft, Methodology, Investigation, Data curation. SW: Writing – review & editing, Data curation. JW: Writing – review & editing, Validation, Resources, Funding acquisition. DW: Writing – review & editing. ZJ: Writing – review & editing, Supervision. YSZ: Writing – review & editing, Resources. HL: Writing – review & editing, Supervision.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Solitary fibrous tumor of the adrenal gland: a case report and review of the literature

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Solitary fibrous tumor (SFT) is a rare mesenchymal tumor, probably of fibroblastic origin, mainly in the extremities and pleura. Primary SFT of the adrenal gland is clinically more rare. Here, we report the case of a 47-year-old woman who detected a left adrenal mass on physical examination, without any symptoms, and no laboratory abnormalities. A computed tomography (CT) examination of the adrenal gland suggested a round-like soft tissue density shadow in the left adrenal area. An unenhanced scan showed uneven density of the mass, with a scattered circular-like cystic low-density shadow inside, and an enhanced scan showed obvious uneven enhancement. We considered it to be adrenal pheochromocytoma. Ultimately, the patient was treated with laparoscopic left adrenalectomy. A pathological examination suggested an adrenal SFT. We reviewed previous case reports of adrenal SFTs and summarized the clinical characteristics of adrenal SFT combined with the relevant literature. For adrenal tumors with uneven low-density shadow and uneven CT enhancement features, we should consider the differential diagnosis of adrenal SFT.

KEYWORDS
solitary fibrous tumor, adrenal tumor, computed tomography, diagnosis, adrenalectomy

## Background

Solitary fibrous tumor (SFT) is a rare spindle cell tumor derived from mesenchymal tissue, accounting for 2% of all soft tissue tumors (1). First reported by Klemperer and Robin in 1931 as a primary pleural neoplasm, SFT mostly originates from the pleura, with cases also reported in the urogenital system, such as the kidney, prostate, and bladder (2, 3). While SFT can occur in endocrine organs, such as the thyroid gland, pancreas, and pituitary gland, primary occurrence in the adrenal gland is even rarer (4–6). A review of the medical literature revealed only 14 cases of adrenal SFTs and one cohort study consisting of 9 cases. This study presents a case of rare adrenal SFT in a 47-year-old woman and provides an overview of previous case reports along with a summary of clinical characteristics combined with relevant literature.

## Case report

A 47-year-old woman presented to the urology department with a left adrenal mass detected during a physical examination. The patient did not exhibit symptoms of abdominal pain, hypertension, dizziness, headache, or fever throughout the course of the disease. Upon physical examination, no lump was palpated in the left upper abdomen, and percussion pain in the left renal area was absent. Adrenal-related hormone levels, including plasma cortisol, aldosterone, and catecholamine, were within normal ranges. In addition, other test results showed no significant abnormalities. A computed tomography (CT) examination revealed a round-like soft tissue density shadow in the left adrenal area measuring approximately 6.9 cm × 4.7cm × 5.9 cm. An unenhanced scan displayed uneven density with scattered circular-like cystic low-density shadows inside, while an enhanced scan showed obvious uneven enhancement suggestive of pheochromocytoma (PHEO) (Figure 1). Due to the large size of the tumor and clear surgical indications, magnetic resonance imaging (MRI) was deemed unnecessary for further evaluation. Subsequently, the patient underwent laparoscopic left adrenalectomy after completing preoperative preparation. The removed mass measured approximately 6 cm × 4 cm × 4 cm and exhibited gray and white coloration with focal cystic changes and clear boundaries. A postoperative pathological examination indicated a spindle cell tumor with the immunohistochemistry (IHC) panel showing CD34(3+), STAT6(3+), Synaptophysin (Syn; 1+), CgA(−), S-100(−), desmin(−), SMA(−), SOX10(−), Alpha-inhibin(−), and Ki-67 at approximately 5% (+) (Figure 2). Finally, the patient was diagnosed with an adrenal solitary fibrous tumor (intermediate type). The patient was discharged on postoperative day 5 and was generally in good condition. The ultrasound and laboratory examination in the third month showed no significant abnormal results. After that, we regularly followed the patient for 8 months with no tumor recurrence.

## Discussion

SFTs mostly originate from the pleura, with origin from the adrenal gland being very rare. According to a search of the medical literature, there are only 14 reported cases of adrenal SFT (Table 1) and one cohort study of 9 cases of adrenal SFT (Table 2). Of all the reported cases of adrenal SFT, 15 were in male patients and 8 were in female patients, indicating a higher incidence in men than in women, at a ratio of approximately 2:1. The age range of patients was 13–77 years (mean age 47 years). The clinical manifestations of adrenal SFT are related to tumor volume; larger tumors that compress surrounding tissues or organs can produce symptoms such as back pain or abdominal pain (13 cases), fever (3 cases), hypertension (2 cases), anemia (1 case), elevated cortisol levels (1 case), and paraneoplastic syndrome presenting with symptoms of hypoglycemia (1 case). Our patient had no symptoms and the SFT was detected during a physical examination. Among the reported cases, there were tumors found in the left adrenal gland in 12 cases, right adrenal gland in 10 cases, and both glands in 1 case, suggesting no significant difference between occurrence on either side of the adrenal gland. Tumor sizes ranged from 22 cm × 17 cm × 20 cm to 2.3 cm × 2.5 cm × 3.0 cm. Our patient's tumor measured 6 cm × 4 cm × 4 cm.

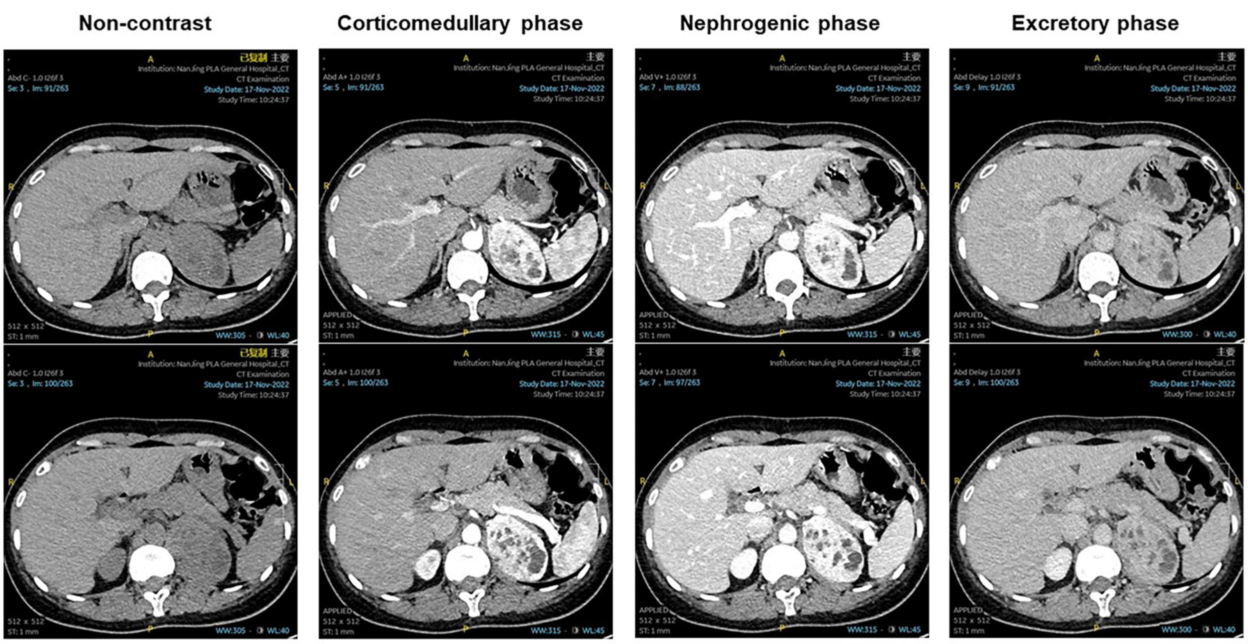


FIGURE 1
Non-contrast: a round-like soft tissue density shadow in the left adrenal area, with a scattered circular-like cystic low-density shadow inside. Corticomedullary phase, nephrogenic phase, and excretory phase showed obvious uneven enhancement, with scattered circular-like cystic low-density shadow inside.

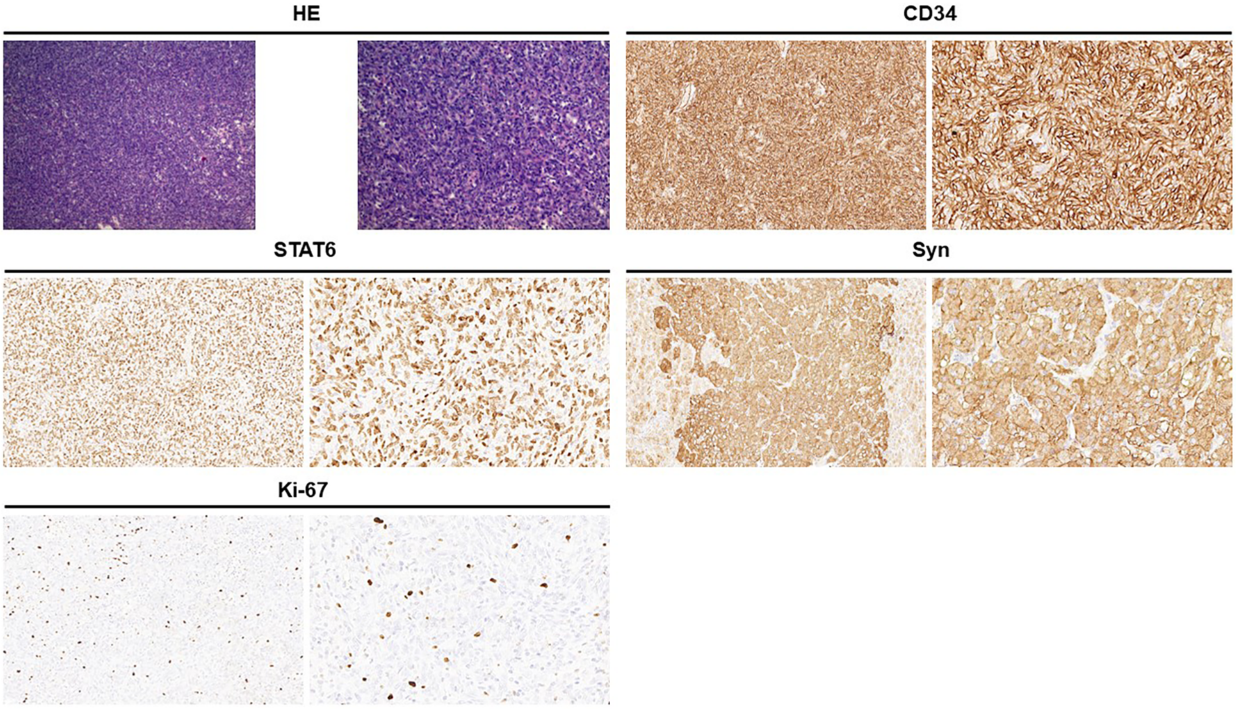


FIGURE 2
Hematoxylin and eosin staining showed that the tumor cells are spindle-shaped and are distributed in a sheet pattern, with blood vessels (left, ×100; right, ×200). Immunohistochemical staining: CD34 positive (3+); STAT6 positive (3+); Syn positive (1+); Ki-67 is approximately 5% (+).

On unenhanced CT scans, the SFT typically presents as a round soft tissue density with well-defined borders, and its density is correlated with the amount of collagen fibers in the tissue. On enhanced scans, the SFT shows moderate to high levels of enhancement, characterized by uneven enhancement, possibly due to necrosis and hemorrhage within the tumor (3). MRI reveals predominantly low to moderate signal intensity on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI), which may be attributed to the presence of collagen fibers within the mass. Kim et al. reported that the signal intensity on T2WI decreases with an increase in collagen components (22). In previously reported cases, one case mentioned uniformly low signal intensity on T1WI and unevenly high and moderate signal intensity on T2WI for adrenal SFT, while two cases noted uneven enhancement during enhanced MRI scans. In our case, the unenhanced CT scan revealed a round soft tissue density shadow with irregular density, including scattered circular cystic low-density shadows; the enhanced scan showed marked irregular enhancement.

Adrenal SFTs require a differential diagnosis, including adrenal PHEO, adrenal cortical carcinoma (ACC), and adrenal metastatic tumor (AMT). PHEO can be qualitatively diagnosed by measuring the concentration of blood-free metanephrines (MNs) or urinary MNs. On unenhanced CT scans, low confounding density is dominant, with some patients showing increased density due to bleeding or calcification. Enhanced CT scans show evident enhancement due to rich blood supply. MRI typically shows mixed signals, with a low signal in T1WI and a high signal in T2WI, significantly enhancing after an enhanced MRI scan. ACC is a rare malignant tumor originating from the adrenal cortex, with 50%–70% exhibiting endocrine function. Unenhanced CT scans show uneven density with irregular, oval, and lobulated shapes as well as cystic changes, necrosis, hemorrhage, and calcification in the lesions. Enhanced scans show irregular ring enhancement. ACC usually invades organs, tissues, or distant metastasis (23, 24). The main common primary tumors of AMT are lung cancer, breast cancer, colon cancer, and thyroid cancer. The CT examination shows diversity; when the tumor is small, it has smooth edges and low uniform density, while larger tumors appear lobulated with blurred edges and uneven density. AMT also exhibits uneven enhancement on both CT and MRI enhanced scans (25).

Adrenal SFTs can be definitively diagnosed through pathological examination and immunohistochemistry. The tumor typically presents with a clear boundary, appearing mostly gray and white in sections, with some instances of mucoid and bleeding necrosis. It has medium hardness, which is related to collagen content. Microscopically, the tumor is characterized by alternating regions of densely packed cells and sparsely distributed cells. The tumor cells themselves are short, spindle-shaped, round, or oval, with abundant red cytoplasm and round, oval, or short spindle nuclei. They are arranged in layers or sheets within the tumor, which also exhibits a rich vascular network forming a typical "hemangiopericytoma-like" area, often containing collagen fibers of varying thickness and shape (26).

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**TABLE 1** Reported cases with SFT diagnosed as adrenal tumor ($n = 14$).

| | Age | Sex | Symptom | Location | Tumor size (cm) | Treatment | F/U (months) | Recurrence during F/U | Positive immunohistochemical staining |
|---|---|---|---|---|---|---|---|---|---|
| 1 (7) | 71 | M | Abdominal pain, blood glucose <50 mg/dl | Left | 22 × 17 × 20 | Surgery | NM | NM | Vimentin, CD99, Bcl-2, STAT6, CD34 |
| 2 (8) | 28 | M | Mild left abdominal and back pain | Left | 6 × 6 × 7 | Surgery | 24 | No | Vimentin, CD34, Ki-67 (5%) |
| 3 (9) | 39 | F | General fatigue, mild anemia | Left | 10 | Surgery | 20 | No | CD34 |
| 4 (10) | 23 | F | Serum and urinary cortisol levels were increased | Left | 9 × 6 | Surgery | NM | NM | Vimentin, CD34, Bcl-2, MIC-2, Ki-67 (6%) |
| 5 (11) | 13 | F | Abdominal mass, dull pain, and low-grade fever | Right | 18 × 15 × 12 | Surgery | 3 | No | NM |
| 6 (12) | 71 | M | Physical examination | Right | 15.5 × 11.5 × 8 | Surgery | NM | NM | Cytokeratin AE1/3, calponin, S-100, CD34 |
| 7 (13) | 62 | F | Back pain | Left | 10 | Surgery | 24 | No | CD34, STAT6 |
| 8 (14) | 77 | M | No symptoms | Right | 4.5 × 3.4 | Surgery | NM | No | STAT6, CD34, Bcl-2 |
| 9 (15) | 54 | M | Hypertension | Both | Right:15 Left:4 | Surgery | 18 | No | CD34, vimentin, Bcl-2, Ki-67 (<10%) |
| 10 (16) | 33 | M | Fever | Right | 2.3 × 2.5 × 3.0 | Surgery | NM | NM | CD34, CD99, Bcl-2 |
| 11 (17) | 52 | M | Right lumbar pain | Right | 11 × 10 × 9 | Surgery | 36 | No | CD34, Actine |
| 12 (18) | 33 | F | Right upper abdominal swelling pain and mass | Right | 14 × 12 × 6 | Surgery + chemotherapy | 36 | Recurrence | CD34, Vimentin, Bcl-2, CD99, Ki-67 (30%) |
| 13 (19) | 37 | F | Abdominal pain, excessive sweating | Left | 7 × 6 | Surgery | NM | NM | NM |
| 14 (20) | 50 | M | Left lumbar abdomen swelling pain | Left | 8 | Surgery + chemotherapy | 21 | Dead | Vimentin, CD99, PDGFR-α, PDGFR-β |

| | CT | Gross appearance | Microscopic features |
|---|---|---|---|
| 1 | Unenhanced: low-density shadow | NM | NM |
| 2 | Unenhanced: low-density shadow; enhanced: uneven enhancement | Clear boundary, section: gray-brown, soft | The cells are arranged in vortex and bundles, consisting of fusiform cells and oval cells, there are numerous blood vessels |
| 3 | Enhanced: uneven enhancement | Clear boundary | The tumor consists of spindle or oval cell proliferation with a laminar pattern |
| 4 | NM | Clear boundary, even gray-white fibrous | Irregular arrangement of spindle cells, with large numbers of blood vessels |
| 5 | Enhanced: uneven enhancement, calcification | NM | The spindle cells and oval cells showed no pattern of proliferation and contained local blood vessels |
| 6 | NM | Section: light pink, partially myxoid | The spindle cells are laminar, bundled and irregularly distributed with "vascular epithelial cells" |
| 7 | Enhanced: uneven mild enhancement | Clear boundary, section: yellowish-white, multinodular | NM |
| 8 | Enhanced: uneven mild enhancement | Clear boundary, section: gray-white | Spindle cell tumors, and the blood vessels were arranged in a hemangiopericytoma-like pattern |
| 9 | NM | NM | NM |
| 10 | NM | Solid mass | Spindle cell hyperplasia |
| 11 | Unenhanced: uneven low density; enhanced: uneven enhancement | NM | The spindle cells showed a short bundle, layered and irregular distribution |
| 12 | Unenhanced: low-density shadow; enhanced: uneven mild enhancement | Section: gray-white, necrosis | Tumor cells are spindle shape, the state is not clear and diffuse hyperplasia |
| 13 | Unenhanced: multilocular cystic low-density zone; enhanced: mild enhancement | Cystic solid | The tumor tissue is arranged in a intermanner |
| 14 | NM | NM | NM |

M, male; F, female; NM, not mentioned; F/U, follow-up.

TABLE 2 Summary of the patients with adrenal solitary fibrous tumor in cohort (21).

| Case | Age | Sex | Laterality | Maximum dimension of the tumor (cm) | Cell type | CD34 | STAT6 | Molecular profile | Treatment | Follow-up (months) | Vital status |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 46 | M | Left | 7 | Spindle | Positive | Positive | ND | Surgery | 7 | Alive |
| 2 | 44 | M | Right | 5 | Spindle | Positive | Positive | NAB2:STAT6 rearrangement | Surgery | 10 | Alive |
| 3 | 70 | M | Left | 2.5 | Spindle | Positive | Positive | ND | Surgery | 23 | Alive |
| 4 | 61 | M | Left | 3 | Spindle | Positive | Positive | NAB2:STAT6 rearrangement | Surgery | 13 | Alive |
| 5 | 55 | M | Right | 2 | Spindle | Positive | Positive | ND | Surgery | LTF | LTF |
| 6 | 64 | M | Left | 5 | Spindle | Positive | Positive | ND | Surgery | 29 | Alive |
| 7 | 27 | F | Right | 7 | Spindle | Positive | Positive | ND | Surgery | LTF | LTF |
| 8 | 58 | F | Right | 10.5 | Spindle | Positive | Positive | ND | Surgery | 7 | Alive |
| 9 | 19 | M | Left | 4 | Spindle | Positive | Positive | NAB2:STAT6 rearrangement | Surgery | 9 | Alive |

LTF, lost to follow-up; ND, not done.

The microscopic findings from reported cases align with this description. While no single marker demonstrates absolute specificity for SFT diagnosis, combined expression of CD34 and Bcl-2 strongly supports the diagnosis of SFT (10). STAT6 protein expression is highly sensitive and specific for SFT; approximately 90% of SFT cases show positive STAT6 protein expression (27, 28). Immunohistochemical analysis from literature reports indicates a 92% positivity rate for CD34, 50% for Bcl-2, and 50% for Vimentin but only 25% for STAT6 (possibly due to absence of STAT6 protein immunohistochemistry). However, another cohort study showed 100% positive results for both CD34 and STAT6. In our case study, immunohistochemical analysis revealed strong positivity for CD34 (3+), STAT6 (3+), as well as weak positivity for Synaptophysin (1+).

Mosquera and Fletcher suggested that the positive rate of CD34 is associated with tumor differentiation. In general, positive expression of CD34 is high in morphologically benign regions, while the expression of CD34 is often decreased or absent in obvious interchanging regions (29). Bishop et al. suggested that Bcl-2 is more sensitive than CD34 in diagnosing malignant SFTs and that negative Bcl-2 is closely related to the high potential for the deterioration of extra-thoracic SFTs (30). Ki-67 serves as a marker of tumor proliferation, and its increased expression level indicates susceptibility to invasion and metastasis. In the case series by Hanau and Miettinen, the positive rate of Ki-67 was lower in all benign SFTs, with a value of 0%–2%, while histologically malignant SFTs showed a higher positive rate (mean 30%, range 20%–40%) (31). Studies have shown that SFT is characterized by reverse rearrangement mutation in 12q13-5 to produce a fusion of NAB2-STAT6 gene, leading to overexpression of STAT6 protein. NAB2-STAT6 gene fusion is considered to be a molecular marker for SFT (three cases in Table 2 underwent genetic testing and all showed NAB2-STAT6). The most common are the NAB2 exon 4—STAT6 exon 3 and NAB2 exon 6—STAT6 exon 16/17 conjunctions. The second most common NAB2-STAT6 genotype is the NAB2 exon 6—STAT6 exon 16/17 conjunction, which is associated with more aggressive clinicopathologic characteristics. This genotype/phenotype variant mostly occurs in extra-thoracic SFTs and mainly affects young patients. STAT6 plays an important role as an immunohistochemical marker for distinguishing SFTs, with a sensitivity of 98% and specificity of nearly100% (32, 33). Therefore, for adrenal SFTs, NAB2-STAT6 gene detection should be performed to increase diagnostic accuracy, assess aggressiveness, guide treatment decisions, and predict prognosis.

Currently, complete surgical resection of the tumor is considered the optimal treatment for adrenal SFTs, with resectability being the key prognostic indicator. Complete resection significantly reduces the recurrence rate of SFTs, although malignant SFTs have a higher recurrence rate compared to cases of benign SFTs (34). The diagnostic criteria for malignant SFTs include the following: (1) abundant and dense cells; (2) cell pleomorphism; (3) nuclear fission elephant ≥4/10 HP; and (4) necrosis and hemorrhage. Tumor edge infiltration also holds significance. Reported cases have mainly undergone complete surgical resection, with postoperative follow-up in the range of 3–36 months showing no tumor recurrence or metastasis in cases of benign adrenal SFTs. In two cases of diagnosed malignant adrenal SFTs, postoperative adjuvant chemotherapy was used to reduce tumor recurrence and metastasis. One case experienced tumor recurrence 36 months after surgery but showed no further recurrence or metastasis after a second surgery at 18 months. The other patient tested positive for platelet-derived growth factor receptors-α (PDGFR-α) and platelet-derived growth factor receptors-β (PDGFR-β) and received oral imatinib mesylate treatment but unfortunately died due to tumor metastasis after 21 months of follow-up. Our patient was classified as having intermediate adrenal SFT and showed no signs of tumor recurrence during an 8-month postoperative follow-up period. Most adrenal SFTs demonstrate benign or intermediate biological behavior, resulting in a good prognosis with rare occurrences of malignancy in this context.

In conclusion, when dealing with adrenal tumors, it is important to consider the possibility of an adrenal SFT diagnosis if an unenhanced CT scan reveals a low-density shadow and an enhanced scan shows uneven enhancement. The definitive diagnosis of adrenal SFT relies heavily on pathological examination and immunohistochemistry. At present, there is no established standard treatment plan, with surgical resection remaining the primary method. The prognosis for cases of benign or intermediate adrenal SFTs is generally favorable; however, cases of invasive and malignant adrenal SFTs are more prone to distant metastasis and require close monitoring and review. Targeted therapy has emerged as a new therapeutic approach in recent years, showing promise for eligible patients; nevertheless, its clinical efficacy still lacks substantial research support. Large-scale research and treatment guidelines for adrenal SFTs are currently lacking, indicating the need for further investigation in this area.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

## Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

## Author contributions

CS: Data curation, Funding acquisition, Writing – original draft. XS: Data curation, Methodology, Writing – original draft. DW: Resources, Writing – original draft. YZ: Visualization, Writing – original draft. DF: Formal Analysis, Writing – review & editing, Methodology. XX: Formal Analysis, Writing – review & editing, Validation. WC: Project administration, Supervision, Writing – review & editing, Conceptualization.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Development and validation of a simulation training platform for the ligation of deep dorsal vein complex in radical prostatectomy

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**Objective:** This study aimed to design a low-cost, simulation training platform for the ligation of deep dorsal vein (DVC) complex in radical prostatectomy and validate its training effectiveness.

**Methods:** A simplified prostate urethra model was produced by 0-degree silica gel and pulse pressure banding. This model was placed on a slope of about 30 degrees using cardboard to thus creating a narrow environment of the pelvis. The DVC ligation was performed by a 2D laparoscopy simulator. A total of 27 participants completed the study include 13 novices, 10 surgical residents and 4 urology experts. The novices were trained five trails with 24 hours interval, the residents and experts completed the DVC ligation once. The construct validity of this simulation training platform was performed by completing time, the GOALS (Global Operative Assessment of Laparoscopic Skills) and TSA (i.e. Task Specific Assessments) score. The face validity and content validity were performed by a specific closed-ended questionnaire.

**Results:** There was no significant difference among three groups in demographic or psychometric variables ($p > 0.05$). Compared to the novices, the residents spend a shorter time to complete the DVC ligation ($p < 0.05$) and had higher GOALS scores ($p < 0.05$), but had no significant difference in TSA scores ($p > 0.05$). Additionally, the experts groups had a better performance compared to residents group in the completing time ($p < 0.05$), GOALS score ($p < 0.05$) and TSA score ($p < 0.05$). The learning curve of novices significantly promoted along with the increased times of training. Almost 90 percent of subjects considered that this simulator had a good performance in the realism and practicability.

**Conclusion:** We developed a novel low-cost a simulation training platform for the ligation of deep dorsal vein complex in radical prostatectomy, and this simulator had a good performance in the construct validity, face validity and content validity.

KEYWORDS

**laparoscopic simulator, deep dorsal vein complex, radical prostatectomy, low-cost, validation**

# 1 Introduction

Prostate cancer is an epithelial malignant tumor that occurs in the prostate, it seriously endangers people's health, and its incidence ranks second in male malignant tumors in Europe and the united states, and it also shows a trend of increasing year by year in our country (1). Laparoscopic radical prostatectomy has become one of the best choices for the treatment of prostate cancer, and has shown significant advantages in clinical applications (2). However, the operation is difficult for junior doctors to learn, and the learning curve is long (3), especially for some key surgical steps, the quality of which will directly affect the prognosis of patients (4).

With the development of teaching mode, simulation training has long been proven to be safe and effective in improving the surgical skills of junior doctors and avoid the risks brought by junior doctors to patients in traditional apprenticeship teaching (5, 6). Many simulation training platforms developed by researchers involve various clinical departments, which are convenient, efficient and safe to improve the skills of junior doctors (7, 8). Therefore, the construction of a simulation training platform for key steps of radical prostatectomy is of great significance for junior urological doctors (9). However, the development of simulation training platforms related to laparoscopic radical prostatectomy is very limited at present, and it is mainly aimed at the steps of bladder neck separation and urethra-vesical anastomosis (10). There is almost no development of simulation training platforms for other steps such as ligation of deep dorsal vein complex (DVC) (11). Ligation of the deep dorsal vein complex is one of the key steps in radical prostatectomy, and the quality of its completion will directly affect the patient's intraoperative blood loss (12). Skilled completion of this step can significantly improve the quality of the operation and speed up the patient's postoperative recovery (13). Therefore, we developed a simple prostate model and combined it with our previously developed simple simulator to build a simulation training platform for junior urological doctors to practice ligation of deep dorsal vein complex during laparoscopic radical prostatectomy steps and validated the effectiveness of this simulation training platform.

# 2 Materials and methods

## 2.1 The design and production of simulation model

The design of our prostate model is inspired by the neck of a beverage bottle. A suitable beverage bottle has a neck portion that is similar in shape and size to the prostate. The portion near the mouth of the bottle can also simulate the periurethral tissue at the front of the prostate. Therefore, we use 0-degree silica gel as the material. After solidification, 0-degree silica gel has similar physical properties to prostate tissue. Then, using a suitable beverage bottle as a mold, 0-degree silicone is poured into the beverage bottle, and a plastic pen holder which is used as the urethral channel is fixed in the middle of the model, and its diameter is of about 0.7cm (similar to the urethra). After 48 hours until the silicone gel solidified, the prostate silicone model was carefully removed, and the plastic pen holder in the middle was pulled out to obtain a prostate model with a urethral channel, then we pass the pulse pressure banding through the prostate model to obtain the prostate urethra model, as shown in Figures 1A–C.

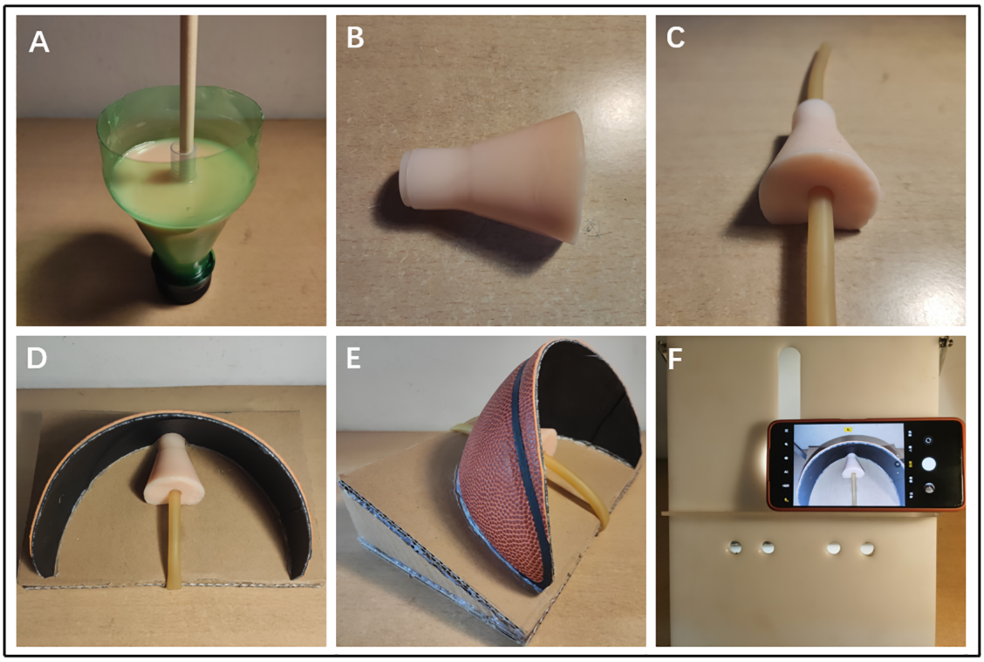


FIGURE 1
**(A–C)** The production process of prostate and urethra model. **(D–F)** The production process of simulation training platform for DVC ligation.

## 2.2 Construction of simulation training platform for DVC ligation

A simulation training platform was constructed using this simplified prostate urethra model for DVC ligation in laparoscopic radical prostatectomy. We designed a ramp frame with a slope of about 30 degrees using cardboard. Placing the simple prostate model on the ramp frame can imitate the patient's head-down position, so that the simulated training operation field will be the same as the real operation field of operation. In addition, we cut about 1/4 of the discarded basketball and fixed it on the ramp to simulate the pelvis, thus creating a narrow environment of the pelvis. Finally, we fixed the pulse pressure banding that passed through the prostate model to the ramp frame. We combined the overall model with our previously developed simple laparoscopy simulator (14) to build a complete simulation training platform, as shown in Figures 1D–F.

## 2.3 Participants and design

A total of 27 participants completed the study include 13 novices, 10 surgical residents and 4 urology experts, and they are all from the Army Medical University and its affiliated hospitals. The inclusion criteria were as follows: (1) The novices have never console laparoscopic surgery; (2) Surgical residents receiving surgical training have done more than 20 laparoscopic surgical procedures; (3)Urology experts have done more than 50 laparoscopic radical prostatectomy; (4)normal or corrected-to-normal vision, normal stereoacuity. This study was approved by the Southwest Hospital Ethics Committee and the informed consent was signed by all participants.

Before the start of the test, all participants watched the instructional video of the steps of ligating the DVC, and an urology expert (completed laparoscopic radical prostatectomy>50) explained it, then conducted a teaching demonstration on the simulation training platform developed by us. After that, all participants will perform familiarization exercises on the platform for about half an hour. After the familiarization is completed, each participant starts to operate the professional laparoscopic instruments (including clamps, scissors, needle holders, 2-0 medical suture needles and sutures) on the platform for operational testing, as shown in Figures 2A–F. Residents and experts completed only one test, while novices completed five times with more than 24 hours interval between two times.

## 2.4 Validation of the simulation training platform

The construct validity of this simulation training platform was performed by completing time, the GOALS (Global Operative Assessment of Laparoscopic Skills) and TSA (i.e. Task Specific Assessments). According to previous studies (15, 16), the GOALS and TSA were validated for the scale for assessing the operation technique of the DVC ligation, which were assessed by 2 experts and 2 assistants without knowing the identity of each participant. The face validity and content validity were performed by a specific closed-

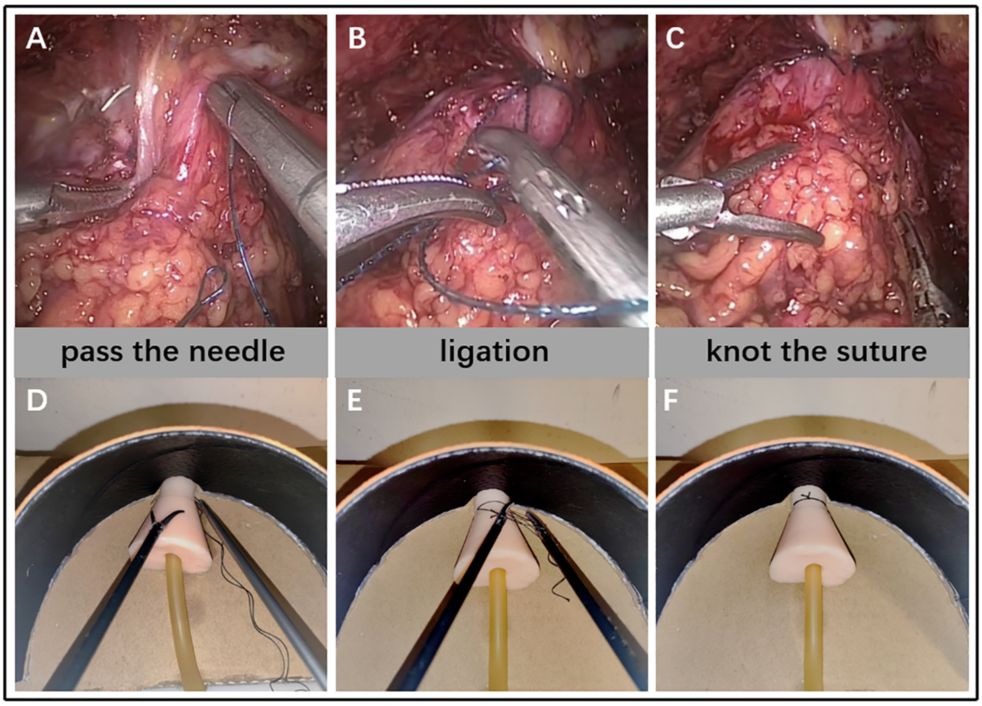


FIGURE 2
The procedure that surgeon ligated DVC under laparoscopy **(A–C)** VS participants ligated DVC on a 2D simulation training platform **(D–F)**.

ended questionnaire (5-point Likert scale from 1 = strongly disagree to 5 = strongly agree).

## 2.5 Statistical analyses

The data conformed to normal distribution are expressed as mean ± standard deviation (SD), otherwise expressed as median (IQR). All statistical analyses were calculated using SPSS 25 (2017; IBM Corp, Armonk, NY, USA). Student's t-test or the Mann-Whitney U test was performed to assess difference between the two groups. A P value of <0.05 was considered statistically significant.

# 3 Result

A total of 27 participants completed the study include 13 novices, 10 surgical residents and 4 urology experts. Demographic experiences are presented in Table 1. The expert group had a mean of 5.13 ± 0.85 years' experience for the radical prostatectomy surgical experience. The Resident group averaged 0.85 ± 0.41 years for the radical prostatectomy surgical experience. Novices had no experience for any surgery.

As shown in the Table 2, The mean completing times of the first trail of novices was 861.85 ± 102.41s, the median (IQR) of GOALS and TSA score were 5(5, 7) and 1(1, 3). Compared to the novices, the residents spend a shorter time to complete the DVC ligation ($p < 0.05$) and had higher GOALS score ($p < 0.05$), but had no significant difference in TSA score ($p > 0.05$). Additionally, the experts groups had a better performance compared to residents group in the completing time ($p < 0.05$), GOALS score ($p < 0.05$) and TSA score ($p<0.05$). In order to further assess the training effect of the simulator for novices, the learning curve of novices was performed by 5 trails with 24h interval. As shown in Figures 3A–C, the mean completing time was significantly reduced along with the increased times of training, the GOALS score and TSA score were significantly increased along with the increased times of training.

TABLE 1 Demographical Information.

| | Novices | Residents | Experts | *P*-Value |
|---|---|---|---|---|
| N | 13 | 10 | 4 | |
| Gender | 8M,5G | 10M | 4M | |
| Mean Age | 20.92 ± 0.76 | 28.2 ± 1.81 | 36.5 ± 1.91 | **0.000** |
| Mean Laparoscopic Surgery Experience(years ± SD) | 0 ± 0 | 2.85 ± 1.08 | 9 ± 1.78 | **0.000** |
| Mean Radical Prostatectomy Surgical Experience(years ± SD) | 0 ± 0 | 0.85 ± 0.41 | 5.13 ± 0.85 | **0.000** |

Bold values indicate significant differences in the comparison.

TABLE 2 Construct Validity Results.

| | GOALS | TSA | Time (S) |
|---|---|---|---|
| Novices | 5(5, 7) | 1(1, 3) | 861.85 ± 102.41 |
| Residents | 21(18.5, 23) | 3(1, 3.5) | 525.40 ± 71.07 |
| Experts | 24(23, 25) | 5(5, 5) | 398.75 ± 26.07 |
| Novices VS Residents | **0.000*** | 0.284 | **0.000*** |
| Residents VS Experts | **0.024#** | **0.024#** | **0.005#** |

*$p < 0.05$: novices VS Residents; #$p < 0.05$: Residents VS Experts.
Bold values indicate significant differences in the comparison.

The face validity of simulator was represented by the realism of simulator from user's judgment and content validity was represented by the practicability of simulator from expert's judgment. As shown in Table 3, almost 90 percent of subjects considered that this simulator had a good performance in the realism and practicability. Majority of participants believe that our simulation training platform can improve the operation level.

# 4 Discussion

There is no standardized training system and process in the training and teaching of minimally invasive technology in our country (17). In most teaching hospitals, the teaching method of minimally invasive surgical skills adopts the traditional "apprenticeship" teaching method of teachers and students on the same stage. Due to the lack of pertinence, the learning efficiency in this way is low and the learning cycle is long, and in the early stage of learning, it is easy to lead to increased surgical complications of patients (18). The teaching method of simulation training can make up for the shortcomings of traditional teaching methods (19). Nowadays, various simulation training platforms are flourishing, and cadaver models are usually the "gold standard" for simulation training, which can 100% reproduce real operations, but they are very few in number and complicated in use, making it difficult to be widely used (20, 21). Animal models are also a good choice, which can highly restore the physical properties of tissues and organs, but there are also problems such as cost, complicated use procedures, and difficulty in popularization (22, 23). 3D printing models have become very popular in recent years, it can accurately restore the anatomical characteristics of organs and tissues, however, its high cost and complicated production process discouraged many unpaid medical students (24, 25). Therefore, our research goal is to create a simple simulation training platform with simple manufacturing, low cost and high simulation degree, so that more medical students or doctors can make and use it by themselves, and use this platform to conduct more efficient training for junior doctors, ensuring they safely complete at least one procedure prior to patient surgery, thereby reducing iatrogenic risk to patients.

In the construction of a simple simulation training platform related to prostate cancer, the prostate is one of the important construction organs, and even determines the quality of the overall simulation training platform. Nur Rasyid et al. used ten different proportions of beef and other materials to construct ten tissue models

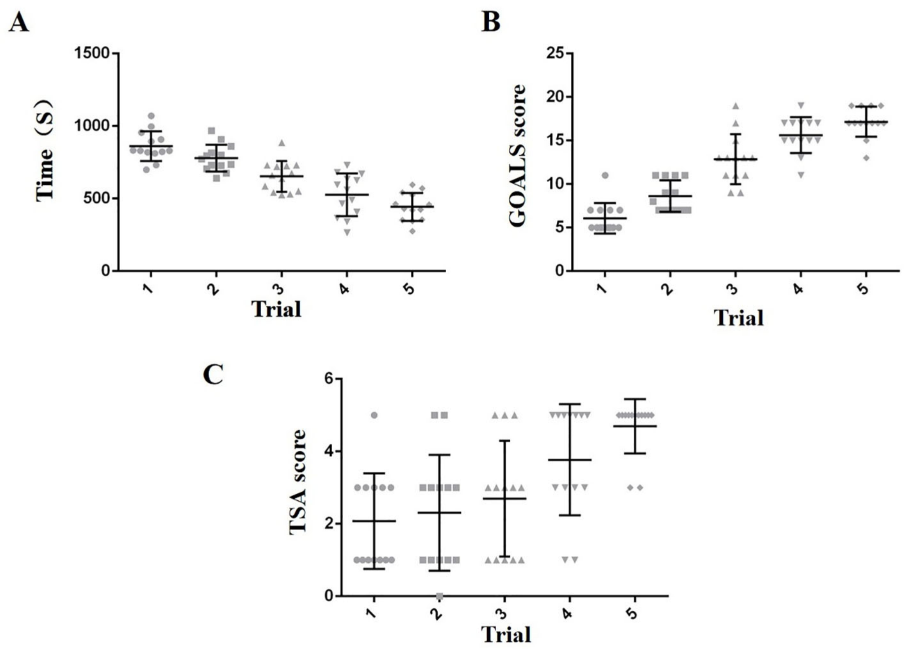


FIGURE 3
Trend chart of five training results for novices **(A–C)**.

with different physical properties, then they used professional measuring instruments to measure the physical properties of these ten tissue models comparing with real human prostate tissue. Finally they find the tissue model that is closest to the physical properties of the human prostate, and use 3D printing technology combined with the tissue model production method to build a highly realistic prostate model for transurethral prostatectomy training (26). Eunjin Choi et al. also aimed at the training of transurethral prostatectomy training, and constructed a high-fidelity prostate model after mixing different materials. After measuring with professional instruments, it was found that it has similar physical properties to human prostate, and cutting it by electrosurgery has similar performance to cutting the human prostate (27). Although the above-mentioned prostate model has a high degree of simulation, it has disadvantages such as complex construction process, high cost, and poor integration with other organ tissue models, it can only be used for the simulation of specific surgical procedures, such as transurethral prostatectomy training. The silicone prostate model developed by us used the bottle mouth as a mold, most commonly used human silica gel as the perfusion material. Its ingenious design, simple production, low cost, high simulation degree, and it can be better combined with other organs and tissues to build different types of simulation training platforms.so our prostate model construction method is worth popularizing, suitable for medical students and researcher.

We used our prostate model combined with simple models such as pelvis and our original laparoscopic simulator previously developed to build a ligation DVC simulation training platform for the training of DVC ligation steps in radical prostatectomy. DVC is a

TABLE 3 Questionnaire results for the face validity and content validity.

| Questionnaire | Strongly Disagree(1) | Disagree(2) | Agree(3) | Strongly |
|---|---|---|---|---|
| Face validity | | | | |
| 1. Accurately simulates the narrow environment of the pelvis | 0 (0%) | 2 (7.41%) | 11 (40.74%) | 14 (51.85%) |
| 2. Accurately simulates the DVC and its surrounding anatomical features | 0 (0%) | 0 (0%) | 17 (62.96%) | 10 (37.04%) |
| 3. Accurately simulates the difficulty of ligating DVC | 0 (0%) | 1 (3.71%) | 17 (62.96%) | 9 (33.33%) |
| 4. Accurately simulate the operation feel of needle threading and suturing | 0 (0%) | 5 (18.52%) | 15 (55.56%) | 7 (25.92%) |
| Content validity | | | | |
| 5. This is a simple and convenient laparoscopy training platform | 0 (0%) | 1 (3.71%) | 12 (44.44%) | 14 (51.85%) |
| 6. It’s a good training tool for ligating DVC for novices | 0 (0%) | 0 (0%) | 10 (37.04%) | 17 (62.96%) |
| 7. It’s a good training tool for ligating DVC for experienced | 0 (0%) | 2 (7.41%) | 13 (48.15%) | 12 (44.44%) |

vascular bundle that exists above the urethra. DVC injury during radical prostatectomy can lead to massive intraoperative bleeding, which can further lead to blurred vision and hinder the progress of surgery. Therefore, efficient intraoperative ligation of DVC is of great significance (28). However, simulation training platforms for DVC ligation steps in radical prostatectomy are rare. Mehrdad Alemozaffar et al. constructed a simulation training platform for key steps of prostatectomy using female porcine genitourinary tract tissue, they used porcine fallopian tube as DVC to simulate ligation of DVC steps, and demonstrated the effectiveness of the platform through novice and expert tests (29). The model uses animal tissue to build a ligation DVC simulation training platform, which is more similar to humans in terms of tissue characteristics, but its female pig reproductive tract is difficult to obtain, the construction process is more cumbersome, the simulation degree of the model shape is low, and there may be ethical issues. The construction materials of the simple ligation DVC platform we built use silica gel, beverage bottles, cardboard, etc., which are easier to obtain, and our production cost will not exceed $10, which is very important for beginners and resident physicians as they do not have a good financial situation. A survey shows that there is very little funding available for training resident physicians in Europe, and I believe this situation may be even more severe in other regions. In addition our model have no ethical issues, and the production process is ingenious and simple. Through measurement, we found that the prostate size, urethral diameter, DVC width and thickness, slope frame angle and other data of our model are very close to the real human situation, so the shape of our model is more simulated and has better face validity. To our knowledge, this is the first simple simulation training platform built for DVC ligation during laparoscopic radical prostatectomy, it will provide new methods for the practice of ligating DVC steps.

We tested our platform to explore its effectiveness by recruiting novices, residents and experts. By comparing novices trial 1,residents and experts, we found that for GOALS scores, novices got a lower score than residents and residents got a lower score than experts. In terms of operating time, novices took more time than residents, and residents took more time than experts, indicating that our platform can differentiate participants in terms of basic laparoscopic skills and complete time. As for TSA scores, novices and residents are not significantly different, and experts performs significantly better than residents, indicating that our platform can differentiate participants in terms of ligating DVC task-specific performance. These can prove that our platform has good construct validity.

Then we conducted five tests on participants in the novices group, their GOALS scores and TSA scores gradually increased, operating time gradually decreased, and through statistical analysis, we found that novices trial 5 had a significant improvement in GOALS scores, TSA scores and operating time than novices trial 1, indicating that our platform can help novices improve basic laparoscopic skills and task completion efficiency.

Finally, all the participants gave a high evaluation to the simulation training platform we developed, proving its face validity and content validity, affirming its role in improving the surgical skills of junior doctors.

Our platform also has some areas for improvement. First of all, although the overall physical characteristics of our prostate model are similar to the real prostate, the details, such as the soft tissue around the urethra, should be softer in the real situation, and the difficulty of puncturing and ligation will be lower. Secondly, the sutures used in real surgery are medical suture needle with thread, and we use medical suture needle that require self-threading for cost and frugal purposes, so the knotting process may be more difficult and time-consuming. Thirdly, our platform mainly trains the step of ligating the deep dorsal vein complex, which is not enough for mastering complex laparoscopic radical prostatectomy, but this basic step can serve as our experience in developing complex steps in the future, we will also continue to explore and research based on the platform's construction ideas, and build more platforms with other steps, or a multi-step integrated platform. In addition, although robotic prostate cancer surgery has gradually become popular and replaced laparoscopic prostate cancer surgery, our platform seems to have been phased out. However, I believe that laparoscopic technology is the foundation of robotic technology, and practicing laparoscopic operation will also improve robotic operation. Finally, our study suffers from the small sample size, small number of tests, and does not assess whether practice on this model will translate into improved performance in the operating room. Future research is needed to determine whether repeated trainings in our platform lead to better GOALS and TSA scores and reduced patient morbidity.

## 5 Conclusion

Our simulation training platform is a reliable educational tool for junior doctors to learn the steps of ligation of the deep dorsal vein complex in laparoscopic radical prostatectomy. In addition, the model can be combined with GOALS and TSA assessment tools for physicians to objectively assess laparoscopic skill levels before performing procedures on patients.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Ethics statement

The studies involving humans were approved by the Ethics Review Committee of the Army Military Medical University, on June 22, 2022 (202243001). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

## Author contributions

YC: Conceptualization, Writing – original draft. QT: Conceptualization, Methodology, Writing – original draft. JZu: Data curation, Formal analysis, Writing – review & editing. LZ:

Data curation, Writing – review & editing. SL: Data curation, Investigation, Writing – review & editing. JZe: Conceptualization, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Clinical efficacy analysis of intelligent pressure-controlled ureteroscopy combined with thulium laser in the treatment of isolated upper urinary tract urothelial carcinoma

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**Objective:** This study aims to investigate the clinical treatment effect of intelligent pressure-controlled ureteroscopy combined with thulium laser for patients with isolated kidney upper tract urothelial carcinoma (UTUC).

**Methods:** This study employed a retrospective analysis approach and focused on six patients with isolated kidney UTUC admitted to our hospital from June 2018 to May 2023, who underwent tumor resection surgery using intelligent pressure-controlled ureteroscopy combined with thulium laser. We collected the perioperative clinical data of these six patients and conducted statistical analysis of the treatment effects.

**Results:** The surgeries of all six patients were completed smoothly, without incidents of surgery termination due to significant bleeding. Postoperative pathology revealed that four patients had low-grade non-invasive papillary urothelial carcinoma, while the other two patients had high-grade invasive urothelial carcinoma. During follow-up period, one patient had a renal pelvis recurrence three months after the surgery, and subsequently underwent thulium laser resection. Additionally, another patient experienced bladder recurrence eight months after the surgery and received transurethral resection of bladder tumor (TURBT) for treatment. The remaining four patients did not experience tumor recurrence during the follow-up.

**Conclusion:** For patients with isolated kidney associated with UTUC, intelligent pressure-controlled ureteroscopy combined with thulium laser represents a feasible treatment option, with good therapeutic effects for low-risk upper tract urothelial carcinoma.

KEYWORDS

**intelligent pressure-controlled, thulium laser, upper tract urothelial carcinoma, ureteroscopy, treatment**

# 1 Introduction

Globally, upper tract urothelial carcinoma (UTUC) is a relatively rare tumor in clinical practice, with an annual incidence rate of approximately 2 cases per 100,000 people in Western countries (1). However, in China, due to specific geographical factors and widespread use of aristolochic acid-containing drugs, the incidence of UTUC is significantly higher than in European countries (2). In treatment of UTUC, radical nephroureterectomy is considered the gold standard treatment for this disease (3). However, performing radical nephroureterectomy (RNU) on patients with solitary kidney and UTUC results in loss of renal function, leading to lifelong dialysis dependency. This significantly impacts long-term survival rates and quality of life. Common complications after RNU include infection, bleeding, thrombosis, and chronic kidney disease due to loss of renal function. These complications occur more frequently in patients with a solitary kidney, as their remaining renal function cannot compensate, failing to significantly improve their overall survival rate (4, 5).

According to the European Association of Urology guidelines on UTUC, conservative treatment is the preferred strategy for patients with a solitary kidney. This approach aims to preserve as much renal function as possible while effectively controlling the tumor. Conservative treatments include local instillation using drugs such as radiotherapy and chemotherapy to reduce the risk of recurrence, and local tumor resection using ureteroscopes or flexible scopes combined with lasers (1, 6, 7). However, local tumor resection using ureteroscopes or flexible scopes combined with lasers requires early repeated ureteroscopic examinations. Studies have shown that early repeated ureteroscopic examinations can effectively detect tumor recurrence and help assess the aggressiveness of the disease, which is crucial for risk stratification in patients undergoing endoscopic treatment for UTUC (8). Therefore, with the informed consent of the patients, we employed intelligent pressure-controlled transurethral flexible ureteroscopy combined with thulium laser for surgical resection in patients with solitary kidney and UTUC, followed by early regular follow-up ureteroscopic examinations. This approach has yielded certain clinical benefits.

# 2 Materials and methods

## 2.1 Study population

This study was approved by the Ethics Committee of Ganzhou People's Hospital, and informed consent was obtained from all patients, who each signed a consent form. We conducted a retrospective analysis on six cases of isolated kidney UTUC patients admitted to our hospital from June 2018 to May 2023.All patients underwent tumor resection using intelligent pressure-controlled ureteroscopy combined with thulium laser, and perioperative clinical data were collected for effectiveness assessment and analysis. This study involved six patients, with four males and two females. There were four cases of renal pelvis tumors and two cases of upper ureteral tumors, all with tumor diameters less than 3 cm. The average preoperative creatinine level of the patients was 98.2 umol/L (range 65-135 umol/L), and the average age of the 6 patients was 58.6 years (ranging from 37 to 76 years). Three patients had hypertension, one had diabetes, and two had coronary heart disease. Four patients were admitted for painless gross hematuria, while the remaining two were diagnosed during routine physical examinations. Preoperative enhanced CT scans showed that all six patients had solitary tumors with diameters less than 3cm.Urine cytology examination revealed urothelial carcinoma cells in two patients. Inclusion criteria for this study: 1. Patients diagnosed with renal pelvis lesions suggestive of UTUC by imaging examinations such as CT or MRI; 2. Patients with absent contralateral kidney or a contralateral kidney GFR <5, indicating non-functional kidney; 3. Patients without distortion or stenosis of the affected ureter, allowing for intelligent pressure-controlled flexible ureteroscopy surgery; 4. Lesions in the affected renal pelvis or calyces categorized as high-risk according to the Chinese Urological Association guidelines. Exclusion criteria: 1. Patients with tumors <2 cm without associated hydronephrosis, categorized as low-risk UTUC; 2. Patients with advanced-stage tumors infiltrating the renal parenchyma or renal fat, making complete resection via flexible ureteroscopy unlikely; 3. Patients with normal or relatively good function of the contralateral kidney; 4. Patients with poor physical condition or bleeding disorders unable to tolerate surgery.

## 2.2 Surgical methods

All patients underwent surgery under general anesthesia in a healthy-side oblique supine position (Figure 1). First, a ureteroscope (7-8.5 Fr, Wolf, USA) was introduced into the patient's ureter and renal pelvis under low-pressure, low-flow perfusion. After confirming the ureter was patent without significant stenosis or distortion, a zebra guidewire was inserted. Along the guidewire, a 12-14 Fr integrated pressure-measuring suction ureteroscope sheath was introduced (Figure 2). The sheath's pressure measurement and suction ports were connected to the intelligent perfusion suction pressure control platform (Figure 3) using pressure and suction tubes, respectively. The platform zeroed the intracavitary pressure and set the intraoperative intracavitary pressure control value (-10 mmHg) and perfusion flow rate (50 ml/min). Then, an electronic flexible ureteroscope (11278VU 8.5 Fr, Storz, Germany) was used. The ureteroscope was connected to the platform perfusion pump, and the platform's automatic switch was activated. The platform could automatically adjust the negative pressure suction capability based on the set intracavitary pressure control value. The ureteroscope was introduced into the sheath, and after locating the tumor (Figure 4), a 200 μm thulium laser (Rekon, China) with a power setting of 25 W was used to enucleate the tumor from the periphery to the center (Figure 5). The excised tumor tissue was extracted intact into a specimen collection bottle through the withdrawal and suction method. The ureteroscope was reintroduced to treat the wound. If any obvious tumor tissue was found around the wound, it was ablated and vaporized using the thulium laser, and thorough hemostasis was ensured. After confirming no significant

FIGURE 1
The healthy side lying on a running position.

tumor tissue or bleeding (Figure 6), the flexible ureteroscope and ureteral sheath were withdrawn, a 6 Fr double-J stent was placed, and a urinary catheter was inserted.

## 2.3 Postoperative management and follow-up

The double-J stents were left in place for 2 weeks in all 6 patients. All patients received 30 mg of pirarubicin bladder instillation within 24 hours postoperatively, with a duration of 30 minutes. Two patients with high-grade infiltrating urothelial carcinoma received "gemcitabine plus cisplatin" chemotherapy as adjuvant therapy, while four patients with low-grade non-invasive papillary urothelial carcinoma did not undergo adjuvant chemotherapy. Postoperatively, all six patients were followed up, with a follow-up rate of 100%. The follow-up period ranged from 6 to 39 months, with an average of (16.57 ± 4.69) months. During follow-up period, patients presenting with symptoms such as hematuria should immediately return to the hospital for enhanced CT of the urogenital system and cystoscopy. If tumor recurrence is detected, further treatment should be initiated promptly. Subsequent arrangements include returning to the hospital every three months for enhanced CT of the urogenital system, complete blood count, renal function tests, urine analysis, and cystoscopy for routine examinations.


FIGURE 2
Medical perfusion attraction platform.

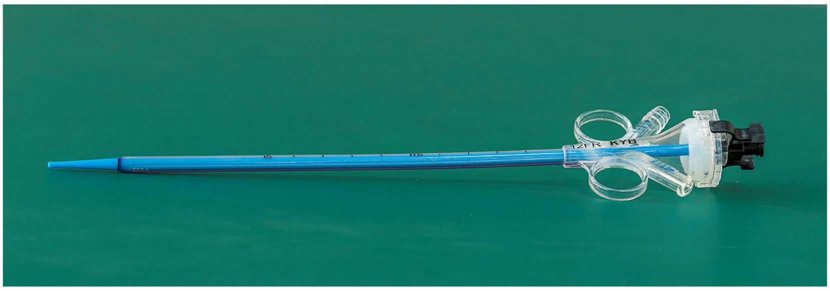

FIGURE 3
Disposable sterile ureteral catheter introducer sheath.

## 3 Results

The surgeries of all 6 patients were successfully completed, with an average operation time of (43 ± 13.45) minutes, and an estimated average intraoperative blood loss of (10 ± 2.26) milliliters. Postoperative pathological examination results showed that 4 patients had low-grade non-invasive papillary urothelial carcinoma, and 2 patients had high-grade invasive urothelial carcinoma. During the follow-up period, one patient with high-grade invasive urothelial carcinoma was found to have renal pelvis recurrence 2 months after the surgery and underwent thulium laser resection treatment. Additionally, one patient with low-grade non-invasive papillary urothelial carcinoma was found to have bladder recurrence 8 months after the surgery, and after transurethral resection and intravesical chemotherapy, the condition was well controlled. The preoperative average serum creatinine level was 98.2umol/L (range 65-135umol/L), while it was 102.4umol/L (range 68-168umol/L) postoperatively. There was no significant statistical difference in serum creatinine changes pre- and postoperatively ($p<0.05$). The recurrence rate of low-grade non-invasive urothelial carcinoma was 14%, with a relatively good prognosis, while the postoperative recurrence rate for patients with high-grade invasive urothelial carcinoma was as high as 50%.

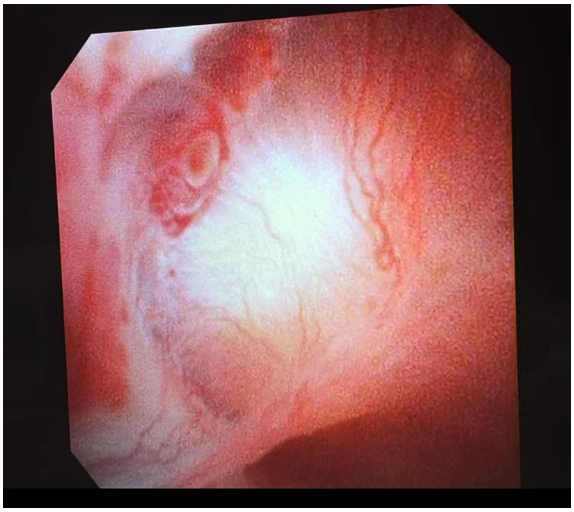

FIGURE 4
Tumor at the top of the renal pelvis.

## 4 Discussion

In recent years, due to unique geographical factors and the use of aristolochic acid medications, the incidence of UTUC in China accounts for approximately 18% of urothelial carcinoma cases, higher than the 5%-10% in Western countries (9). Radical nephroureterectomy is considered the “gold standard” for treating this disease, but for some patients with a solitary kidney or impaired renal function, undergoing radical surgery would lead to lifelong hemodialysis, severely impacting the quality of life (10). Therefore, for such patients, minimally invasive tumor resection via a natural orifice approach is considered an alternative treatment modality (11). With the advancement of ureteroscopy and laser technology, minimally invasive surgery through natural orifice for treating UTUC is becoming increasingly common (12–14).

During the procedure, the intelligent pressure-controlled ureteroscope utilized a self-developed intelligent pressure control device, which includes an intelligent irrigation and suction pressure monitoring platform and an integrated pressure-sensing ureteroscope insertion sheath for guidance. The functions of the

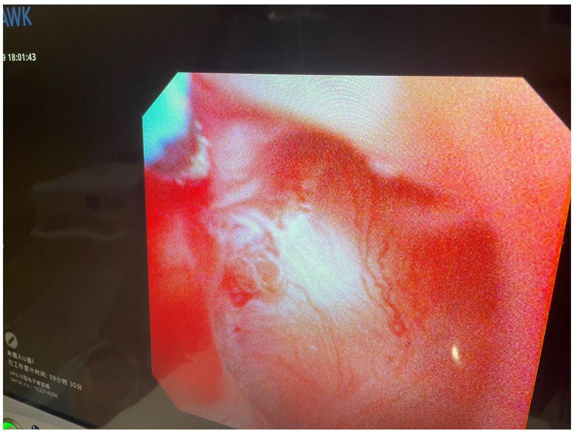

FIGURE 5
Thulium laser resection of the tumor.

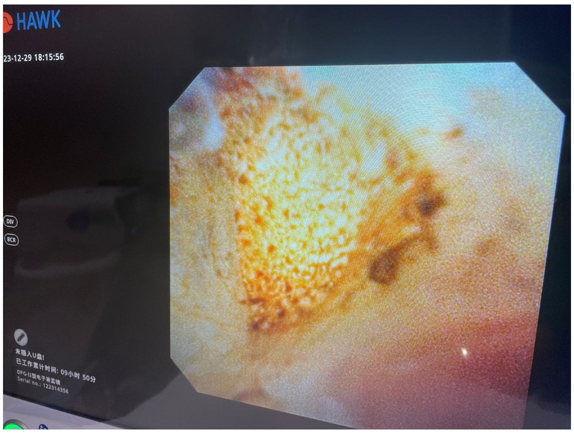


FIGURE 6
The tumor has been removed.

intelligent pressure control platform include: setting the required irrigation flow rate for surgery, controlling the renal pelvic pressure, setting the warning pressure for renal pelvic pressure, and the upper limit of renal pelvic pressure. It also receives pressure data from the ureteroscope suction sheath for renal pelvic pressure monitoring and, utilizing pressure feedback control technology based on the set renal pelvic pressure control value, automatically adjusts negative pressure suction to maintain the renal pelvic pressure within the predetermined safe range (15, 16). Internal diameter of the ureteroscope insertion sheath is 12Fr, the external diameter is 14Fr, and the length ranges from 20 to 45cm. It integrates pressure sensing and suction devices, enabling connection to the pressure control instrument for real-time monitoring of renal pelvic pressure during stone retrieval using negative pressure suction. The sheath is made of transparent material, facilitating observation of the surroundings during surgery and aiding in tumor localization.

Previous studies have shown that among UTUC patients who underwent minimally invasive treatment via the urethra, the postoperative upper urinary tract tumor recurrence rate was 65% (range 15% to 90%), and the bladder tumor recurrence rate was 44% (range 19% to 70%). In comparison, patients undergoing standard radical surgery had a bladder recurrence rate of 11% to 36% (17, 18). Regarding survival rates, studies have indicated that patients undergoing nephron-sparing surgery had a 2-year overall survival rate of 35% to 100% and a tumor-specific survival rate of 70% to 100% (19, 20). In this study, we utilized a self-developed intelligent pressure control device in conjunction with ureteroscopy and thulium laser therapy for six elderly UTUC patients. Postoperative pathological results revealed that 4 cases were low-grade non-invasive papillary urothelial carcinoma, of which 1 case had a bladder tumor recurrence 18 months after the surgery. Additionally, 2 cases were high-grade invasive urothelial carcinoma, with 1 case experiencing renal pelvis recurrence 3 months postoperatively. During the follow-up period, none of the six patients experienced distant organ metastasis, and they were still in good health with a tumor-specific survival rate of 100%.

In this study, we achieved high-volume irrigation under ureteroscopy using an intelligent pressure control device, which continuously applied negative pressure to actively remove irrigating fluid containing blood and tumor cells in real-time, promoting fluid circulation within the cavity. This approach not only maintained a clear surgical field but also prevented iatrogenic tumor dissemination due to leakage of irrigating fluid caused by high renal pelvis pressure, and reduced laser-related collateral damage resulting from severe hematuria. Thulium laser is currently the shallowest penetrating laser in medical use, with a depth of penetration of only 0.2 mm. It enables precise tissue cutting, rapid hemostasis, and efficient vaporization (21). As a continuous-wave laser, compared to conventional holmium lasers, thulium lasers have a faster tissue heating rate, better vaporization effect, and superior hemostatic performance (22). When performing thulium laser ablation and vaporization therapy, we used a low power setting of 25W.arefully cutting along the tumor edge towards the tumor base and laser cauterizing visible vessels under the scope to prevent bleeding, thereby occluding the blood supply around the tumor and avoiding severe bleeding caused by direct tumor excision, which may impact surgical outcomes. When resecting upper ureteral tumors, avoid cutting too deeply to prevent ureteral perforation that could facilitate tumor implantation and metastasis, excessive damage to the muscle layer of the ureter may lead to ureteral stricture. In this study, leveraging the advantages of two devices and unique positioning, none of the 6 patients experienced major bleeding, ureteral perforation, tearing, renal rupture, or severe infection during the surgical procedures. During the follow-up period, no distant organ metastases to the liver, lungs, or other organs were observed in these 6 patients. Therefore, it can be concluded that combining intelligent pressure-controlled ureteroscopy with thulium laser therapy for upper urinary tract urothelial carcinoma in solitary kidney patients is a safe and reliable treatment method. However, following UTUC nephron-sparing treatment, patients require long-term intensive imaging and endoscopic follow-up (23). Hence, the overall treatment costs and duration are also important considerations.

This study has the following limitations: Firstly, the number of cases is relatively small, the follow-up period is short, and it is a retrospective study. Although the results show some efficacy, the small sample size introduces selection bias, which is an unavoidable limitation of retrospective studies. Additionally, the equipment used is currently only available in China and has not yet been approved by the FDA, potentially leading to regional limitations of the findings. Furthermore, during intraoperative procedures, the completeness of tumor ablation was judged solely based on endoscopic appearance, which cannot accurately determine whether the tumor was entirely resected, thus affecting the assessment of postoperative tumor staging. Lastly, intraluminal nephron-sparing surgery for solitary kidney high-risk urothelial carcinoma is still in the exploratory stage, with large-scale clinical studies being rare both domestically and internationally. Despite these limitations, this small retrospective study suggests that this technique can achieve clinical efficacy in managing relatively early high-risk upper tract urothelial carcinoma. We plan to apply for a multi-center clinical study in the future to further demonstrate the safety and efficacy of this technique.

In summary, for patients with UTUC, intelligent pressure-controlled flexible ureteroscopy combined with thulium laser is an effective treatment option that clinicians can consider. However, close imaging and endoscopic follow-up are necessary after the procedure.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving humans were approved by Ethics Committee of Ganzhou People's Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. The animal study was approved by Ethics Committee of Ganzhou People's Hospital. The study was conducted in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

## Author contributions

HC: Writing – original draft, Writing – review & editing. TL: Validation, Writing – review & editing. JX: Formal analysis, Writing – original draft. JG: Writing – original draft.

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# Extrarenal renal cell carcinoma in the adrenal region: a case report

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This case report describes a rare instance of extrarenal clear cell renal cell carcinoma (ccRCC) in a 48-year-old woman who presented with a loss of consciousness. Abdominal CT revealed a 24 × 31 mm mass in the left adrenal region, with no kidney involvement. The mass was surgically excised, and histopathological examination confirmed the diagnosis of ccRCC. Immunohistochemical analysis revealed positive markers, including CA9, CD10, PAX-8, and vimentin. The patient did not undergo adjuvant therapy, and a 6-month follow-up showed no signs of recurrence or metastasis. This case emphasizes the importance of considering extrarenal ccRCC in differential diagnoses of adrenal masses.

KEYWORDS

**extrarenal renal cell carcinoma, adrenal region, case report, adrenal masses, clear cell renal cell carcinoma**

## Introduction

Renal cell carcinoma (RCC) is a prevalent malignancy within the urinary system, with clear cell renal cell carcinoma (ccRCC) being the most common histological subtype, accounting for approximately 70% of RCC cases (1). Extrarenal RCC, however, is extremely rare, with only a few cases documented in the literature (2–4). In this report, we present a case of extrarenal ccRCC located in the adrenal region.

## Case report

A 48-year-old woman was treated in a tertiary hospital for "loss of consciousness." The patient denied any symptoms related to upper abdomen discomfort, abdominal distension, hematuria, or fever. Physical examination revealed no tenderness in the upper abdomen or lumbar region, and no palpable abdominal masses were detected. An abdominal computed tomography (CT) scan identified a 24 × 31 mm soft tissue mass in the left adrenal region. A contrast-enhanced CT scan confirmed mild, uneven enhancement of the mass, with indistinct margins relative to the left adrenal gland. The bilateral kidneys were intact and showed average size, location, and enhancement. No mass was found in either kidney (Figures 1a–c). The plasma concentrations of adrenal-related hormones, including catecholamine, cortisol, renin, and aldosterone, were within normal ranges. Based on these findings, a preliminary diagnosis of a left adrenal mass was established. The differential diagnosis included adrenal cortical tumor, adrenal medullary tumor, extra-adrenal paraganglioma, and adrenal metastasis. The patient underwent laparoscopic surgery via a retroperitoneal approach to excise the mass. Intraoperatively, a 30 × 25 × 20 mm mass with an intact capsule was identified near the left adrenal gland. The mass was successfully resected outside the capsule, without involvement of the left kidney, spleen, or other adjacent organs.

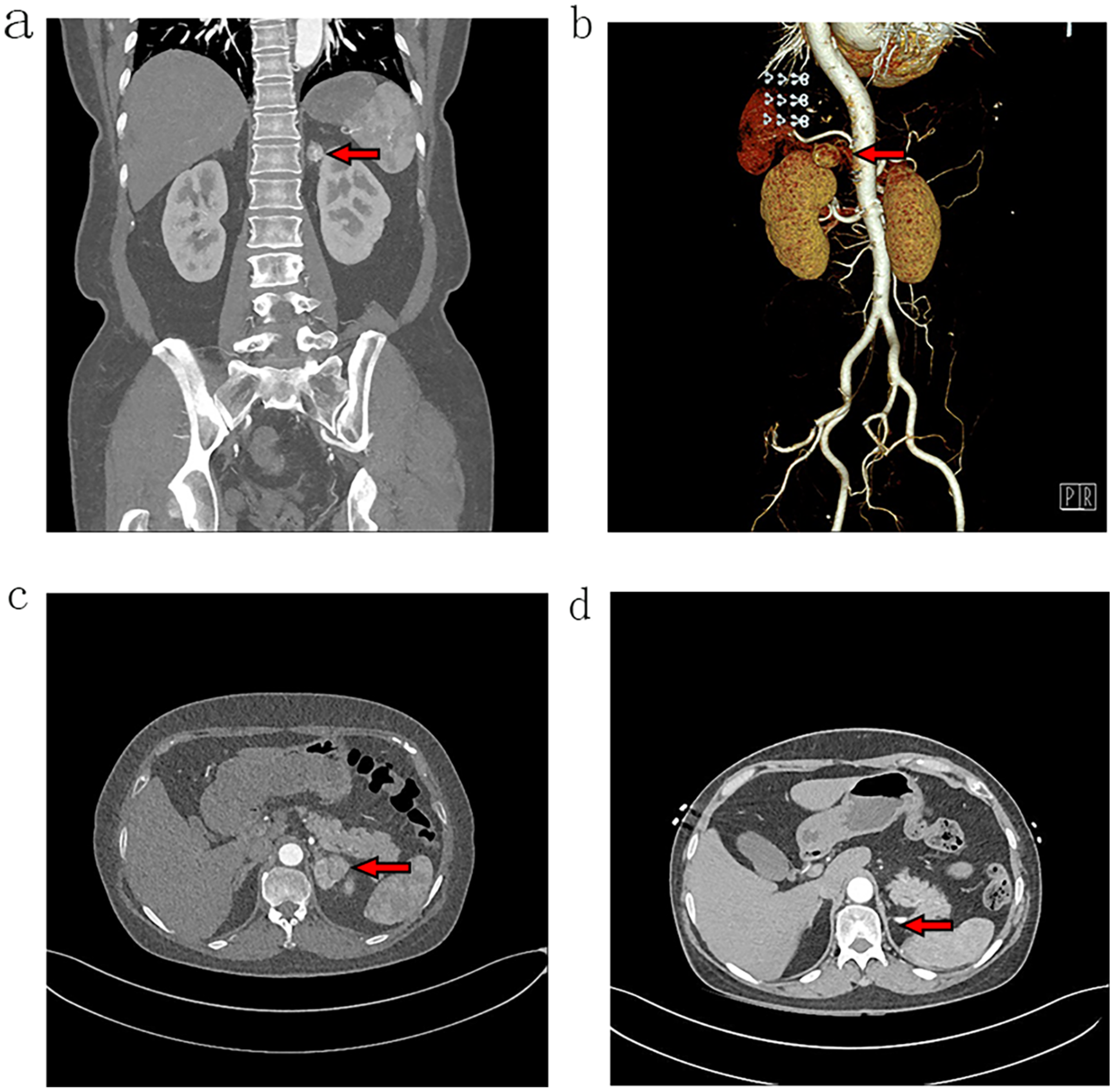


FIGURE 1
Abdominal CT images with contrast enhancement. Coronal views (a,b) and a cross-sectional view (c) reveal a soft tissue mass in the left adrenal region, characterized by mild and uneven enhancement. (d) The follow-up cross-sectional view at 6 months postoperatively hows no evidence of tumor recurrence in the left adrenal region.

Histopathological examination revealed a well-encapsulated mass with a clear boundary from the surrounding tissues. Normal renal tissue was absent, but some normal adrenal tissue was observed in the surrounding area. Hematoxylin and eosin (H&E) staining showed tumor cells arranged in nest-like and adenoid structures, with a rich vascular network. The tumor cells were round to polygonal, with abundant clear cytoplasm and centrally located nucleus (Figures 2a,b). Immunohistochemistry results deemed the tumor cells positive for expression of Ki-67 (+, about 15%), PAX-8 (+), carbonic anhydrase 9 (CA9) (+), vimentin (foci +), CD10 (+) and negative for expression of markers such as chromogranin A (CgA) (-), melan-A (-), a-inhibin (-), calretinin (-), cytokeratin 7 (CK7) (-), RCC (-), and CD117 (-) (Figures 2c,d). These findings led to a pathological diagnosis of clear cell renal cell carcinoma (ccRCC), WHO/ISUP nuclear grade G2. There was no evidence of tumor involvement or invasion of the surrounding adrenal gland, and no normal renal tissue was found in the resected specimens.

The patient did not receive any adjuvant therapy postoperatively. At the 6-month follow-up, thoracoabdominal CT scans showed no signs of tumor recurrence or distant metastasis in the left adrenal area, thorax, or abdomen (Figure 1d). Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

## Discussion

Clear cell renal cell carcinoma (ccRCC) is the most common histological subtype of renal cell carcinoma (RCC). However,

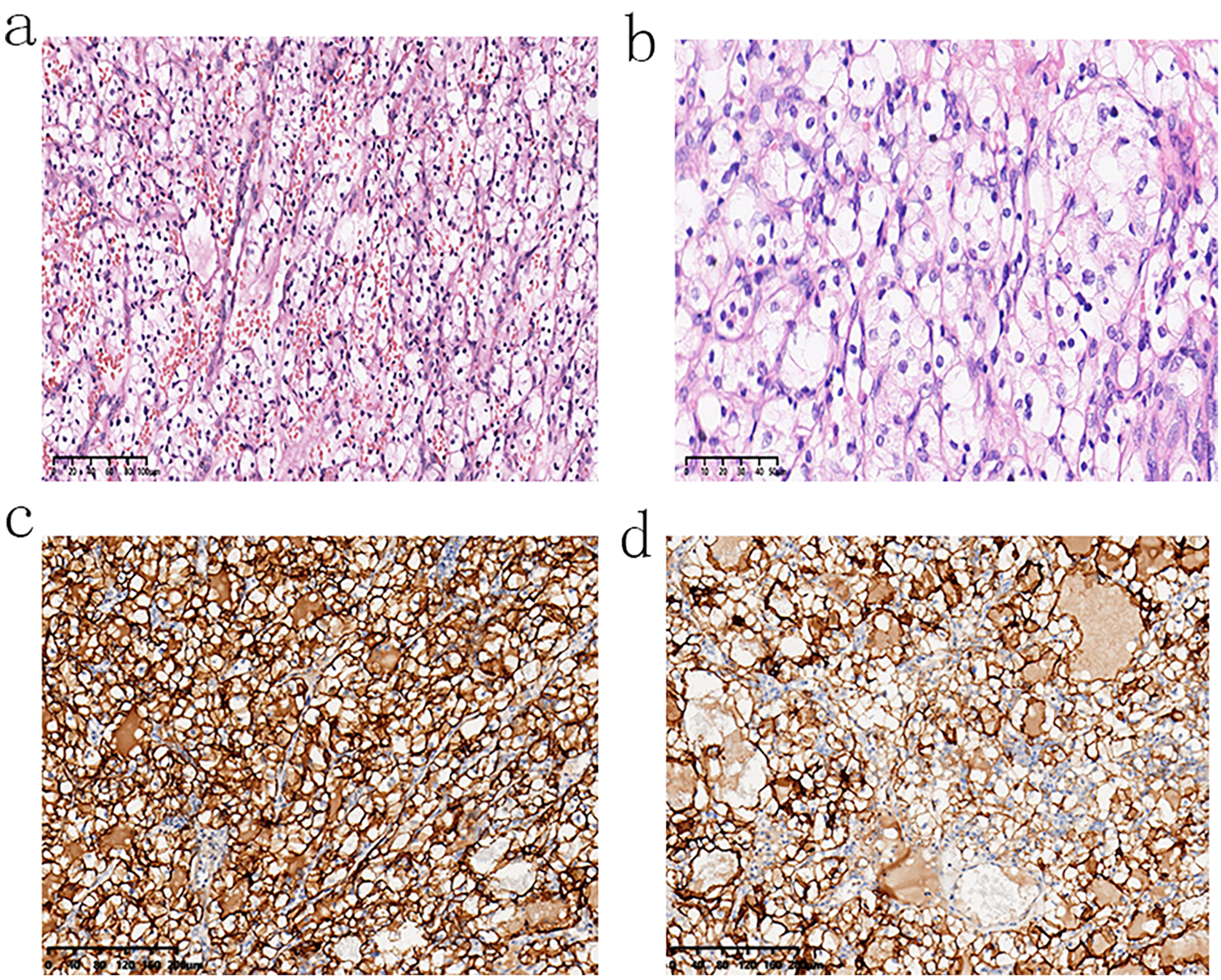

FIGURE 2
Microscopic examination of the tumor consistent with clear cell renal cell carcinoma: **(a)** at ×20 magnification and **(b)** at ×40 magnification. Immunohistochemical staining shows positive expression of **(c)** CA9 at ×40 magnification and **(d)** CD10 at ×40 magnification.

cases of extrarenal ccRCC are rare. Extrarenal ccRCC is believed to represent renal carcinoma arising from either remnants of embryonic kidney tissue or from an early developmental anomaly where kidney tissue remains in an extrarenal location (2).

Computed tomography (CT), magnetic resonance imaging (MRI), and contrast-enhanced ultrasound (CEUS) are commonly used in the diagnosis of renal and adrenal tumors. MRI offers high soft-tissue resolution and multi-parametric imaging, which is helpful in distinguishing benign from malignant tumors. However, the examination time is longer compared to other modalities. CEUS provides real-time dynamic observation of tumor blood perfusion, making it a simple and non-invasive option, but its field of view is limited and heavily dependent on the operator's technical skill. Preoperative biopsy can help determine the tumor's nature, but it carries risks such as damage to surrounding organs and tissues, potential bleeding, tumor seeding, and false-negative results. CT, on the other hand, remains the standard imaging modality for evaluating suspected renal and adrenal masses due to its fast scanning speed, multi-phase imaging capability, and broad applicability.

In the present case, CT imaging revealed a mass in the left adrenal region with mild, uneven enhancement and indistinct differentiation from the adrenal gland. The bilateral kidneys appeared normal in size, shape, and enhancement, making it challenging to distinguish this mass from primary adrenal tumors based solely on imaging. The imaging characteristics were similar to those seen in adrenocortical carcinoma. AlShalabi et al. reported a similar case where abdominal CT identified a large, irregularly enhanced tumor in the adrenal area, which was later confirmed as clear cell carcinoma following laparotomy and histopathological examination (5). Additionally, endoscopic ultra-sonography has been utilized in preoperative diagnosis of adrenal masses, though its use in extrarenal ccRCC remains limited (6).

The differential diagnosis for the mass included benign adrenal tumors, pheochromocytoma, adrenocortical carcinoma, metastatic carcinoma, and adrenocortical carcinoma. The absence of abnormal catecholamine, aldosterone, and cortisol levels, along with the lack of clinical symptoms associated with hormonal excess, effectively ruled out pheochromocytoma. Furthermore, the small size of the tumor, lack of local tissue invasion, and normal hormonal profile made adrenocortical carcinoma unlikely (7). No evidence of primary tumors elsewhere in the body was found on preoperative imaging, excluding metastatic carcinoma. Both kidneys were normal, and there was no anatomical or functional connection between the tumor and the left kidney.

Further, the tumor capsule was intact, which excluded the possibility of renal cancer invading the surrounding tissues or metastatic RCC. During the surgical procedure, the patient's kidneys on both sides remained undamaged and were not linked to the tumor. However, there was no obvious boundary with the adrenal gland. The tumor and a portion of the adrenal gland were completely excised. Pathological examination confirmed the diagnosis of extrarenal RCC, as no normal renal tissue was identified in the resected specimens.

Postoperative immunohistochemical analysis further supported the diagnosis of ccRCC, with positive staining for CA9, CD10, PAX-8, and vimentin, and negative staining for markers such as CgA, inhibin, melan-A, and calretinin. The negative staining for chromogranin A (CgA) ruled out pheochromocytoma, while the absence of melan-A, inhibin, and calretinin excluded adrenocortical tumors (8). The intact capsule and normal adrenal tissue adjacent to the mass indicated that the tumor had not infiltrated the adrenal gland.

The management of extrarenal ccRCC parallels that of typical ccRCC, with surgical resection being the primary treatment for localized tumors. In this case, the tumor was completely removed, and no recurrence was observed during the follow-up period. However, further studies are required to confirm the long-term efficacy of this approach. Robotic radiosurgery (RRS) has emerged as a non-invasive alternative to traditional renal mass surgery. Michael Staehler et al. demonstrated that RRS provided similar overall survival outcomes to open partial nephrectomy in elderly and high-risk patients (9).

Currently, there is no evidence to suggest that patients with locally advanced tumors benefit from regional or extended lymph node dissection, nor is there documented evidence supporting the efficacy of ipsilateral adrenalectomy in the management of locally advanced tumors. In fact, a large-scale study by the Mayo Clinic found no oncological benefit from routine ipsilateral adrenalectomy during radical nephrectomy for locally advanced renal cancer. The study also noted that ipsilateral adrenalectomy does not prevent contralateral adrenal metastasis, as the risk of metastasis is equivalent on both sides. Therefore, routine ipsilateral adrenalectomy is not recommended unless there is evidence of adrenal involvement or metastasis (10).

In summary, the treatment of advanced or metastatic extrarenal RCC remains reliant on systemic therapies, with palliative surgery or radiotherapy serving as adjuncts for managing primary or metastatic lesions. Diagnosing extrarenal ccRCC preoperatively, especially when tumors are located in the adrenal region, poses significant challenges. Future research should focus on optimizing the diagnostic and therapeutic strategies for this rare entity.

## Conclusion

This report presents a rare case of extrarenal clear cell renal cell carcinoma (ccRCC). The exact origin of extrarenal ccRCC remains unclear, potentially arising from embryonic remnants of renal tissue. Due to its rarity and the complexities of its development, extrarenal ccRCC poses diagnostic and therapeutic challenges. In accordance with established guidelines for renal cell carcinoma, complete surgical resection is the recommended treatment for localized extrarenal ccRCC. For cases that are advanced or metastatic, systemic therapy remains the cornerstone of management.

## Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving humans were approved by the Ethics Committee of the 363 Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

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# Impacts of completely endophytic renal masses on perioperative, oncologic, and functional outcomes in robot-assisted partial nephrectomy: a systematic review and meta-analysis

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**Background:** The objective of this study was to perform a comprehensive pooled analysis aimed at comparing the efficacy and safety of robot-assisted partial nephrectomy (RAPN) between completely endophytic tumors (CERT) and non-completely endophytic tumors (non-CERT).

**Methods:** This study adhered rigorously to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to conduct a systematic review and meta-analysis. We performed a systematic search in the PubMed, Embase, Web of Science, and Cochrane Library databases, focusing on studies published in English up to May 2024. Our analysis primarily evaluated key outcomes, specifically perioperative, functional, and oncological outcomes.

**Results:** A total of 2126 patients across six studies were included in the analysis. Compared to non-CERT, CERT was associated with significantly higher rates of major complications (Odds Ratio [OR]: 2.47; 95% CI: 1.14 to 5.34; $p = 0.02$), longer warm ischemia times (Weighted Mean Difference [WMD]: 3.27 min; 95% CI: 0.61 to 5.39; $p = 0.02$), a greater decline in estimated glomerular filtration rate (eGFR) (WMD: 2.93 ml/min/1.73 $m^2$; 95% CI: 0.75 to 5.11; $p = 0.008$), and relatively lower trifecta achievement rates (OR: 0.63; 95% CI: 0.41 to 0.96; $p = 0.03$). However, no statistically significant differences were observed between the two groups in terms of operative time, length of stay, blood loss, transfusion rates, intraoperative complications, overall complications, positive surgical margins, and local recurrence.

**Conclusions:** Although CERT was associated with greater declines in eGFR and lower rates of trifecta achievement, it yielded perioperative, functional, and oncologic outcomes comparable to those of non-CERT in RAPN. Our findings suggest that RAPN for completely endophytic renal masses can achieve acceptable outcomes when performed in centers with substantial expertise in robotic surgery.

**Systematic review registration:** https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=555067, identifier CRD42024555067.

KEYWORDS

completely endophytic tumors, non-completely endophytic tumors, robot-assisted partial nephrectomy, outcomes, meta-analysis

# 1 Introduction

Partial nephrectomy (PN) is widely recognized as the preferred therapeutic strategy for small renal tumors, in alignment with recommendations from the American Urological Association (AUA) and the European Association of Urology (EAU) guidelines (1, 2). Beyond yielding surgical outcomes and cancer control comparable to those of radical nephrectomy, PN offers the distinct advantage of nephron preservation. This preservation is pivotal not only for maintaining renal function but also for enhancing postoperative quality of life in patients (3). In recent years, the advent of robotic technology has revolutionized the field of PN, leading to substantial advancements in both instrumentation and surgical techniques. As a result, robot-assisted partial nephrectomy (RAPN) has gained ascendancy over traditional laparoscopic PN. This shift is characterized by significant enhancements in perioperative outcomes and a marked reduction in the learning curve, making RAPN an increasingly favored approach in urological surgery (4–6).

The Complete Endophytic Renal Tumor (CERT) is typically evaluated using the 'E' domain of the RENAL Nephrometry Score, which assesses the extent of tumor invasion into the normal renal parenchyma (7). Tumors are classified into three groups based on their growth patterns: exophytic, mesophytic, and endophytic. Moreover, many surgeons contend that the complexity of tumors, particularly those that are entirely endophytic, substantially increases the difficulty of surgical procedures. These complex tumors pose numerous challenges for the surgeon, requiring advanced skills and careful planning (8). Despite previous studies indicating that RAPN can be safely performed even on completely endophytic tumors (9), a significant barrier to drawing definitive conclusions is the reliance on research characterized by small sample sizes and conducted within the confines of single institutions. These limitations hinder the ability to achieve robust and universally applicable results, calling for broader multi-institutional studies to validate these findings.

Therefore, the objective of this study is to synthesize comparative research data to evaluate the efficacy and safety of RAPN for CERT versus non-CERT. This research aims to provide a comprehensive analysis of the available evidence, thereby informing and guiding clinical decision-making processes.

# 2 Methods

This study was officially registered with PROSPERO and adhered meticulously to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, in accordance with the recommendations of the 2020 statement (10, 11). Additionally, it has been documented in the PROSPERO registry under the identification number: CRD42024555067.

## 2.1 Literature search strategy, study selection, and data collection

We conducted exhaustive searches across multiple databases including PubMed, Embase, Web of Science, and the Cochrane Library, capturing data up to May 2024. Our search methodology employed a combination of terms specific to the intervention and relevant to patient characteristics, structured as follows: [(Robotic PN OR Robot-assisted PN OR Robot-assisted nephron-sparing surgery) AND (Intrarenal OR Endophytic OR Completely endophytic) AND (Renal tumors OR Renal masses)]. Additionally, we conducted manual searches of relevant references to ensure thoroughness and broaden the scope of our investigation.

The inclusion criteria were established utilizing the PICOS framework: P (Patients)—included patients diagnosed with localized renal tumors; I (Intervention)—patients with CERT who underwent RAPN; C (Comparator)—patients diagnosed with non-CERT, also treated with RAPN; O (Outcome)—evaluated outcomes encompassed perioperative metrics, complications, renal functionality, and oncologic effectiveness; S (Study Type)—the studies considered were randomized controlled trials (RCTs), along with prospective and retrospective comparative studies. Exclusion criteria were delineated as follows: (1) specific types of publications, such as case reports, meeting abstracts, editorial comments, and any unpublished research; (2) studies lacking crucial data required for inclusion in a meta-analysis; (3) studies that failed to provide comparative data.

Each selected study was meticulously reviewed by two independent evaluators. The extracted data included: (1) General study details such as the first author, year of publication, and country of the study; (2) Participant demographics, which covered sample size, age, gender, body mass index (BMI), RENAL scores, and follow-up duration; (3) Perioperative outcomes, including operative time, hospital stay duration, warm ischemia time, blood loss, intraoperative complications, major complications (Clavien grade ≥ 3), and overall complications (Clavien grade ≥ 1) (12); (4) Renal function and oncologic outcomes, encompassing preoperative estimated glomerular filtration rate (eGFR), trifecta achievement, tumor diameter and site, clinical stage, tumor pathology, local recurrence, and positive surgical margins (PSM). All discrepancies were resolved through consensus or following consultation with a third reviewer.

This study employed the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) framework to evaluate non-RCTs (13). The quality of the literature was independently assessed by two evaluators. Discrepancies in the evaluations were resolved through detailed discussion between the evaluators.

## 2.2 Statistical analysis

For data analysis, we utilized the RevMan5.4 software provided by the Cochrane Collaboration (Oxford, UK). Odds ratios (ORs) and weighted mean differences (WMD) for dichotomous and continuous variables were calculated separately, with results presented including a 95% confidence interval (CI). To determine heterogeneity among the included studies, the $I^2$ test was applied (14). In light of expected significant heterogeneity, a random-effects model was adopted for all statistical analyses, with a p-value of less than 0.05 indicating statistical significance. Sensitivity analyses were also conducted on results with marked heterogeneity to explore the sources of such variability between studies and to verify the robustness of our analyses.

## 2.3 Publication bias

In our study, we employed Begg's funnel plot method to systematically assess and identify potential evidence of publication bias.

# 3 Results

## 3.1 Baseline characteristics

In our systematic review, we initially identified 71 relevant studies. After the removal of duplicates, 11 studies remained for detailed assessment. Further screening of titles and abstracts led to

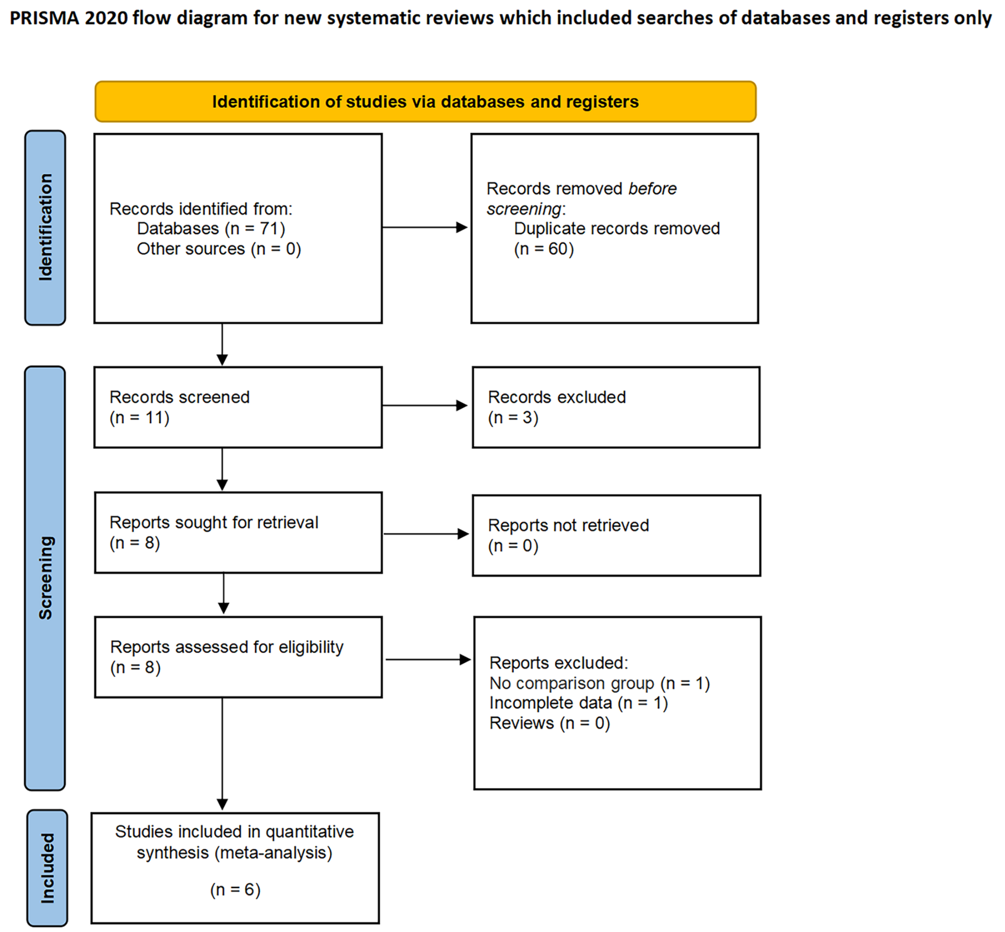


FIGURE 1
PRISMA flow diagram for the systematic review.

the exclusion of three studies, as they were not controlled studies, and an additional two were discarded following an exhaustive full-text review. Consequently, our meta-analysis ultimately included six studies, involving a total of 2,126 patients, comprising 389 diagnosed with CERT and 1,737 with non-CERT conditions, as illustrated in Figure 1. The cohort for analysis consisted of six non-RCTs, all of which were retrospective comparative studies (15–20). Of these, two studies were multi-institutional (15, 17), while the others were conducted at single centers. The scope of the research was international, with studies originating from Japan, the United States, Europe, and Korea. None of the included studies used propensity scoring analysis. Table 1 offers a meticulous summary of the key characteristics of the studies, including preoperative variables and interventions—detailing sample size, age, gender, and BMI. The duration of follow-up for the studies included ranged from 12 to 48 months. Tables 2, 3 provide an exhaustive summary of the functional and oncological outcomes.

The analysis demonstrated that individuals within the CERT group were on average younger than those in the non-CERT group, with a WMD of -3.48 years (95% CI: -5.39 to -1.57; p = 0.0004). Additionally, patients in the CERT group presented with higher RENAL scores compared to the non-CERT group, evidenced by a WMD of 3.32 (95% CI: 1.72 to 4.92; p < 0.0001). However, comparative analyses regarding BMI, tumor diameter, and preoperative eGFR between the two groups did not exhibit any statistically significant differences, with p-values of 0.36, 0.18, and 0.58, respectively, as detailed in Table 4.

## 3.2 Assessment of quality

All studies included in the analysis conducted comparative evaluations, with the majority being published between 2014 and 2024. An assessment of the risk of bias indicated that five studies were categorized as having a moderate risk, while one exhibited a high risk of bias (18). These assessments are comprehensively detailed in Supplementary Table 1.

## 3.3 Outcome analysis

### 3.3.1 Perioperative effectiveness

The pooled results from six studies indicated no significant difference in operative time between the CERT and non-CERT groups (WMD 5.99 min, 95% CI -5.56 to 16.75; p = 0.33) (15–20). Additionally, the meta-analysis, which included four studies, reported that the cumulative findings showed no significant differences in the length of hospital stay between the two groups (WMD -0.09 day, 95% CI -0.47 to 0.28; p = 0.62) (16, 17, 19, 20), as depicted in Figure 2.

The analysis revealed no statistically significant differences in blood loss between the CERT and non-CERT tumor groups (six studies; WMD 6.31 ml, 95% CI -20.27 to 32.90; p = 0.64) (15–20). Similarly, cumulative analysis showed no significant differences in transfusion rates between the two groups, based on data from four studies (OR: 1.76; 95% CI: 0.52 to 6.02; p = 0.36) (16, 17, 19, 20), as depicted in Figure 3.

TABLE 1 The trials included in the systemic review.

| Reference | Year | Country | Propensity scoring analysis | Center | Patients | | Age(y) | | Male/Female | | BMI ($kg/m^2$) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic |
| Ito | 2024 | Japan | No | multi-institutional | 76 | 590 | 62.2(12.8) | 62.7(12.9) | 63/13 | 412/178 | 24.5(3.6) | 24.5(4.3) |
| Motoyama | 2022 | Japan | No | single-center | 26 | 127 | 64.5(12.5) | 68(15.75) | 18/8 | 83/44 | 24.8(5.43) | 24.2(8.05) |
| Carbonara | 2020 | USA and Europe | No | multi-institutional | 147 | 510 | 57.7(11.8) | 60.9(12.7) | 93/54 | 296/214 | 27.4(5.7) | 27.7(5.2) |
| Curtiss | 2015 | USA | No | single-center | 30 | 267 | 54.5(10) | 60.9(10.4) | 14/16 | 170/97 | 30.2(6.7) | 29.4(5.9) |
| Komninos | 2014 | Korea | No | single-center | 45 | 64 | 50(9.63) | 51(10.37) | 31/14 | 30/34 | 26.1(3.33) | 25.5(3.7) |
| Autorino | 2014 | USA | No | single-center | 65 | 179 | 56(1.4) | 61.2(0.9) | 31/34 | 111/68 | 29.4(6.3) | 31.2(7.4) |

BMI, Body mass index; Mean (SD).

TABLE 2 The trials included in the systemic review.

| Reference | Tumor diameter (cm) | | Tumor site (Lt/Rt) | | Preoperative eGFR (ml/min/1.73 $m^2$) | | RENAL score | | Follow-up duration (month) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic |
| Ito | 2.4(0.84) | 2.9(1.3) | NA | | 71.6(16.2) | 68.6(19.1) | 8.9(1.3) | 6.8(1.7) | 12(46.7) | 12.5(62.2) |
| Motoyama | 1.9(1.0) | 2.9(1.75) | 8/18 | 63/64 | NA | | 9(1.25) | 6(1.5) | NA | |
| Carbonara | 4.2(2.5) | 3.2(4.1) | NA | | 84.2(22.7) | 83.6(21.4) | 10(1.48) | 4(1.48) | 21.6(20) | 32.3(25.4) |
| Curtiss | 2.3(1.1) | 2.7(1.4) | NA | | NA | | 9(1.5) | 6(2.2) | 10.6 | |
| Komninos | 2.6(1.56) | 2.5(2.96) | 26/19 | 29/35 | 84.4(10.37) | 90(14.07) | 9(1.48) | 5.5(2.22) | 48(28.89) | 38(34.82) |
| Autorino | 2.6(1.0) | 3.7(2.1) | 32/33 | 90/89 | 89.6(22.9) | 80.1(23.2) | 8.7(1.4) | 6.4(2.2) | 12.6(11.0) | 14.5(13.8) |

eGFR, estimated glomerular filtration rate; Mean (SD).
N/A, not application.

### 3.3.2 Complications

Analysis from four studies indicated that the difference in the incidence of intraoperative complications between the CERT and non-CERT cohorts was not statistically significant (OR: 1.19; 95% CI: 0.51 to 2.79; p = 0.69) (17–20). In the CERT cohort, major complications occurred in 3.8% of cases (12 out of 313), whereas in the non-CERT cohort, the rate was 2.0% (23 out of 1147). However, the analysis revealed a statistically significant higher risk of major complications in the CERT group compared to the non-CERT group (OR: 2.47; 95% CI: 1.14 to 5.34; p = 0.02) (16–20). Furthermore, our meta-analysis of four studies that focused on overall complication rates showed that the CERT group experienced a complication rate of 18.1% (52 out of 287 cases), while the non-CERT group experienced a rate of 15.4% (157 out of 1020 cases). Nonetheless, the difference in overall complication rates between the CERT and non-CERT cohorts was not statistically significant (OR: 0.83; 95% CI: 0.35 to 1.96; p = 0.66) (17–20), as shown in Figure 4.

### 3.3.3 Renal functional

The quantitative analysis of six studies focused on warm ischemia time revealed that the CERT group experienced longer warm ischemia durations compared to the non-CERT group (WMD 3.27 min, 95% CI 0.61, 5.93; p = 0.02) (15–20). Additionally, a subsequent meta-analysis, which included data from four studies, indicated a greater decline in eGFR in the CERT group (WMD 2.93 ml/min/1.73 $m^2$, 95% CI 0.75 to 5.11; p = 0.008) (15, 17, 19, 20), as depicted in Figure 5.

### 3.3.4 Oncologic outcomes

In the CERT group, the analysis indicated statistically significantly lower rates of trifecta achievement compared to the non-CERT group (five studies; OR 0.63, 95% CI 0.41 to 0.96; p = 0.03) (15–17, 19, 20). However, the analysis found no statistical significance in PSM between CERT and non-CERT across six studies (OR 1.77, 95% CI 0.94 to 3.31; p = 0.08) (15–20). Regarding local recurrence, the CERT group reported a rate of 1.7% (5 incidents out of 287 cases), while the non-CERT cohort had a rate of 0.5% (6 incidents out of 1020 cases). A meta-analysis of four studies showed that there was no statistically significant difference in local recurrence rates between the CERT and non-CERT groups across six studies (OR 2.38, 95% CI 0.72 to 7.89; p = 0.16) (17–20), as illustrated in Figure 6.

## 3.4 Heterogeneity

Our research findings generally demonstrate moderate heterogeneity. Despite including studies of moderate to high quality, we observed considerable heterogeneity in three outcomes: operative time ($I^2$ = 74%), overall complications ($I^2$ = 75%), and warm ischemia time ($I^2$ = 92%).

## 3.5 Sensitivity analysis

In this investigation, we noted significant heterogeneity across three clinical parameters: operative time, overall complications, and

TABLE 3 Oncologic outcomes.

| Reference | Tumor stage | | Tumor pathology | |
|---|---|---|---|---|
| | Completely endophytic | Non-completely endophytic | Completely endophytic | Non-completely endophytic |
| Ito | pT1a:62; pT1b:1; pT2a:0; pT3a:5 | pT1a:438; pT1b:68; pT2a:1; pT3a:31 | Clear cell: 54; Papillary: 3; Chromophobe: 6; Others: 13 | Clear cell: 426; Papillary: 48; Chromophobe: 37; Others: 79 |
| Motoyama | NA | | Clear cell: 18; Others: 2; Benign: 6 | Clear cell: 75; Others: 24; Benign: 28 |
| Carbonara | pT1a:68; pT1b:33; pT2a:13; pT2b:2; pT3a:10 | pT1a:307; pT1b:70; pT2a:9; pT2b:4; pT3a:18 | Benign: 31; Malignant: 116 | Benign: 121; Malignant: 389 |
| Curtiss | pT1a:19; pT1b:0; pT2a:0; pT3a:1 | pT1a:161; pT1b:31; pT2a:3; pT3a:31 | Clear cell: 15; Papillary: 2; Chromophobe: 0; Others: 3 | Clear cell: 110; Papillary: 45; Chromophobe: 20; Others: 33 |
| Komninos | pT1a:30; pT1b:9; pT2:1; pT3a:0 | pT1a:30; pT1b:10; pT2:4; pT3a:2 | Benign: 5; Malignant: 40 | Benign: 18; Malignant: 46 |
| Autorino | pT1a:47; pT1b:3; pT2:0; pT3a:2 | pT1a:84; pT1b:41; pT2:4; pT3a:11 | Benign: 17; Malignant: 48 | Benign: 40; Malignant: 139 |

N/A, not application.

warm ischemia time. To pinpoint the primary sources of this heterogeneity and assess the robustness of our findings, we conducted a sensitivity analysis by systematically excluding one study at a time. It's important to highlight that for outcomes where the number of included studies was three or fewer, sensitivity analyses were deemed inapplicable. Ultimately, this process did not reveal any substantial changes in the levels of heterogeneity associated with operative time, overall complications, and warm ischemia time. This suggests that the observed heterogeneity is a consistent characteristic across the included studies.

## 3.6 Publication bias

To evaluate the presence of publication bias, we analyzed indicators such as operative time, blood loss, warm ischemia time, and PSM. The distribution of studies exhibited near symmetry for these variables, suggesting a minimal likelihood of publication bias. These findings are detailed in Figure 7.

# 4 Discussion

This study aims to evaluate the perioperative, functional, and oncologic outcomes of RAPN for CERT and non-CERT. Additionally, several significant findings from this study warrant further discussion.

Due to the larger and deeper resection of normal renal parenchyma surrounding the tumor, a longer surgical time is typically required to completely remove an endophytic tumor. However, there was no statistically significant difference in surgical time between the two groups. Besides tumor characteristics, numerous other factors can influence surgical time, such as the experience of the surgeon and assistant, the patient's BMI, and intraoperative complications (21). In the included studies, all procedures were performed by operators with extensive experience in minimally invasive surgery, which may partially explain this result. In most of the included studies, the average hospital stay for patients was 4 days. Robotic surgery helps to reduce intraoperative blood loss, maintain a clear surgical field, and protect surrounding tissues (22). Additionally, minimally invasive surgery aids in the recovery of bowel function and reduces complications associated with prolonged bed rest, thereby shortening the hospital stay. There was no statistically significant difference in hospital stay between the two groups. However, the hospital stay for robotic surgery is mainly influenced by the surgeon's expertise and the volume of procedures at the institution, rather than the surgical method itself (23). It is also important to note that differences in healthcare systems and insurance policies across regions may lead to variations in hospital stay (24).

The combined results indicated no statistically significant difference in blood loss between the CERT and non-CERT groups ($p = 0.64$). Despite this, the CERT group generally exhibited greater blood loss across most included studies. This lack of statistical

TABLE 4 Comparison of baseline characteristics of patients.

| Baseline characteristic | CERT VS non-CERT group | Heterogeneity $I^2$ (%) | *p* value |
|---|---|---|---|
| Age WMD (95% CI) | -3.48(-5.39 to -1.57) | 71 | 0.0004 |
| BMI WMD (95% CI) | -0.24(-0.77 to 0.28) | 0 | 0.36 |
| Tumor diameter WMD (95% CI) | -0.35(-0.87 to 0.17) | 89 | 0.18 |
| RENAL score WMD (95% CI) | 3.32(1.72 to 4.92) | 99 | < 0.0001 |
| Preoperative eGFR WMD (95% CI) | 1.56(-3.73 to 6.85) | 81 | 0.56 |

CERT, completely endophytic tumors; non-CERT, non-completely endophytic tumors; eGFR, estimated glomerular filtration rate.

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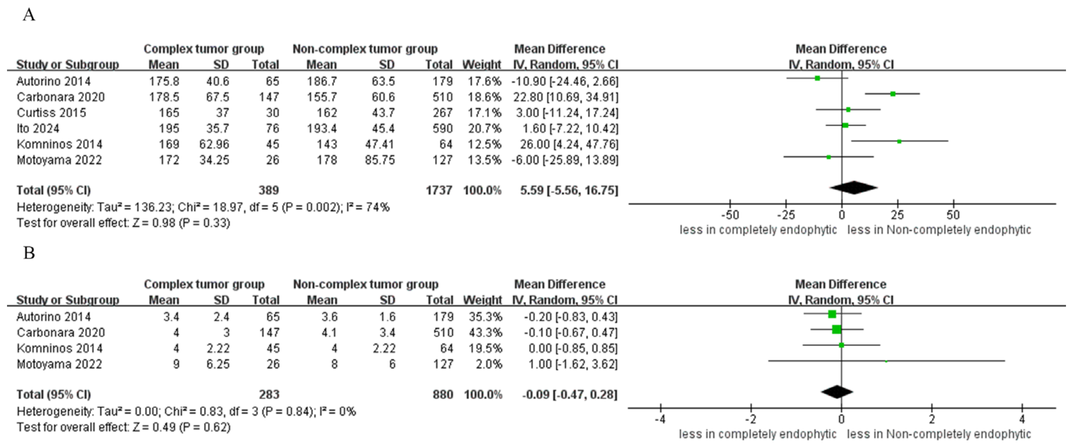


FIGURE 2
Forest plots of perioperative outcomes **(A)** operative time, **(B)** length of hospital stay.

significance may be due to the limited number of studies analyzed. However, the increased blood loss in the CERT group was not likely to be clinically significant, as there was no significant difference in transfusion rates between the two groups (p = 0.36). The transfusion rates observed in both the CERT and non-CERT groups may also be influenced by the surgeon's expertise and the hospital's blood transfusion guidelines (25).

The analysis revealed that the CERT group exhibited a higher incidence of major complications compared to the non-CERT group (p=0.02). This finding may be attributed to the increased complexity of RAPN in tumor reconstruction and resection. It is noteworthy that no patients succumbed to major complications. Furthermore, cumulative analysis indicated no significant differences in intraoperative (p = 0.69) and overall complications between the two groups (p = 0.66). Therefore, despite the increased incidence of major complications in the CERT group, RAPN can still yield acceptable outcomes. In greater detail, two studies reported on the intraoperative conversion to radical nephrectomy in both patient groups, finding no significant differences in conversion rates between them. Similarly, one study noted that there were no cases requiring embolization for hemorrhage in either group (15, 18). However, more evidence is required to validate these conclusions.

For completely endophytic renal tumors, RAPN poses significant challenges in tumor localization and excision, leading to prolonged warm ischemia time. A quantitative analysis of five studies focusing on warm ischemia time revealed that the CERT group experienced longer warm ischemia durations compared to the non-CERT group (p = 0.02). However, certain aspects warrant attention, particularly the optimal time of warm ischemia during PN, which remains a topic of debate in the urological community. Several studies suggest that warm ischemia time should be limited to 25 or 30 minutes to minimize the risk of renal function impairment (26–28). It is noteworthy that the warm ischemia times included in our analysis were all less than 30 minutes. Considering these factors, the ischemia time in the CERT group

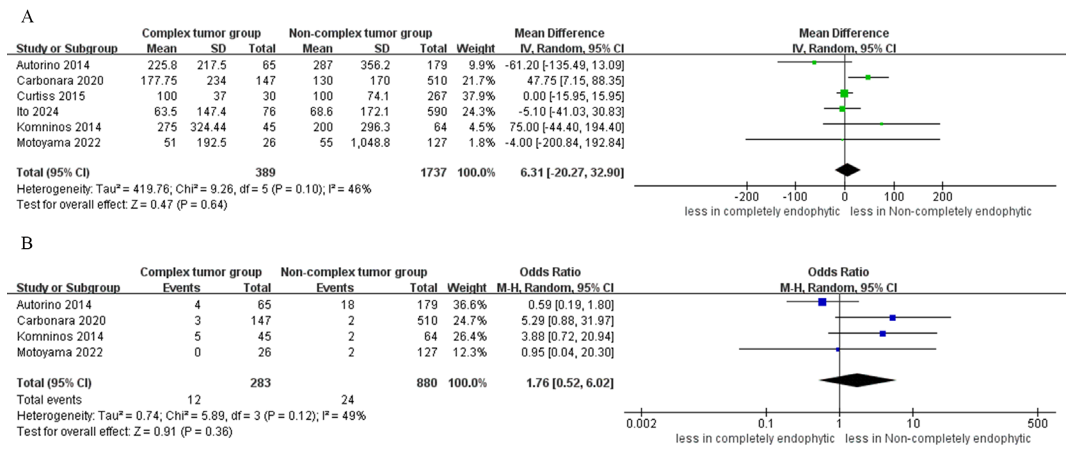


FIGURE 3
Forest plots of perioperative outcomes **(A)** blood loss, **(B)** transfusion rates.

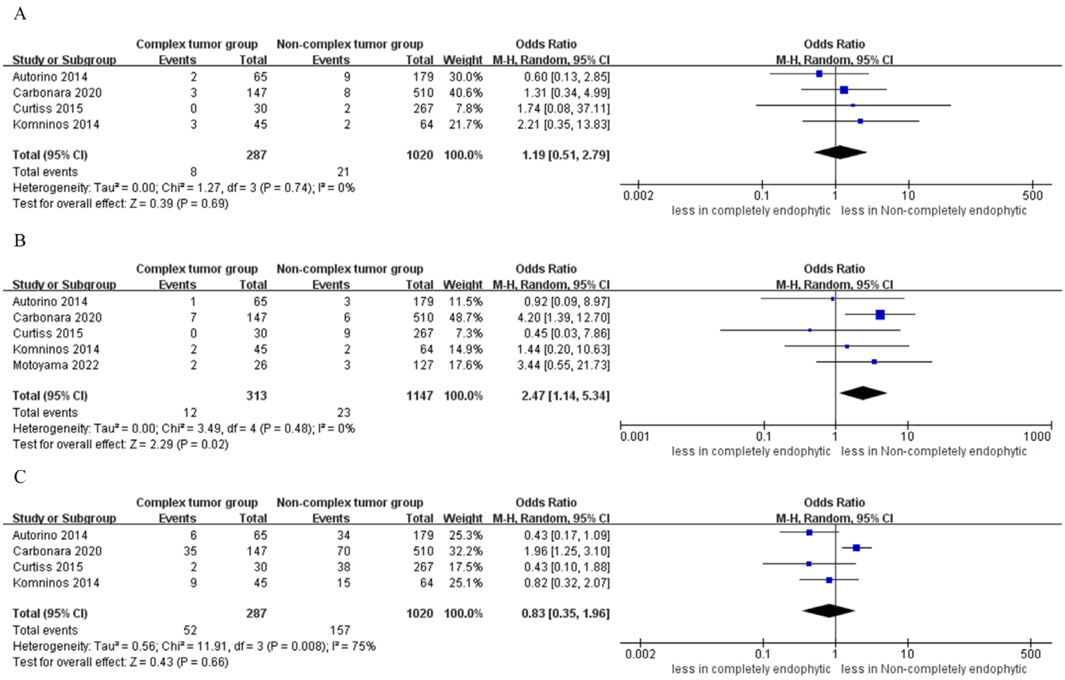


FIGURE 4
Forest plots of complication **(A)** intraoperative complications, **(B)** major complication **(C)** overall complications.

is deemed acceptable. Postoperative renal function is crucial, especially for endophytic tumors (18). The meta-analysis, which included data from four studies, indicated a greater decline in eGFR in the CERT group. A meta-analysis including data from four studies indicates that the CERT group experienced a greater decline in eGFR. However, certain aspects deserve attention. First, recent studies suggest that preoperative renal function and the number of kidneys preserved are major factors significantly associated with long-term renal function outcomes (29, 30). Second, the work of Fergany et al. (31) highlights the critical role of age in the postoperative recovery of renal function. Additionally, the included studies did not report the number of patients who progressed to advanced stages of CKD during follow-up. Nonetheless, this result may not translate into clinical harm for patients. Therefore, this result should be interpreted with caution.

In our study, the trifecta achievement rate in the CERT group for treating CERT was lower at 48.6% (171 out of 352 cases) compared to reports on small renal masses in RAPN series (32). Factors influencing trifecta achievement include tumor size and complexity, with patients in the CERT group presenting higher RENAL scores than those in the non-CERT group, making these findings expected. Additionally, our results are consistent with

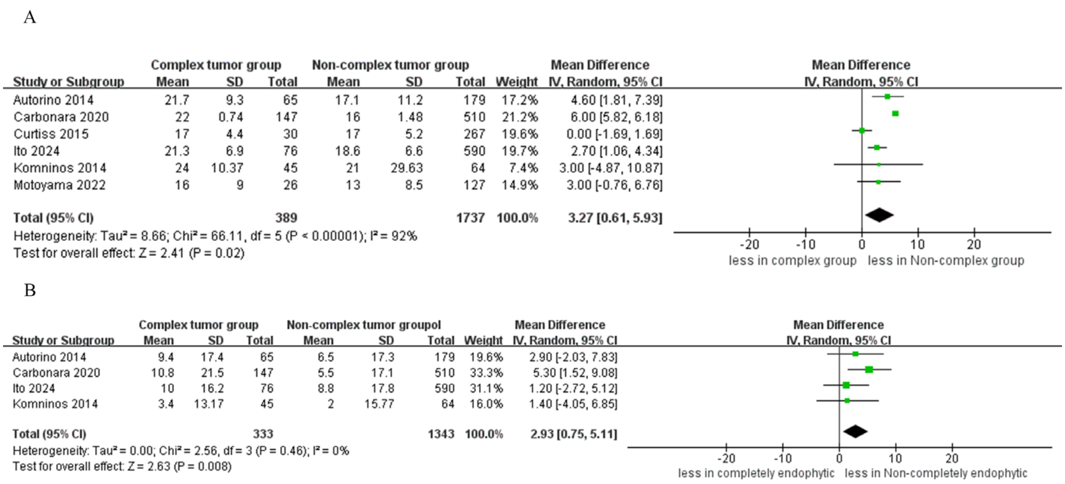


FIGURE 5
Forest plots of renal functional outcomes **(A)** warm ischemia time, **(B)** eGFR decline.

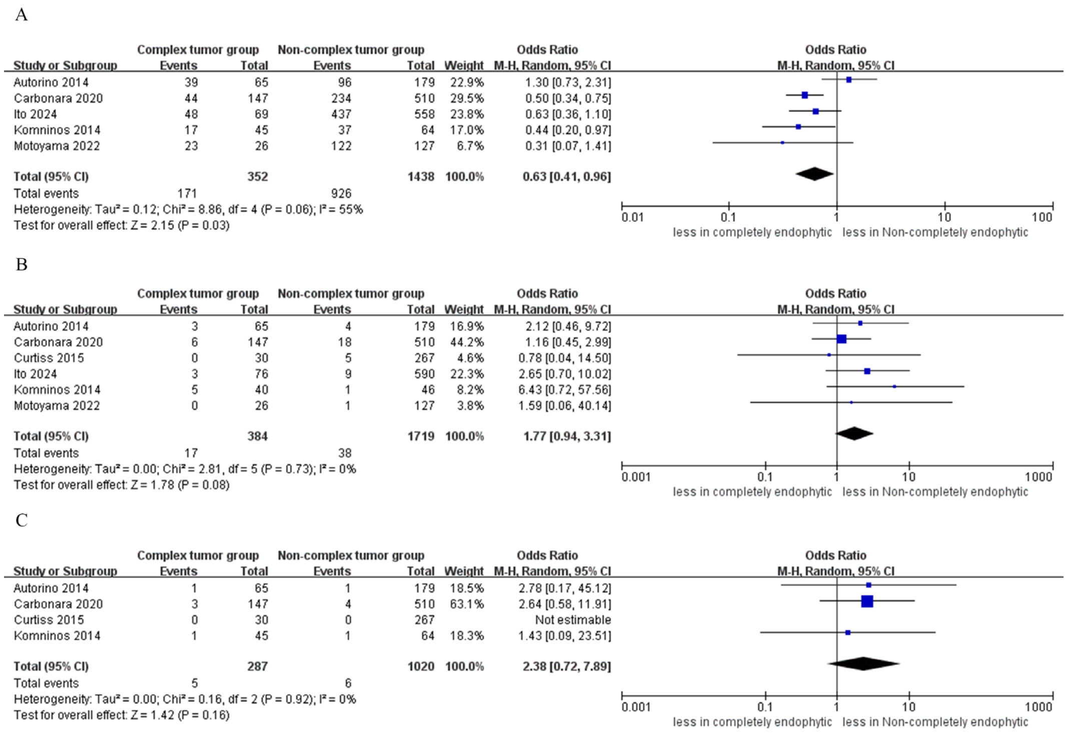


FIGURE 6
Forest plots of oncologic outcomes **(A)** trifecta achievement, **(B)** PSM, **(C)** local recurrence.

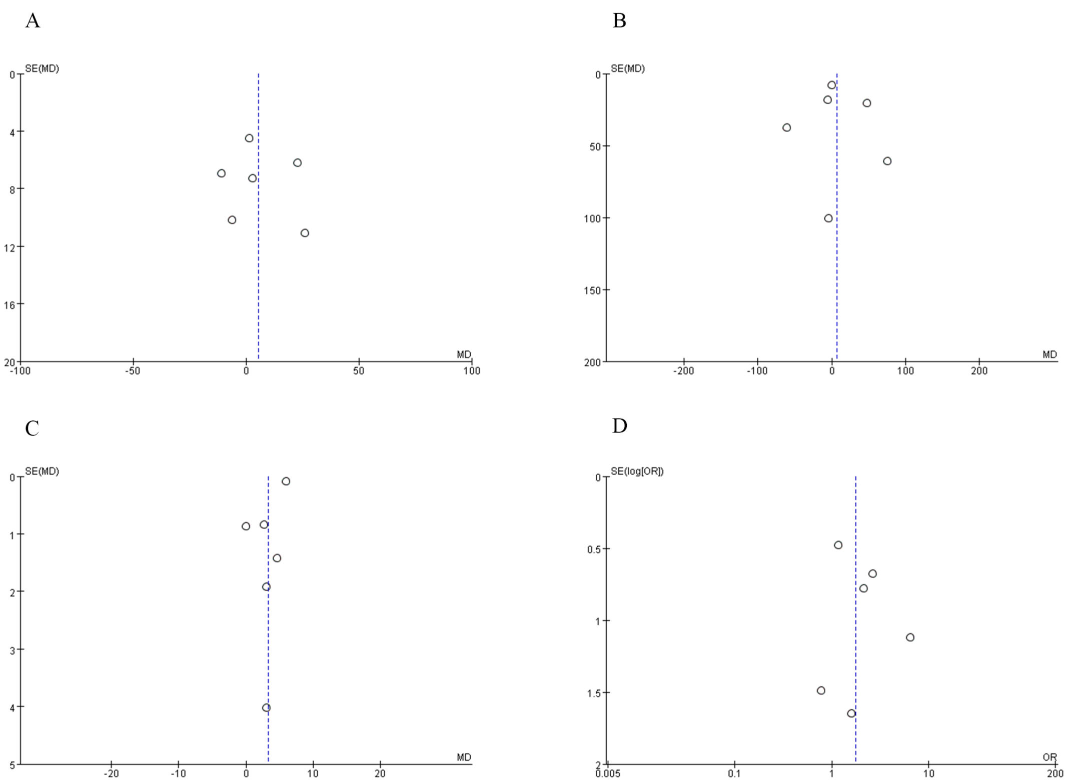


FIGURE 7
Funnel plot **(A)** operative time, **(B)** blood loss, **(C)** warm ischemia time, **(D)** PSM.

those published by Bertolo et al. (33), who reported a trifecta achievement rates of 49% among patients with larger renal tumors treated with RAPN. The prolonged warm ischemia time in the complex tumor group appears to be a contributing factor affecting trifecta achievement. Nonetheless, trifecta achievement does not assess long-term renal function and oncological outcomes, indicating the necessity for further long-term follow-up studies to evaluate these results comprehensively. Among the included studies, no significant difference in PSM was observed between the CERT and non-CERT groups. The incidence of PSM in the CERT group was 4.42%, compared to 2.21% in the non-CERT group. The PSM rate of 4.42% in the CERT group aligns with the range reported by high-volume institutions performing RAPN, where rates vary from 0% to 3.7% (34). Several important aspects of this finding merit further discussion. Firstly, Marszalek et al. (35) suggested that PSM might not be a decisive factor for recurrence. Secondly, various factors could influence PSM, including tumor staging, surgical approach (transperitoneal or retroperitoneal approaches), and tumor diameter (36). Consequently, further research is essential to validate our findings. Furthermore, our study showed that there was no statistically significant difference in local recurrence rates between the CERT and non-CERT groups across six studies.

Other important issues requiring in-depth discussion include the choice of surgical approach. First, the studies we included utilized different surgical approaches, such as transperitoneal or retroperitoneal approaches. The retroperitoneal approach offers certain benefits; for example, it may result in shorter operative times and shorter hospital stays, particularly for posteriorly located tumors (37). However, compared to the transperitoneal approach, the retroperitoneal approach also has drawbacks, such as limited working space. The debate over whether to choose the retroperitoneal or transperitoneal approach remains controversial. Therefore, further research with higher-quality evidence is necessary to determine the most suitable surgical method for CERT. Second, three-dimensional (3D) virtual models have shown a positive impact. Grosso et al. (38) conducted a study reporting that 3D virtual models are promising tools, as they can provide a reliable assessment of surgical planning. However, with increasing complexity of the renal masses, the advantages offered by 3D reconstruction become more apparent. Additionally, another study reported that the use of 3D virtual models in RAPN resulted in a lower incidence of global ischemia and a higher enucleation rate compared to the control group (39). Therefore, the importance of surgical planning is crucial for RAPN for complete endophytic renal masses. Third, recent studies have compared the outcomes of open and robotic PN (enucleation, enucleoresection, or resection), focusing on predictors of trifecta failure in patients with highly complex renal tumors (40, 41). These studies have shown that tumor complexity and surgical approach are independent predictors of trifecta failure following PN for highly complex renal tumors. Fourth, the endophytic renal masses are only one determinant of tumor complexity. The complexity of renal tumors primarily depends on several tumor-associated factors, such as tumor size and type, including endophytic, hilar, and cystic renal tumors (42). Additionally, the RENAL and PADUA scores are among the most commonly used renal scoring systems, with complex renal tumors identified as those having a RENAL or PADUA score of 7 or higher (7, 43). Lastly, RAPN is a challenging surgical procedure that requires continuous learning and adaptation, influenced by various patient, tumor, and surgeon-related factors. Beyond the complexity of the tumor and the increasing volume of cases managed by surgeons, prior surgical experience significantly impacts perioperative outcomes (44). Incorporating research from different institutions may introduce some heterogeneity in the results. Therefore, more research is needed to confirm our conclusion.

The limitations of this study must be acknowledged. Firstly, all included studies were non-randomized controlled trials, inherently carrying a risk of potential bias. Secondly, the absence of subgroup analyses based on surgical approaches (retroperitoneal versus transperitoneal) in the included studies may have introduced subtle differences in outcomes. Thirdly, the lack of reported oncological outcomes such as cancer-specific survival (CSS), overall survival (OS), and recurrence-free survival (RFS) results in insufficient data for a comprehensive evaluation of oncological results. Fourth, the relatively short follow-up periods (10-12 months) in some studies constrain the ability to compare renal function and oncological outcomes between the two groups effectively. Finally, endophyticity may include different grades according to the amount of parenchyma above the lesion. However, the included studies did not report the amount of parenchyma above the lesion, which may cause some heterogeneity in the results.

# 5 Conclusions

Our study confirms that while CERT is associated with a greater decline in eGFR and a lower rate of trifecta achievement, its perioperative, functional, and oncological outcomes are comparable to non-CERT in RAPN. In centers with appropriate robotic surgical expertise, RAPN can be considered a minimally invasive surgical treatment for these lesions. However, to strengthen the evidence base and affirm the veracity of the findings, further extensive and meticulous research is indispensable, encompassing a larger sample size and comprehensive data from high-volume medical centers.

# Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

## Author contributions

H-XG: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. JL: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Supervision, Writing – original draft, Writing – review & editing. YL: Conceptualization, Data curation, Funding acquisition, Investigation, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. H-LW: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2024.1444477/full#supplementary-material

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