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JOURNAL OF ENDOUROLOGY

& Urotechnology, Minimally Invasive and Robotic Urology

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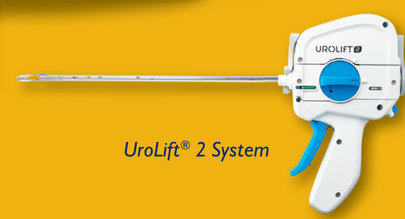

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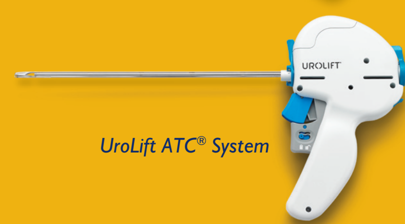

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(continued)

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Ureteroscopy and Percutaneous Procedures

Long-Term Oncologic Outcomes of Endoscopic Management of High-Risk Upper Tract Urothelial Carcinoma: The Fundació Puigvert's Experience

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Abstract

Objectives: Many patients with upper tract urothelial carcinoma (UTUC) outside of the low-risk criteria may possess low absolute risks of distant progression. Herein, we hypothesized that careful selection of high-risk patients undergoing an endoscopic approach could result in acceptable oncologic outcomes.
Materials and Methods: Patients with high-risk UTUC managed endoscopically between 2015 and 2021 were retrospectively identified from a prospectively maintained single academic institution database. Elective and imperative indications for endoscopic treatment were considered. Regarding elective indications, the decision to perform endoscopic treatment was systematically proposed to high-risk patients in whom macroscopically complete ablation was deemed feasible, excluding invasive appearance on CT scan, and without histologic variant.
Results: A total of 60 patients with high-risk UTUC met our inclusion criteria (29 imperative and 31 elective indications). The median follow-up in patients without any event was 36 months. At 5 years, the estimated overall survival, cancer-specific survival, metastasis-free survival, UTUC recurrence-free survival, radical nephroureterectomy-free survival, and bladder recurrence-free survival were 57% (41–79), 75% (57–99), 86% (71–100), 56% (40–76), 81% (70–93), and 69% (54–88), respectively. All oncologic outcomes were similar between patients with elective and imperative indications (all log-rank $p > 0.05$).
Conclusions: In conclusion, we report the first large series of endoscopic treatment in patients with high-risk UTUC, arguing that promising oncologic outcomes can be achieved in properly selected candidates. We encourage multi-institutional collaborative work as a large cohort of high-risk patients treated endoscopically may allow subgroup analyses to define the best candidates.

Keywords: upper tract, urothelial carcinoma, high risk, endoscopic, oncologic outcomes

Introduction

Owing to the refinement of endoscopic armamentarium, indications of renal sparing surgery have been progressively expanded over time and is now recommended[1] as a primary treatment option for patients with low-risk upper tract urothelial carcinoma (UTUC) because of excellent long-term oncologic outcomes.[2] Radical nephroureterectomy (RNU) with bladder cuff excision remains the gold standard for the treatment of nonmetastatic high-risk UTUC.[1] However, many patients outside of the low-risk criteria may possess low absolute risks of distant progression.

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Several large-scale retrospective cohorts based on RNU specimens have attempted to refine patient selection for an endoscopic approach, but they are limited by the use of a surrogate endpoint (i.e., ≥pT2 and/or N+ tumors), which limits the generalizability of the results since redirection of patients to RNU favored selection of aggressive disease.[3,4] To date, there is a lack of long-term data on endoscopic treatment in patients with high-risk UTUC. Herein, we hypothesized that careful selection of high-risk patients undergoing an endoscopic approach could result in acceptable oncologic outcomes, as compared with those achieved after radical treatment in the same risk-category population.

Methods

Patients with high-risk UTUC managed endoscopically between 2015 and 2021 were retrospectively identified from a prospectively maintained single academic institution database (IRB approval: FP2014/17). High-risk disease was defined according to the European Association of Urology (EAU) criteria[1] by the presence of any of the following factors: multifocal disease, tumor size ≥20 mm, high-grade cytology, high-grade ureteroscopy (URS) biopsy, local invasion on CT, hydronephrosis, previous radical cystectomy for high-grade bladder cancer, and variant histology.

Elective and imperative indications for endoscopic treatment were considered. Imperative indications included solitary kidney, severe chronic kidney disease (estimated glomerular filtration rate ≤30 mL/[min·m^2]), bilateral disease, contraindication to RNU, and genetic predisposition. Regarding elective indications, we offered endoscopic treatment of high-risk tumors if the following criteria were met: 1/complete surgical removal was achieved; 2/no invasive appearance of the tumor on CT scan; and 3/no histological variant. The final decision was routinely validated at a multidisciplinary meeting.

Our endoscopic technique has been described previously.[5] In brief, careful exploration of the upper tract is systematically undertaken using a semirigid and then a digital flexible URS (Flex XC; Karl Storz, Germany, URF-V; Olympus, Japan) with the aid of image enhancement modalities (Image1S; Karl Storz, Narrow Band Imaging; Olympus). A 10F to 12F ureteral access sheath is then inserted with its upper end under the target lesion or the ureter pelvis junction.

According to lesion size and morphology, different biopsy devices were used, including 3F ureteroscopic forceps, 6F back-loading forceps (BIGopsy; Cook Medical), and a 2.2F Nitinol basket (N-Circle; Cook Medical). For tumors that could not be safely treated by pure retrograde access, a combined percutaneous approach was performed. Tumor ablation was performed with thulium–YAG laser (standard setting: 10–15 W). For large lesions, we used the combination of thulium and holmium–YAG lasers (standard setting: 0.8–1.2 J and 8–12 Hz), which allows removing any necrotic layer developed by the photothermic coagulative effect of thulium laser and so to show up any residual tumor tissue.[6]

An example of the surgical technique is provided in Supplementary Video S1. At the end of the procedure, the ureteral access sheath was removed under endoscopic visual control to assess whether any ureteral injuries occurred, and a final retrograde pyelography was performed to detect any possible leakage. A 6F to 7F Double-J or Mono-J ureteral stent was placed and maintained for a variable timeframe according to the findings of the pyelography. Postoperative complications were graded according to Clavien–Dindo classification.

Surgical specimens were evaluated by a dedicated genitourinary pathologist (F.A.). All patients underwent strict follow-up including CT scan, flexible cystoscopy, and urine cytology every 6 months. Kaplan–Meier curves were used to illustrate oncologic outcomes after treatment: UTUC recurrence-free survival, bladder recurrence-free survival, RNU-free survival, metastasis-free survival (MFS), cancer-specific survival (CSS), and overall survival (OS). UTUC recurrence-free survival included only ipsilateral recurrence. The decision to perform RNU was usually based on grade progression, invasive aspect on CT scan, recurrence unfit for endoscopic treatment, or functional loss of the renal unit. Oncologic outcomes were compared between elective and imperative indications with the log-rank test. All statistical

Table 1. Baseline Characteristics

Total no. of patients	60
Age, years	74 (65–81)
Gender	
Male	50 (83)
Female	10 (17)
Age-adjusted Charlson comorbidity index	6 (4–7)
Smoking status	
Current smoker	13 (22)
Ex-smoker	25 (41)
Never smoker	22 (37)
Chronic kidney disease (eGFR ≤60/mL/m^2)	30 (50)
History of urothelial carcinoma	
Previous UTUC	19 (32)
Previous NMIBC	30 (50)
Previous MIBC	6 (10)
Hydronephrosis	18 (30)
Tumor number	
Single	37 (62)
Multiple	23 (38)
Tumor localization	
Ureter	30 (50)
Kidney	26 (43)
Both	4 (7)
Maximum tumor size (mm)	
<20	26 (43)
≥20	26 (43)
Not reported	8 (14)
Cytology	
Not performed	25 (42)
Not valuable	2 (3)
Negative	15 (25)
Positive	18 (30)
Biopsy grade	
Not performed	3 (5)
Not valuable	9 (15)
Low grade	30 (50)
High grade	18 (30)
Carcinoma *in situ*	3 (5)

Data are presented as median (interquartile range) or number (percentage).

eGFR = estimated glomerular filtration rate; MIBC = muscle-invasive bladder cancer; NMIBC = nonmuscle invasive bladder cancer; UTUC = upper tract urothelial carcinoma.

Table 2. Indications of Conservative Treatment

Elective indication	*31 (52)*
Imperative indication	
Severe CKD (eGFR ≤30 mL/[min·m^2])	6 (10)
Previous contralateral UTUC	5 (8)
Unfit for RNU	5 (8)
Lynch syndrome	2 (3)
Solitary kidney	11 (19)

Data are presented as numbers and percentages.
CKD = chronic kidney disease.

analyses were performed using R software version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 60 patients with high-risk UTUC met our inclusion criteria. Baseline characteristics are summarized in Table 1. The indication for endoscopic management (Table 2) was considered imperative in 29 patients (48%) as a result of the presence of a single kidney in 11 patients (19%), severe chronic kidney disease in 6 patients (10%), bilateral disease in 5 patients (8%), contraindication to RNU in 5 patients (8%), and Lynch syndrome in 2 patients (3%). The remaining indications were elective ($n = 31$; 52%). Six (10%) patients experienced minor complications (Clavien–Dindo 2) and two (3.3%) major complications (Clavien–Dindo 3a and 3b) after treatment. The median follow-up in patients without any event was 36 months.

Figure 1 shows the Kaplan–Meier survival curves and Table 3 gives the estimated survival. Overall, three patients developed metastases over follow-up and 16 patients died, including 5 patients with disease-specific mortality. The estimated OS, CSS, and MFS were 94% (89–100), 98% (94–100), and 98% (94–100), respectively at 1 year, 75% (63–89), 95% (88–100), and 94% (87–100), respectively, at 3 years, and 57% (41–79), 75% (57–99), and 86% (71–100), respectively, at 5 years. A total of 18 patients experienced 26 upper tract recurrences over follow-up, most of them were treated endoscopically. The estimated UTUC recurrence-free survival was 83% (74–94) at 1 year, 70% (58–84) at 3 years, and 56% (40–76) at 5 years.

A total of nine patients proceeded to RNU over follow-up. The estimated RNU-free survival was 87% (79–96) at 1 year, 84% (75–95) at 3 years, and 81% (70–93) at 5 years. Finally, a total of 12 patients experienced bladder recurrence, all of

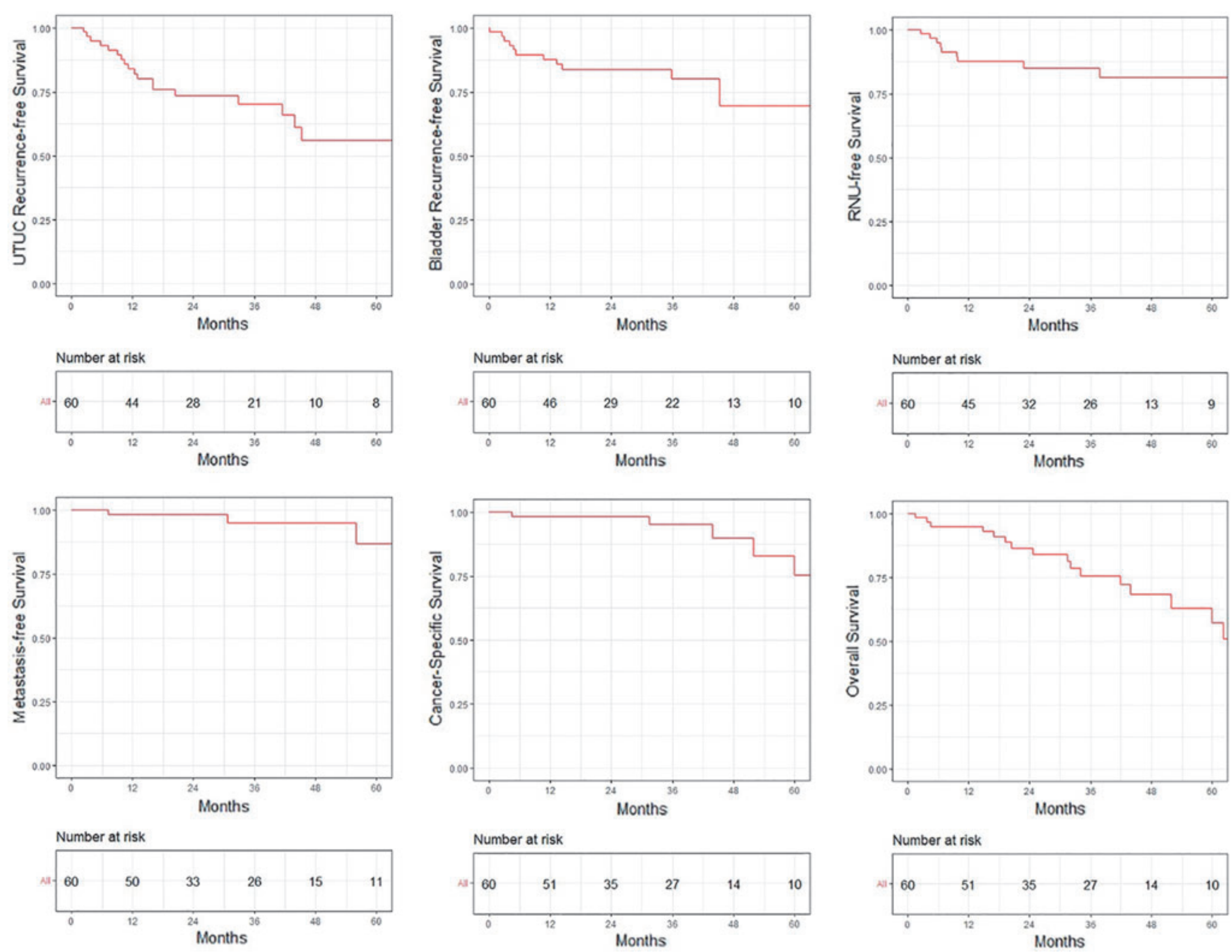

FIG. 1. Kaplan–Meier curves. RNU = radical nephroureterectomy; UTUC = upper tract urothelial carcinoma. Color graphics are available online.

Table 3. Oncologic Outcomes

	Prob 1 year (95% CI)	Prob 3 years (95% CI)	Prob 5 years (95% CI)
UTUC recurrence-free survival	83 (74–94)	70 (58–84)	56 (40–76)
Bladder recurrence-free survival	87 (79–96)	80 (69–92)	69 (54–88)
RNU-free survival	87 (79–96)	84 (75–95)	81 (70–93)
Metastasis-free survival	98 (94–100)	94 (87–100)	86 (71–100)
Cancer-specific survival	98 (94–100)	95 (88–100)	75 (57–99)
Overall survival	94 (89–100)	75 (63–89)	57 (41–79)

Data are presented as median (interquartile range) or number (percentage).
CI = confidence interval; Prob = probability; RNU = radical nephroureterectomy.

whom were classified as nonmuscle-invasive bladder cancer. The estimated bladder recurrence-free survival was 87% (79–96) at 1 year, 80% (69–92) at 3 years, and 69% (54–88) at 5 years. All oncologic outcomes were similar between patients with elective and imperative indications (Table 4, all log-rank *p*-values >0.05).

Discussion

Endoscopic management of UTUC is an effective treatment in patients with low-risk disease. Conversely, patients with high-risk features and normal contralateral kidney are usually submitted to radical treatment since poorer oncologic outcomes are expected in high-grade, multifocal, or large tumors. Nevertheless, we hypothesized that not all high-risk patients are equal and that some of them could benefit from conservative endoscopic treatment. In this study, we provide sound evidence that endoscopic conservative management offers effective oncologic control with an acceptable CSS when high-risk patients with UTUC are properly selected.

In a recent systematic review and meta-analysis, Kawada et al. reported similar survival outcomes between RNU and endoscopic treatment in UTUC.[7] Although the majority of included patients had low-risk disease, up to 24% of endoscopically treated patients had multifocal tumors, and up to 68% had high-grade tumors. Similarly, despite all the patients included in our study being defined as having high-risk disease, only 30%, 38%, and 43% of patients had high-grade, multifocal, and large disease (>2 cm), respectively, and these patients achieved comparable oncologic outcomes with that reported in the literature after RNU.

According to these findings, it is clear that although the EAU risk classification helps in identifying those patients with more aggressive clinical behavior to be submitted to prompt radical treatment, a non-negligible portion of high-risk patients is possibly being overtreated.

Table 4. Oncologic Outcomes in Patients with Elective *vs* Imperative Indication

	HR	95% CI	p
UTUC recurrence-free survival	2.68	0.95–7.53	0.06
Bladder recurrence-free survival	0.55	0.17–1.77	0.3
Overall survival	0.43	0.15–1.19	0.1

Data are presented as median (interquartile range) or number (percentage).
HR = hazard ratio.

Thus, our results corroborate that a subset of patients with high-risk UTUC may benefit from conservative treatment and that UTUC risk categories should be also refined. In this regard, the selection of high-risk patients for endoscopic management remains a matter of debate. The success of endoscopic management depends on the ability to identify preoperative features that distinguish patients with a low risk of progression who can be managed appropriately with endoscopic kidney-sparing surgery from those who will require definitive and radical treatment.[3,8]

Several large-scale retrospective studies have attempted to change the two-level currently recommended classification of UTUC.[3,4] However, the exclusion of patients with UTUC who received a primary kidney-sparing surgery treatment partly limits the strength of their findings. Although not comparative, our study also provides some useful information regarding the selection criteria for endoscopic treatment in high-risk UTUC. Excluding patients with high-burden tumors, invasive CT appearance, and/or variant histology, we have shown that similar results can be obtained in selected high-risk patients compared with previously published data in low-risk patients (including some high-risk patients).[9]

Further large-scale studies are needed to refine the criteria for selecting high-risk patients for endoscopic treatment, ideally on a prospective cohort of patients treated with endoscopy. In these future studies, an interesting debate will concern the ideal criteria that should be used to define success/failure of endoscopic management in high-risk UTUC. In our opinion, RNU should not be considered a primary endpoint, as delayed RNU still has the advantage of delaying RNU-related side effects, such as impaired renal function and cardiovascular events.[10] MFS and CSS appear to be more robust clinical criteria and should ideally be incorporated into future studies.

Finally, the benefit of endoscopic treatment is mainly associated with a lower risk of impaired renal function and long-term cardiovascular events.[11] However, when discussing such alternative strategies with high-risk UTUC patients, the potential benefit of preserving renal function must be weighed against the disadvantages of endoscopic management, such as rigorous long-term monitoring and the burdensome nature of repeated procedures that can have a physical and psychologic impact on individuals.[12]

Some limitations should be acknowledged. First, the main limitation of this study lies in its retrospective design. Second, a selection bias is recognized as endoscopic treatment was offered to selected high-risk patients without an invasive aspect on CT scan and in whom complete endoscopic treatment was considered feasible. Only a randomized trial will overcome this selection bias, which also affects all large retrospective studies conducted on RNU, as radically treated patients are more likely to harbor aggressive disease.[3,4] Finally, all procedures were conducted in an expert tertiary center with its own endoscopic technique, and the results are not generalizable to all institutions.

Conclusions

In conclusion, we report the first large series of endoscopic treatment in patients with high-risk UTUC, arguing that promising oncologic outcomes can be achieved in properly selected candidates. We encourage multi-institutional collaborative work as a large cohort of high-risk patients treated endoscopically may allow subgroup analyses to define the best candidates.

Authors' Contributions

Conception and design of study were contributed by M.B., An.T., A.G., and A.B. Acquisition of data was done by P.V., A.V., G.B., Al.T., J.A., and P.I. Analysis and/or interpretation of data were carried out by M.B., An.T., A.G., and A.B. Drafting the article was by M.B. Revising the article critically for important intellectual content was done by J.M.G., J.H., O.R.F., F.S., F.A., J.P., and A.B. Statistical analysis was taken care by M.B. Supervision was by A.B.

Data Availability Statement

Data are available upon reasonable request from the corresponding author.

Author Disclosure Statement

The authors have nothing to disclose.

Funding Information

The study was not funded.

Supplementary Material

Supplementary Video S1

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Abbreviations Used

CI = confidence interval
CKD = chronic kidney disease
CSS = cancer-specific survival
CT = computed tomography
eGFR = estimated glomerular filtration rate
HR = hazard ratio
MFS = metastasis-free survival
MIBC = muscle-invasive bladder cancer
NMIBC = nonmuscle invasive bladder cancer
OS = overall survival
RNU = radical nephroureterectomy
UTUC = upper tract urothelial carcinoma

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Robotic Partial *vs* Radical Nephrectomy for Clinical T3a Tumors: A Narrative Review

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Abstract

Introduction: T3a renal masses include a diverse group of tumors that invade the perirenal and/or sinus fat, pelvicaliceal system, or renal vein. The majority of cT3a renal masses represent renal cell carcinoma (RCC) and have historically been treated with radical nephrectomy (RN) given their aggressive nature. With the adoption of minimally invasive approaches to renal surgery, the combination of improved observation, pneumoperitoneum, and robotic articulation has allowed urologists to consider partial nephrectomy (PN) for more complex tumors. Herein, we review the existing literature regarding robot-assisted PN (RAPN) and robot-assisted RN (RARN) in the management of T3a renal masses.
Methods: A literature search was performed using PubMed for articles evaluating the role of RARN and RAPN for T3a renal masses. Search parameters were limited to English language studies. Applicable studies were abstracted and included in this narrative review.
Results: T3a RCC caused by renal sinus fat or venous involvement is associated with $\sim$50% lower cancer-specific survival than those with perinephric fat invasion alone. CT and MRI can both be used to stage cT3a tumors, however, MRI is more accurate when assessing venous involvement. Upstaging to pT3a RCC during RAPN does not confer a worse prognosis than pT3a tumors treated with RARN; however, patients who undergo RAPN for T3a RCC with venous involvement have relatively higher rates of recurrence and metastasis. Intraoperative tools including drop-in ultrasound, near-infrared fluorescence, and 3D virtual models improve the ability to perform RAPN for T3a tumors. In well-selected cases, warm ischemia times remain reasonable.
Conclusions: cT3a renal masses represent a diverse group of tumors. Depending on substratification of cT3a, RARN or RAPN can be employed for treatment of such masses.

Keywords: renal cancer, robotics, partial nephrectomy, renal mass, T3 renal cell carcinoma, radical nephrectomy

Introduction

Renal masses comprise a diverse group of tumors ranging from benign tumors to aggressive malignancies. The majority of renal masses will be malignant, even at small sizes, with clear cell histology analysis being the most common type. When intervention is indicated, the management of localized renal cell carcinoma (RCC) is predominantly surgical, either through partial nephrectomy (PN) or through radical nephrectomy (RN). In the case of small renal masses, PN is strongly preferred given excellent oncologic outcomes with the added benefit of nephron preservation.[1,2]

Although there are many considerations in how to perform PN including modality (open, laparoscopic, and robot-assisted) and approach (transperitoneal and retroperitoneal), robot-assisted partial nephrectomy (RAPN) is now the most common surgical approach in the United States.[3]

Although clinical T1 (cT1) and cT2 RCC, by definition, are only differentiated by size, cT3 RCC comprises a more heterogeneous group of renal masses. Although organ-

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confined RCC carries a 5-year cancer-specific survival (CSS) of up to 90% (cT1–T2), this decreases to 75% to 80% for tumors involving perinephric fat[4] and, even worse, approaches 50% with venous involvement.[5] As such, most cT3 renal masses have been classically managed with RN. Oncologic outcomes, however, must be carefully weighed against functional outcomes, as RN increases the risk of chronic kidney disease (CKD) and may exclude some patients from necessary systemic therapy.

In select patients with T3a renal masses and pre-existing proteinuria or CKD, or an anatomic or functional solitary kidney, PN is more imperative and should be considered. RAPN of these more complex tumors can be challenging and associated with a higher risk of perioperative complications.[6] In this article, we aim to review the existing literature regarding the use of RAPN and robot-assisted radical nephrectomy (RARN) in the treatment of cT3a renal masses.

Staging of cT3a Renal Tumors

cT3a renal masses are defined by invasion into the perinephric fat, renal sinus fat, pelvicaliceal system, and/or renal veinous system (Fig. 1). In earlier classification systems, tumors with direction extension into the ipsilateral adrenal gland were also considered cT3a renal tumors, but this was later changed to T4 disease in the seventh edition American Joint Committee on Cancer TNM Staging System given significantly worse oncologic outcomes in this population.[7] This underscores the critical nature of accurate clinical staging given the impact it has on surgical decision making.

Although all patients with solid renal masses require multiphase cross-sectional imaging, either with CT or with MRI, there are some differences in the diagnostic accuracy of CT and MRI when assessing T3a tumors, specifically. The specificity and sensitivity of CT in detecting perinephric fat invasion are 32% to 96% and 85% to 93%, respectively.[8] MRI is slightly more sensitive in detecting perinephric invasion than CT because of a more visible capsule on fat-subtraction images, but similarly lacks specificity.[9] CT has a sensitivity of 71% to 88% in detecting renal sinus fat invasion, whereas its ability to detect renal vein involvement ranges from 59% to 69%.[10] Large right-sided tumors can distort the short right renal vein and make clear delineation of the renal vein–vena cava interface difficult on CT. Conversely, MRI offers superior soft tissue resolution using T2-weighted and diffusion-weighted imaging sequences, which improves the sensitivity to 64% to 89% in detecting tumor thrombi.[11] MRI is also better able to differentiate between bland and tumor thrombus. For these reasons, it is generally prudent to obtain an MRI when there is suspicion for renal vein invasion.

Oncologic Outcomes Based on Subclassification of T3a Renal Tumors

In contrast to the size-driven designation of T1 and T2 RCC, T3 classification is based on anatomic extension alone, as mentioned above. Yet, there is still evidence to support tumor size as an important prognostic factor in T3a disease. Patients with resected T3a RCC ≤7 cm have a 5-year disease-specific survival (DSS) of 63%, whereas DSS decreases to only 46% when tumor size is >7 cm.[12] In patients with T3a RCC secondary to fat invasion only, each 1 cm increase in tumor size is associated with a 9% decrease in DSS.[12]

In light of the homogeneous categorization, quite heterogeneous outcomes are noted among the various cT3a subtypes. Patients with sinus fat involvement are at 1.47 times higher risk of RCC-related death than those with perinephric fat invasion alone,[13] which may be because of increased access to the venous system. Venous involvement was historically thought to be a poor prognosticator, with main renal vein involvement carrying a worse prognosis than segmental vein invasion alone.[14] However, recent reports have demonstrated acceptable outcomes assuming the primary tumor is confined to the kidney and negative surgical margins are obtained.[5]

This supports other work that has demonstrated that the metastatic potential of RCC with tumor thrombi is quite heterogeneous and invasion not universally driven by the most aggressive clone.[15] The metastatic potential of RCC remains incompletely understood and further research may provide insight into subpopulations that may derive maximal benefit from RAPN as compared with RARN. Unsurprisingly, T3a tumors with multiple patterns of extension (i.e., renal vein thrombus and perinephric fat invasion) are associated with an increased risk of disease progression and

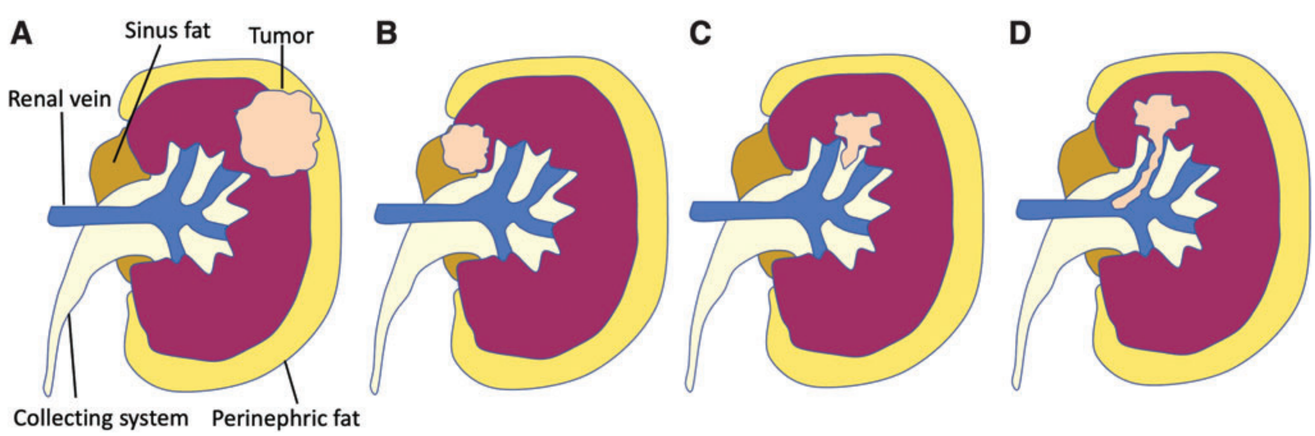

FIG. 1. Subclassification of T3a renal tumors. **(A)** Perinephric fat invasion, **(B)** renal sinus fat invasion, **(C)** collecting system invasion, **(D)** segmental or main renal vein invasion. Color images are available online.

cancer-related death after surgery, and, therefore, should be managed more aggressively.[16]

Given the diversity of cT3a renal masses, it is critical that physicians consider anatomic patterns of extension and the ability to achieve a negative margin when counseling patients on surgical options (RAPN or RARN).

Oncologic Outcomes After RN and PN for cT3a Tumors

Open RN has traditionally been the preferred treatment for most patients with cT3 renal masses with an average 5-year CSS of 80% in a large review of >18,000 patients with T3a, T3b, and T3c tumors.[17] Beginning in the 1990s, laparoscopic radical nephrectomy (LRN) was adopted as an acceptable alternative to open RN, demonstrating equivalent oncologic outcomes for T3 RCC.[18] Although there was some initial concern that minimally invasive RN could result in port site metastases, these are quite rare and felt to be an indicator of overall disease progression rather than an isolated result of surgical technique.[19]

The use of RARN in the United States has been increasing 11.8% annually since 2004, whereas the use of LRN has been decreasing 5.5% annually.[20] In a study comparing 941 patients with ≥cT2 renal masses undergoing RARN or LRN, of whom 18% were cT3 specifically, RARN and LRN were associated with equivalent overall survival (OS) and recurrence-free survival (RFS). More patients who underwent RARN *vs* LRN had hilar tumors (28% *vs* 10%) and ≥cT3 tumors (21% *vs* 16%), suggesting that surgeons prefer the robotic approach for more complex and high-risk tumors.[20]

Much of our knowledge regarding the oncologic efficacy of PN for T3a RCC stems from patients with pathologic upstaging from T1/T2 to T3, which ranges from 6% to 13%.[21,22] Factors associated with upstaging to T3a including patient age, tumor size, central tumor location, and Fuhrman grade.[23] OS is 13% to 26% lower in patients who have cT3a renal tumors compared with those who are upstaged from cT1 to pT3a renal tumors at the time of surgery,[24] likely because of the grossly more advanced nature of disease visible on preoperative imaging.

Compared with RN, PN does not jeopardize cancer control in those with upstaged pT3a RCC.[25–28] In fact, two studies have suggested that PN may confer an RFS advantage.[26,27] This may be because of selection bias or increased opportunity to receive adjuvant therapy caused by preserved renal function. Although the data support the safety of RAPN in T3a tumors, it should be interpreted with caution as tumor size, location, type of T3a disease (vascular *vs* sinus invasion *vs* perinephric invasion *vs* multiple), and surgeon comfort/ability should drive surgical decision making. Ultimately, complete resection with negative margins is the most important outcome to achieve.

Several studies specifically assessing the role of RAPN for T3a tumors have been published (Table 1).[29–34] A large single-institution retrospective series compared 140 patients who underwent RAPN or RN in a matched-control manner.[30] At a median follow-up duration of 20 months, there was no difference in OS, CSS, or RFS, and the only factor associated with increased mortality on multivariable analysis was ≥2 aggressive tumor features (positive margin, necrosis, lymphovascular invasion, Grade ≥3, or presence of sarcomatoid elements). Another study retrospectively compared patients who underwent RAPN or open PN for pT2 or pT3 RCC.

Of the 35 patients reviewed, 26 had pT3a renal tumors.[33] There was no difference in the positive margin rate or local RFS between RAPN and open PN, though ischemia time, complication rates, and length of stay all favored RAPN. Yim et al. recently published a multi-institutional study from the Robotic Surgery for Large Renal Mass (ROSULA) collaborative group of 157 patients undergoing RAPN for cT3a renal masses.[32]

In this group, the median tumor size was 7 cm and 66% of tumors were cT3a because of extension into the renal sinus or perinephric fat. Ninety-six percent of patients achieved negative margins, and 5-year RFS, CSS, and OS rates were 82%, 93%, and 91%, respectively. These survival rates are similar to those in studies evaluating upstaged pT3a RCC, and suggest that with adequate surgical planning, outcomes are acceptable despite clinically evident aggressive growth patterns of cT3a tumors.

Given the diversity of cT3a tumors, researchers have investigated the role of RAPN specifically in patients with T3a tumors secondary to venous involvement. Abaza and colleagues first reported on RAPN for T3a tumors with venous involvement in 2013.[29] This included three patients with only T3a disease and one patient who was pT4 because of liver involvement. Despite negative margins in all patients, two of the four patients developed metastatic disease within 6 months. A more recent study by Morgan and colleagues evaluated 45 patients who underwent RAPN for pT3a tumors secondary to venous involvement, of whom only 25% had suspected T3a disease based on preoperative imaging.[34]

The positive margin rate was 6.7% and after a median follow-up duration of 29 months, two patients developed a local recurrence and four developed distant metastases. Two years local RFS and metastasis-free survival was 95.4% and 95.3%, respectively. The relatively high rate of both local and distant recurrence in patients with pT3a RCC secondary to renal vein involvement undergoing PN is not surprising given the potential for hematogenous spread.

Renal Function Preservation After PN and RN for T3a Tumors

The implications of developing CKD are broad and severe. Risk factors for CKD, such as hypertension and diabetes, are common in patients with RCC, and thus, many patients before intervention already have some level of nephron impairment. Preoperative CKD stage 3 and above has been shown to be an independent risk factor for survival in patients undergoing renal surgery.[35] Nevertheless, although several retrospective studies have shown a lower incidence of CKD and overall mortality in patients with renal masses undergoing PN compared with RN, the landmark EORTC 30904 trial, in which patients with T1–T2 tumors ≤5 cm were prospectively randomized to RN or PN, showed that 10-year OS was 5% higher in the RN group and cardiovascular deaths were also less common.[36–38]

Although the EORTC study had multiple limitations, including low accrual, no information on the quality/extent of parenchyma resected in the PN group, and high rate of crossover (15% planned PN received RN), we did learn that PN reduced the incidence of moderate CKD (stage 3) but had

Table 1. Reports of Robot-Assisted Partial Nephrectomy for cT3a Masses Over the Past 10 Years (Since 2012)

Reference	*Total number/ number with cT3a*	*Pathologic staging details*	*Treatment*	*Tumor size*	*Survival/recurrence*	*Change in renal function*	*Follow-up, months*
Abaza and Angell (2013)	4/3	4 (100%) pT3a (all with venous involvement)	4 (100%) underwent RAPN	7.8 cm[a]	2 (50%) developed metastases	ΔeGFR 6 months postoperatively: -21.5 mL/min/m^2	9.4[b]
Andrade et al. (2017)[30]	140/NR	140 (100%) pT3a	70 (50%) underwent RAPN 70 (50%) underwent RN	3.8 cm[b] (RAPN) 4.7[b] (RN)	3-years OS 90% (RAPN) *vs* 84% (RN), $p=0.4$ 3-years CSS 94% (RAPN) *vs* 95% (RN), $p=0.8$ 3-years RFS 95% (RAPN) *vs* 100% (RN), $p=0.03$	Renal preservation 86% (RAPN) *vs* 70% RN, $p<0.001$	20[b]
Marra et al. (2018)[31]	2549/NR	821 (3.2%) pT3a	42 (1.6%) underwent PN 2507 (98.4%) underwent RN	5.3 cm[a] (PN) 7.3 cm[a] (RN)	5-years OS 57% (PN) *vs* 46% (RN), $p=0.19$ 5-years CSS 71% (PN) *vs* 52% (RN), $p=0.02$[c]	ΔeGFR 9 months postoperatively: -27% (PN) *vs* -41% (RN), $p=0.13$	27.3[b]
Yim et al. (2021)[32]	157/157	157 (100%) cT3a	157 (100%) underwent RAPN	7.0 cm[b]	5-years OS 91.3% 5-years CSS 92.3% 5-years RFS 82.1%	ΔeGFR 12 months postoperatively: -7 mL/min/m^2	26[b]
Beksac et al. (2022)[33]	35/NR	26 (74%) pT3a	20 (57.1%) underwent RAPN 15 (42.9%) underwent OPN	5.8 cm[b] (RAPN) 6.0 cm[b] (OPN)	3 (8.6%) developed local recurrence 4 (11.4%) developed metastases	79% eGFR preservation at 1 year in RAPN group	21.1[b]
Morgan et al. (2022)[34]	45/11	43 (100%) pT3a (all with venous involvement)	45 (100%) underwent RAPN	4.3 cm[a]	2 years local RFS 95.4% 2 years MFS 95.3%	ΔeGFR 25 months postoperatively: -6.6 mL/min per m^2	28.5[b]

[a]Values reported as mean.
[b]Values reported as median.
[c]Results not significant after matching.
CSS = cancer-specific survival; eGFR = estimated glomerular filtration rate; MFS = metastasis-free survival; NR = not recorded; OPN = open partial nephrectomy; OS = overall survival; PN = partial nephrectomy; RAPN = robot-assisted partial nephrectomy; RFS = recurrence-free survival; RN = radical nephrectomy.

similar rates of severe CKD (stages 4 and 5) as RN. Taken together, although most healthy patients with a functional contralateral kidney will have acceptable renal function after RN, nephron-sparing approaches should be considered when feasible and oncologically sound for those with pre-existing CKD or risk factors for development of CKD.

With that said, CKD caused by surgical removal of nephrons has been shown to be different than CKD caused by medical causes and is associated with less CKD progression and improved survival.[39] This conceptually makes sense given that surgical CKD results in fewer but functional filtration units as compared with more numerous, but diseased, filtration units. A recent meta-analysis assessed renal functional outcomes in T3a tumors and found that renal function, as assessed through estimated glomerular filtration rate (eGFR), was improved in patients undergoing PN for T3a renal tumors as compared with RN (weight mean difference 12.48 mL/min).[40]

In patients wherein there is concern for significant postoperative renal dysfunction, validated equations can be used to predict postnephrectomy GFR.[41] In the case of asymmetric kidneys on preoperative cross-sectional imaging, a renogram may be useful in determining differential function. Patients with a high risk of CKD progression after surgery, as evidenced by a preoperative GFR <45, proteinuria, CKD in the setting of diabetes, or if postoperative GFR is expected to be <30, should be referred to nephrology preoperatively to assess risk of CKD progression and address any modifiable risk factors.[42]

Surgical determinants of renal function after PN include the number of nephrons spared (maximal parenchymal preservation) and the duration of warm ischemia time (WIT). The use of enucleation for complex tumors has been associated with greater renal function preservation compared with a wide margin resection.[43] Furthermore, more peripherally located and lower complexity tumors have also been associated with improved postoperative renal function.[44] This may stem from the potential for ischemia-related parenchymal loss as part of the renorrhaphy.

With regard to ischemia, WIT is recommended to be limited to 25 to 30 minutes if possible.[45] Although performing an off-clamp or selectively clamped RAPN is possible in certain situations, T3a tumors are often centrally located and may be best excised under complete ischemia. This allows for a relatively bloodless field and optimized observation during resection (optimizing the potential for negative margins), as well as guards against the possibility of tumor thrombus embolism.

Although laparoscopic PN for central tumors is associated with a longer WIT than for peripheral tumors, a multicenter study of 157 RAPNs for cT3a renal masses, of which 22% had venous involvement, reported a median WIT of 19 minutes.[32] There was only a 7 mL/min per 1.72 m^2 median decrease in eGFR, and 55% of patients had a ≥90% preservation of eGFR. Additional studies on RAPN for T3a tumors secondary to venous invasion report WITs of 9 to 30 minutes.[29,34] These data support the notion that RAPN for T3a tumors can be performed without prolonged ischemia or significant postoperative compromise of renal function.

Technical Considerations of RAPN for T3a Tumors

RAPN for complex T3a renal masses can be challenging and surgeons should be aware of the techniques and tools available when attempting such cases. First and foremost, a thorough review of preoperative imaging is essential to understanding the anatomic relationship of the tumor and other structures. Tumors can be approached transperitoneally or retroperitoneally based on patient and tumor factors and surgeon preference. A transperitoneal approach is likely more familiar to most surgeons and allows increased working space and better access to the renal vein for tumors with venous involvement. Multiple adjunctive tools, including intraoperative ultrasound with small drop-in probes, virtual 3D anatomic models, near-infrared fluorescence (NIRF), and TilePro™,[46–49] can better facilitate RAPN for complex tumors.

Early and frequent use of intraoperative ultrasound is critical to delineate the location of the tumor and characterize the tumor's interface with perinephric fat, renal sinus fat, and renal vasculature. Both laparoscopic and drop-in robotic ultrasound probes exist, however, the smaller drop-in probes allow greater rotational mobility and improved surgeon autonomy.[46] When there is concern for perinephric fat involvement on preoperative imaging, ultrasound is helpful in determining the tumor location before incising Gerota's fascia to leave some of the perinephric fat on top of the tumor in the case of RAPN.

Intraoperative ultrasound is also useful in identifying the extent of tumor thrombus in the renal vein either for clamping in the case of RAPN or for ligation in the case of RARN. The operating room team should be well versed in using the ultrasound machine, as often, the overall gain or time-gain compensation need to be adjusted to better observe deeper structures such as renal sinus fat.

There is an increasing interest in the use of 3D virtual models (VMs) in augmenting intraoperative ultrasound, improving preoperative surgical planning/counseling, and assisting in intraoperative navigation and decision making. Three-dimensional VMs utilize the preoperative CT or MRI to generate a 3D virtual reconstruction of the kidney, tumor, kidney vasculature, and collecting system. The VM can then be viewed and manipulated by the surgeon at the console intraoperatively and the transparency of the anatomic structures can be adjusted to provide cognitive fusion.

Surgeons report better spatial orientation and understanding of the anatomy when using a 3D VM, and it impacts the decision to perform an RAPN or RARN in 20% of cases.[47] A randomized controlled trial showed that the use of an intraoperative 3D VM decreased intraoperative blood loss, but not operative or clamp times when performing RAPN.[50] The utility of 3D VMs in cT3a tumors remains to be defined.

NIRF utilizes an NIR camera specific to a wavelength of 700 to 1000 nm and a fluorescent dye such as indocyanine green (ICG) that allows preferential fluorescence of well-vascularized structures. NIRF can be used to confirm complete ischemia if the main renal artery is clamped or to guide selective clamping by confirming that the tumor to be excised is not fed by any other arterial branches aside from the one being clamped.[51] Although many cT3a tumors are centrally located and not typically amenable to selective clamping, NIRF may prove useful in intraoperative assessment of margin status during resection.

As ICG binds the transmembrane protein bilitranslocase, which is expressed in normal proximal convoluted tubules but not malignant tissue, normal renal parenchyma fluoresces under NIR, but malignant tissue does not.[52] Differential fluorescence is noted in 90% of RCC and 72% of oncocytomas.[53] To use differential fluorescence for this purpose, 0.25 to 0.5 mL of ICG is administered before clamping the artery. During resection, one can use NIRF to help confirm that the tumor margin fluoresces green, and, therefore, represents nonmalignant renal parenchyma. In one single-surgeon series of 361 RAPNs, the use of NIRF resulted in a 0.33% positive margin rate.[53] When using NIRF to confirm ischemia, a larger dose of ICG (1.5–2.5 mL) is administered after clamping the artery.

RAPN for T3a tumors because of venous involvement provides a unique challenge given the vascular involvement. Small tumor thrombi in intraparenchymal veins can often simply be excised with the tumor and the vein closed as part of the renorrhaphy. If there is invasion into a subsegmental or segmental vein, the main renal vein is dissected out to the segmental branches, and the tumor-containing vein branch is clipped, cut and oversewn, or stapled. Thrombus extending into the main renal vein necessitates a more complex resection and reconstruction.

Intraoperative ultrasound should be used to delineate the distal extend of the thrombus and the vein should be clamped distal to this point with enough space between the clamp and thrombus to allow for reconstruction. Clamping the renal vein also helps avoid a CO_2 embolism while the tumor-containing venous branch is open. When opening the main renal vein, all additional nonrenal venous branches should be controlled before opening the vein. For a left renal vein thrombus, the left adrenal and gonadal vein should be ligated or clamped to avoid blood loss during thrombectomy. In addition, the renal vein should be incised longitudinally and the tumor thrombus removed en bloc with the tumor.[29] The renal vein can then be repaired with a fine nonabsorbable monofilament suture such as polypropylene.

Conclusions

T3a renal masses represent a diverse group of tumors that should be approached on an individual basis, taking into account clinical characteristics and surgeon experience/expertise. Although MRI does not provide much benefit over CT in detecting perinephric or sinus fat invasion, it is preferred when evaluating for a tumor thrombus. Oncologic outcomes for T3a RCC treated with RAPN are acceptable provided a negative margin can be obtained, however, cT3a RCC secondary to renal vein invasion carries a higher recurrence risk. Improved stratification of these diverse tumors using clinical parameters or biomarkers will hopefully further improve our ability to counsel patients in the role of RARN and RAPN in T3a renal masses.

Authors' Contributions

T.E.S. contributed to conceptualization, methodology, investigation, data curation, writing—original draft, writing—review and editing, and project administration.

P.T.G. was involved in investigation, writing—original draft, and writing—review and editing.

C.R.T. carried out investigation, writing—original draft, and writing—review and editing.

R.L.S. was in charge of conceptualization, methodology, writing—original draft, writing—review and editing, and supervision.

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Abbreviations Used

CKD = chronic kidney disease
CSS = cancer-specific survival
CT = computed tomography
cT1 = clinical T1
DSS = disease-specific survival
eGFR = estimated glomerular filtration rate
ICG = indocyanine green
LRN = laparoscopic radical nephrectomy
MFS = metastasis-free survival
MRI = magnetic resonance imaging
NIRF = near-infrared fluorescence
NR = not recorded
OPN = open partial nephrectomy
OS = overall survival
PN = partial nephrectomy
RAPN = robot-assisted partial nephrectomy
RARN = robot-assisted radical nephrectomy
RCC = renal cell carcinoma
RFS = recurrence-free survival
RN = radical nephrectomy
VM = virtual model
WIT = warm ischemia time

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Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique in Right Nephrectomy and Inferior Vena Cava Tumor Thrombectomy: A Novel Surgical Technique and Long-Term Outcomes from a Large Chinese Center

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Abstract

Purpose: To explore the safety and effectiveness of the Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique (PREP-IT) in laparoscopic radical nephrectomy (LRN) and inferior vena cave (IVC) tumor thrombectomy for right renal-cell carcinoma (RCC) with level Mayo I to III venous tumor thrombus (VTT).
Patients and Methods: From May 2015 to September 2020, 92 patients with right RCC and Mayo I to III VTT were retrospectively reviewed, including 57 patients who underwent retroperitoneal LRN and IVC thrombectomy using PREP-IT, and 35 patients who underwent open surgery. PREP-IT refers to dissecting the retroperitoneum and temporarily placing the right kidney into the abdominal cavity to enlarge the retroperitoneal workspace for a safer and faster IVC operation.
Results: Compared with the open surgery group, the PREP-IT group had a larger tumor diameter, while a larger proportion of Mayo I tumor thrombus and smaller maximum tumor thrombus width. Two patients (3.5%) in the PREP-IT group had a history of abdominal surgery. No conversion to open surgery or standard laparoscopic surgery occurred in PREP-IT group. Laparoscopic surgery with PREP-IT was characterized by shorter operative time, less surgical blood loss, shorter postoperative hospital stay, and lower postoperative complication rate. With a 33-month (ranges: 2–86) follow-up time period, the estimated mean overall survival time was 57.2 ± 5.3 and 58.1 ± 71.5 months in the PREP-IT group and open surgery group, respectively. Log-rank test indicated no significant difference between the two groups in terms of overall survival and cancer-specific survival.
Conclusions: The PREP-IT is relatively safe and feasible for retroperitoneal LRN with right renal tumor and IVC tumor thrombus, allowing for a large workspace and wide exposure for IVC operations.

Keywords: renal-cell carcinoma, retroperitoneal laparoscope, venous tumor thrombus, surgical technique

Introduction

Renal-cell carcinoma (RCC) is a malignant tumor characterized by a tendency to invade the venous system, accounting for 2% to 3% of all cancers. Inferior vena cava (IVC) tumor thrombus is found in 4% to 10% of locally advanced patients, which is significantly associated with the presence of clinical symptoms and poor prognosis.[1] Venous tumor thrombus (VTT) derived from the right renal tumor is more likely to extend into the IVC and therefore more commonly seen than the left one, as the right renal vein (RV) is shorter compared with the left one. Radical nephrectomy

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and IVC tumor thrombectomy are the main treatment for RCC with IVC tumor thrombus. Laparoscopic surgery offers a minimally invasive choice, with a similar therapeutic effect to open surgery.

The approach for laparoscopic radical nephrectomy (LRN) and IVC tumor thrombectomy includes the transperitoneal approach and retroperitoneal approach.[2] The former is used more widely in general, as it provides a large workspace, which is especially essential for IVC operation. However, the retroperitoneal approach has its advantages in comparison, such as reduced blood loss because of the easy access to the renal artery (RA) and lumber veins, a short time of operation, less bowel irritation, and prevention of peritoneal implantation.[3,4] Still, the narrow workspace and long learning period limit its wide application.[5]

To solve these drawbacks, we purpose the Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique (PREP-IT), aimed to enlarge the workspace in tumor thrombectomy for right RCC with IVC tumor thrombus. In brief, the PREP-IT technique refers to dissecting the retroperitoneum and temporarily placing the right kidney into the abdominal cavity to enlarge the retroperitoneal workspace for a safer and faster IVC operation. Herein, we introduced the detailed procedure of the technique and discussed its safety and efficacy based on the short-term outcomes from our center.

Patients and Methods

Patients

Three hundred thirteen patients with renal masses and VTT were adopted in our center from May 2015 to September 2020, and we retrospectively analyzed the clinical data of patients with right RCC and level I to III IVC tumor thrombus according to the Mayo classification. The exclusion criteria include (1) bilateral tumors and (2) only underwent IVC tumor thrombectomy. In total, we enrolled 57 patients who underwent laparoscopic surgery with PREP-IT and 35 who underwent open surgery. LRN with PREP-IT was performed by four experienced urologic surgeons. The indication of the PREP-IT includes right RCC with Mayo I to III IVC tumor thrombus by enhanced CT or MRI scans preoperatively.

The relative contraindications for this technique include the following: (1) a history of abdominal surgery, especially right upper abdominal surgery including gallbladder removal, pancreatectomy, and duodenectomy; (2) severe scoliosis; (3) large renal mass (generally diameter ≥10 cm); (4) fixed masses based on palpation; and (5) preoperative imaging indicating hepatic vein invasion. All the patients underwent pure retroperitoneal LRN and IVC thrombectomy, using the PREP-IT technique. Before the surgery, the benefits and risks were informed to each patient, and informed consent was signed.

An overall preoperative evaluation covers the demographics, clinical symptoms, physical examinations, laboratory tests, and radioactive examinations. Ultrasound, enhanced CT, and IVC MRI were performed to evaluate the side, size, and nature of the primary tumor, the length, width, and border of the VTT, presence of perirenal fat invasion, adrenal invasion, IVC wall invasion, lymph node metastasis, and distant metastasis (Fig. 1). Besides, the presence of bland thrombus and RV branch tumor thrombus was recorded as these manifestations are associated with long-term outcomes.[6,7] The American Society of Anesthesiologists (ASA) score was used to evaluate the tolerance of patients to anesthesia.

Intraoperative parameters including the operative time, blood loss, blood transfusion rate, and IVC blocking time were recorded. Postsurgical outcomes, including intensive care unit transfer rate, days to surgical drain removal, days to oral feeding, days to full ambulation, postoperative hospital stays, and postoperative complications, were documented. The severity of the postoperative complications was assessed with the Clavien–Dindo classification system.

The study was approved by Peking University Third Hospital Medical Science Research Ethics Committee (approval no. IRB00006761-M2022597). Informed consent was waived by our Institutional Review Board for the retrospective nature of the study.

Surgical technique

Patients' position and trocar placement. With the retroperitoneal approach, all the patients were placed in the left lateral position after induction of general anesthesia. A 2-cm longitude skin incision was made anterior to the right psoas major muscle under the 12th lib, and blunt dissection was carried down through the incision. The musculature and lumbodorsal fascia were split to enter the retroperitoneal space. The extraperitoneal fat was detached first by index finger, and then, a balloon dilator was placed for further expansion. Usually, 15 to 18 times of inflation, with 50 to 60 mL gas each time is enough. A 12 mm trocar was placed via the incision, and pneumoperitoneum was established with a maintained pressure at 12 mm Hg.

Institute of Urology, Peking University technique can be applied by placing the laparoscope and expanding the retroperitoneal space bluntly with the laparoscope body.[8] Then, another 12 mm trocar was placed in the right anterior axillary line under the rib, and an 11 mm trocar was placed above the right iliac crest. In addition, a 5 mm trocar was placed in the anterosuperior iliac spine for auxiliary.

Renal mobilization. After entering the retroperitoneum, the dorsal Gerota's fascia was incised and perirenal fat was removed. The right RA in the hilum was dissected and clipped with Hem-o-lok clips, and then cut off (Fig. 2A). We dissected along the kidney's dorsal side to mobilize the tumor-bearing IVC (Fig. 2B), followed by the ventral side (Fig. 2C). It is necessary to preserve the perirenal fat for clamping, since in the PREP-IT procedure, the kidney was taken out from the abdominal cavity via the clamped fat.

Next, a kidney-upturning technique was used in most cases to facilitate the exposure of the medial, inferior, and ventral side of the kidney, taking advantage of the upper pole suspension. First, we mobilized the inferior pole by dissecting the fascia and cutting off the right ureter (Fig. 2D), and then, upturning the kidney by lifting the inferior pole to the upper side with a vascular clamp. This technique allows for exposing the peritoneum and hilum (Fig. 2E). Moreover, the upper pole suspension could provide the kidney with a reliable attachment to the retroperitoneum after it was placed in the abdominal cavity during the PREP-IT procedure, preventing it from dropping down. Then, the distal end of the IVC, left RV, right RV,

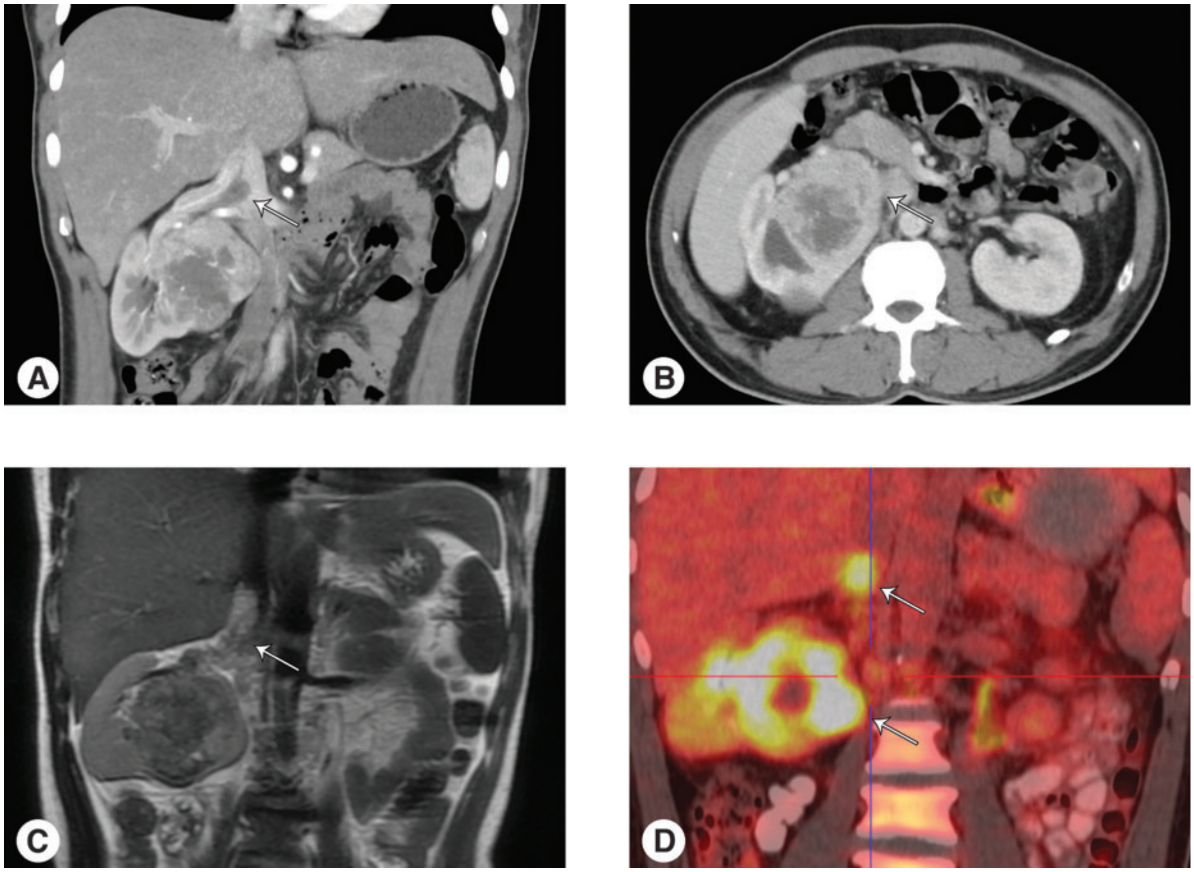

FIG. 1. Images of renal tumor thrombus. **(A)** Coronal CT scan of primary tumor and tumor thrombus. **(B)** Cross-sectional scan of primary tumor and tumor thrombus. **(C)** Coronal CT scan of primary tumor and tumor thrombus. **(D)** PET-CT scan of primary tumor and tumor thrombus. Tip of the primary tumor or venous tumor thrombus (*arrow*). Color images can be found online.

and the proximal end of IVC were dissected and blocked with vessel tourniquets successively.

PREP-IT and tumor thrombus resection. To develop a larger workspace in the retroperitoneum, PREP-IT was used. A transverse incision was made on the peritoneum in front of the renal capsule, allowing for a renal pass-through (Fig. 2F). We prefer a relatively inferior and lateral incision to avoid bowel or liver damage. Still, this procedure should be performed with caution. Once the incision was performed, the high carbon dioxide pressure was conducted from the retroperitoneum to the abdominal cavity, pushing the bowels aside and thus creating a local hollow space, which was large enough to bear the kidney. Then, we placed the kidney into the abdominal cavity by pushing it with vascular forceps. Hence, the retroperitoneal workspace was expanded. During this procedure, the retroperitoneal space was first oppressed by the filled abdominal cavity, but the workspace would be soon expanded visibly after the kidney was placed in the abdomen.

As with usual tumor thrombectomy, the IVC wall was incised, then the tumor thrombus and invaded vascular wall was resected and collected in a retrieval bag *en bloc* (Fig. 2G). The IVC was perfused with heparinized saline and sutured continuously with a 4-0 nonabsorbable suture (Fig. 2H). Then the vessel tourniquets of the proximal end of IVC, left RV, and the distal end of IVC were released successively. The kidney in the abdominal cavity was taken out by clamping the perirenal fat and was collected in a retrieval bag following complete dissection (Fig. 2I). The peritoneal incision was closed routinely to prevent the internal hernia, a rare but notable consequence of untreated peritoneal tears as reported.[9,10] A demo video is provided to show the surgery procedures (Supplementary Video S1).

Postoperative care and follow-up

Prophylaxis for deep vein thrombosis included lower limb exercise on the bed, elastic socks, elastic bandage, and early ambulation. Prophylactic anticoagulation was not used routinely because of the bleeding risk. Antibiotics, analgesics, and fluids were given according to the center protocol.

The follow-up period was defined from the date of surgery to the latest documented date of telephone or clinical follow-up, including the survival status, tumor recurrence or metastasis, and postoperative renal function.

Statistical analysis

The Shapiro–Wilk test was used to determine the normality of continuous variables. Categorical variables are

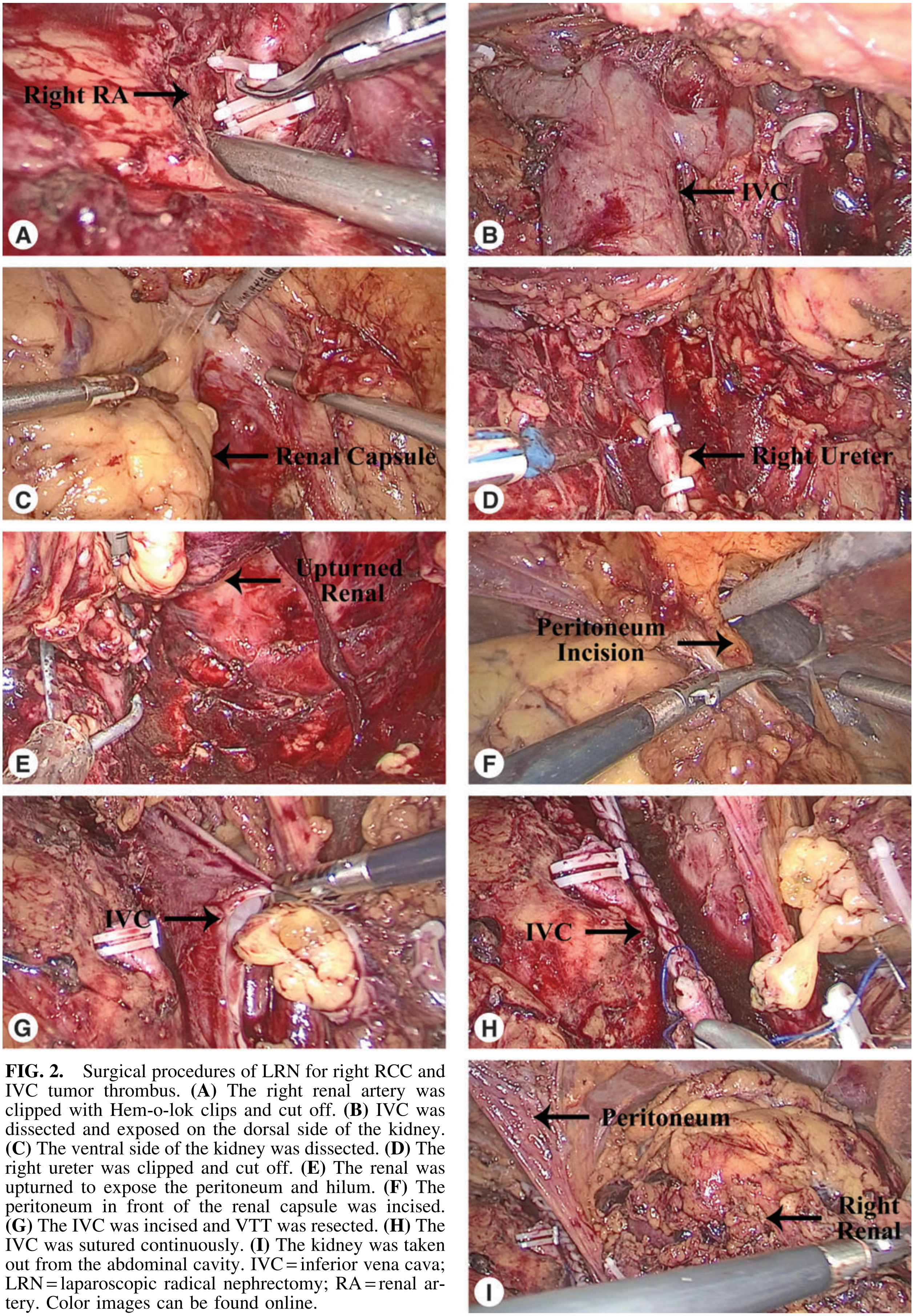

FIG. 2. Surgical procedures of LRN for right RCC and IVC tumor thrombus. **(A)** The right renal artery was clipped with Hem-o-lok clips and cut off. **(B)** IVC was dissected and exposed on the dorsal side of the kidney. **(C)** The ventral side of the kidney was dissected. **(D)** The right ureter was clipped and cut off. **(E)** The renal was upturned to expose the peritoneum and hilum. **(F)** The peritoneum in front of the renal capsule was incised. **(G)** The IVC was incised and VTT was resected. **(H)** The IVC was sutured continuously. **(I)** The kidney was taken out from the abdominal cavity. IVC = inferior vena cava; LRN = laparoscopic radical nephrectomy; RA = renal artery. Color images can be found online.

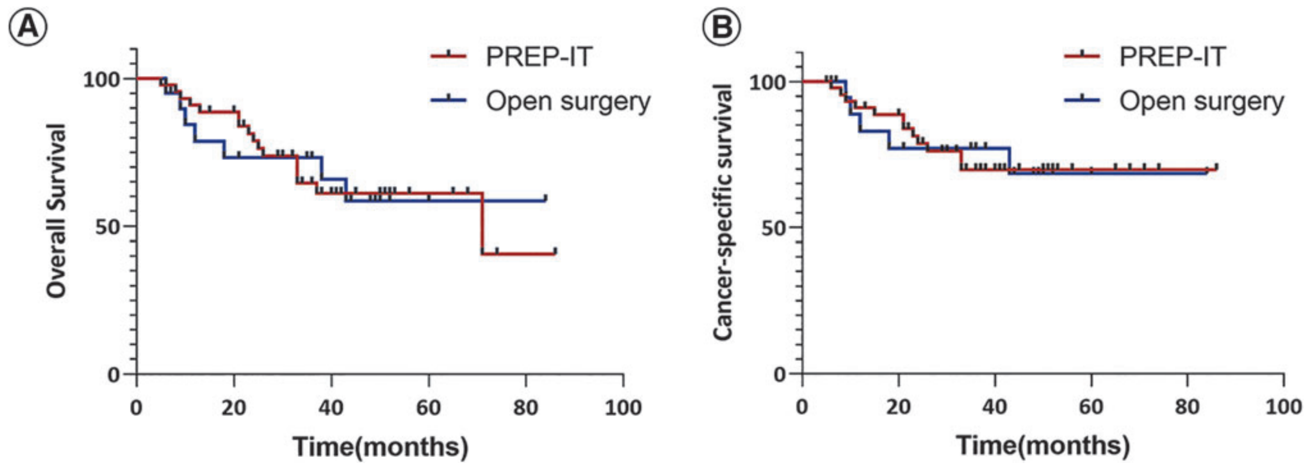

FIG. 3. Overall survival **(A)** and cancer-specific survival **(B)** were determined by the Kaplan–Meier analysis. PREP-IT = Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique. Color images can be found online.

given as percentages or frequencies. Continuous variables in accordance with normal distribution are given as mean ± standard derivation, otherwise are given as medians and interquartile ranges. Comparisons between groups were performed using independent *t*-test (normal distribution) or Mann–Whitney U-test (non-normal distribution) for continuous variables, and chi-square test for categorical variables. Differences in survival were evaluated using the log-rank test. *p*-Value <0.05 was considered statistically significant.

Table 1. Baseline Characteristics of Patients Receiving Radical Nephrectomy and Inferior Vena Cave Tumor Thrombectomy Using Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique

Variable	*PRAP-IT,* n (%)	*Open surgery,* n (%)	p
Gender			1.000
Male	39 (68.4)	26 (74.3)	
Female	18 (31.6)	9 (25.7)	
Age, years, median (IQR)	61 (54–68)	61 (55–68)	0.535
BMI, kg/m^2, mean ± SD	24.0 ± 3.4	23.8 ± 3.2	0.710
ASA grade			0.586
1	5 (8.8)	2 (5.7)	
2	49 (86.0)	28 (80.0)	
3	3 (5.2)	4 (11.4)	
4	0	1 (2.9)	
Clinical symptoms			0.363
No clinical symptoms	14 (24.6)	5 (14.3)	
Local symptoms	31 (54.4)	21 (60.0)	
Systemic symptoms	4 (7.0)	1 (2.9)	
Both	8 (14.0)	8 (22.9)	
Previous abdominal surgery	2 (3.5)	4 (11.4)	0.419
Thrombus level (Mayo)			**0.001**
I	25 (43.9)	3 (8.6)	
II	29 (50.9)	25 (71.4)	
III	3 (5.3)	7 (20.2)	
Tumor diameter, cm, median (IQR)	8.0 (6.1–9.9)	6.6 (5.1–8.6)	**0.027**
Maximum width of VTT, mm, median (IQR)	17.8 (15.7–19.5)	26.3 (22.1–31.5)	**<0.001**
Maximum width of the RV entrance, mm, mean ± SD	15.2 ± 5.0	16.12 ± 5.50	0.524
Hemoglobin, g/L, mean ± SD	124.7 ± 21.6	116.6 ± 31.7	0.396
Platelet count, × 10^9/L, mean ± SD	266.5 ± 80.0	238.3 ± 119.3	0.063
Neutrophil counts, × 10^9/L, median, (IQR)	4.36 (3.44–5.61)	4.32 (3.17–5.22)	0.398
Serum calcium, mg/dL, median, (IQR)	5.3 (4.8–6.0)	2.25 (2.15–2.33)	0.940
Albumin, g/L, median (IQR)	39.8 (36.0–42.4)	39.05 (35.07–43.30)	0.822
Alkaline phosphatase, U/L, median (IQR)	85.5 (65.0–110.0)	82.5 (68.3–112.3)	0.507

Bold font indicates *p* value ≤0.05.

ASA = American Society of Anesthesiologists; BMI = body mass index; IQR = interquartile range; PREP-IT = Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique; RV = renal vein; SD = standard derivation; VTT = venous tumor thrombus.

Results

Table 1 depicts the baseline characteristics of patients. Compared with the open surgery group, patients in the PREP-IT group were characterized by significantly larger tumor diameters (8.0 cm *vs* 6.6 cm, $p = 0.027$), a higher proportion of low-level (Mayo I) tumor thrombus (43.9% *vs* 8.6%, $p = 0.002$), and smaller maximum width of VTT (17.8 *vs* 26.3 mm, $p < 0.001$). Other baseline characteristics, including gender, age, body mass index (BMI), ASA grade, and previous abdominal surgery, showed no significant difference between the two groups.

The clinicopathologic characteristics are summarized in Table 2. There was no significant difference between the two groups in cN1 stage, cM1 stage, pN1 stage, perirenal fat invasion, ipsilateral adrenal gland invasion, and presence of bland thrombus. However, patients in PREP-IT groups were less comorbid with RV branch tumor thrombus (5.3% *vs* 33.3%, $p = 0.005$), including the left adrenal vein, the left gonadal vein, and the left ascending lumbar vein.

Compared with the open surgery group, the PREP-IT group was characterized by shorter operative time (290.0 *vs* 363.3 minutes, $p = 0.015$), less surgical blood loss (200.0 *vs* 1330.6 mL, $p < 0.001$), less transfusion receiving rate (24.6%

Table 2. Clinicopathologic Characteristics of Patients Receiving Radical Nephrectomy and Inferior Vena Cave Tumor Thrombectomy Using Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique

Clinicopathologic characteristics	*PREP-IT,* n *(%)*	*Open surgery,* n *(%)*	p
Operative time, mean ± SD	290.0 ± 82.0	363.3 ± 157.6	**0.015**
Surgical blood loss, mL, median (IQR)	200.0 (87.5–500.0)	1330.6 ± 1074.2	**<0.001**
Patients receiving transfusion	14 (24.6)	28 (80.0)	**<0.001**
Transfer to intensive care unit	23 (40.4)	24 (68.6)	**0.009**
Days to surgical drain removal, days, median (IQR)	5 (4–6)	7 (5–8)	**<0.001**
Days to full ambulation, days, median (IQR)	2 (2–3)	3 (3–6)	**0.004**
Days to oral feeding, days, median (IQR)	2 (1–2)	3 (2–4)	**<0.001**
Postoperative hospital stays, days, median (IQR)	8 (8–9)	10 (7–13)	**0.005**
IVC transverse resection	8 (14.0)	17 (48.6)	**<0.001**
IVC blocking time, minutes, median (IQR)	25 (13–30)	20 (11–28)	0.265
Postoperative complications	7 (12.3)	14 (40.0)	**0.002**
I	2 (3.5)	2 (5.7)	
II	2 (3.5)	10 (28.6)	
IVa	2 (3.5)	2 (5.7)	
IVb	1 (1.8)	0	
Major complications	2 (3.5)	2 (5.7)	1.000
Preoperative serum creatine, μmol/L, median (IQR)	92 (81–111)	90 (84–111)	0.944
Serum creatine 1 week after operation, μmol/L, median (IQR)	106 (87–126)	100 (83–138)	0.604
Serum creatine at follow-up (3 months; μmol/L), median (IQR)	105 (88–130)	108 (83–111)	0.604
Clinical N stage			0.378
cN0	23 (40.4)	11 (31.4)	
cN1	34 (59.6)	24 (68.6)	
Clinical M stage			1.000
cM0	45 (78.9)	27 (77.1)	
cM1	12 (21.0)	8 (22.9)	
Pathologic N stage			0.294
pN0	56 (98.2)	32 (91.4)	
pN1	1 (1.8)	3 (8.6)	
Perirenal fat invasion	10 (17.5)	6 (18.8)	1.000
Ipsilateral adrenal gland invasion	3 (5.3)	1 (2.9)	1.000
Presence of bland thrombus	6 (10.5)	6 (17.1)	0.525
Presence of renal vein branch tumor thrombus	3 (5.3)	10 (33.3)	**0.005**
Pathologic type			0.248
Clear cell renal-cell carcinoma	48 (84.2)	30 (85.7)	
Papillary renal-cell carcinoma	4 (7.0)	5 (14.3)	
Undifferentiated renal-cell carcinoma	4 (7.0)	0	
Chromophobe renal carcinoma	1 (1.8)	0	
Nuclear grade			0.611
1	0	1 (2.9)	
2	21 (36.8)	12 (34.3)	
3	23 (40.4)	14 (40.0)	
4	13 (22.8)	8 (22.9)	
Sarcomatoid feature	5 (8.8)	4 (11.4)	0.477

Bold font indicates p value ≤0.05.
IVC = inferior vena cava.

vs 80.0%, $p<0.001$), less intensive care unit transfer rate (40.4% *vs* 68.6%, $p=0.009$), fewer days to surgical drain removal (5 *vs* 7 days, $p<0.001$), days to full ambulation (2 *vs* 3 days, $p=0.004$), days to oral feeding (2 *vs* 3 days, $p<0.001$), and postoperative hospital stays (8 *vs* 10, $p=0.005$). The PREP-IT group received fewer IVC transverse resections (14.0% *vs* 48.6%, $p<0.001$). IVC blocking time showed no difference between the two groups.

The postoperative complication rate was significantly lower in the PREP-IT group (12.3% *vs* 40.0%, $p=0.002$), while the major complication rate indicated no significant difference. Overall, 7 (12.3%) patients in PREP-IT group experienced postoperative complications. Two patients had mild renal dysfunction. One patient had postoperative infection and one experienced atrial fibrillation, both improved after medications. Three patients had IV complications: two had acute renal dysfunction requiring dialysis, and one patient experienced a combination of heart failure, respiratory failure, and acute liver dysfunction after a pulmonary embolism. For patients with severe complications, no death occurred within 9 months after the surgery.

The median follow-up time was 33 (range: 2–86) months. In PREP-IT group and open surgery group, respectively, the mean overall survival time was 57.2 ± 5.3 and 58.1 ± 71.5 months, and the mean cancer-specific survival time was 70.3 ± 4.3 and 65.0 ± 9.7 (Fig. 3). The median overall survival time was 71.0 ± 28.9 months in PREP-IT group. Log-rank test indicated no significant difference between the two groups in terms of overall survival ($p=0.864$) and cancer-specific survival ($p=0.971$).

Discussion

For radical nephrectomy and IVC tumor thrombectomy, although open surgery is the traditionally preferred approach that can provide wide exposure and safe vascular operation, especially involving Mayo III to IV VTT, its operative wound and surgical blood loss are notable. Recently, there is a gradual transformation toward minimally invasive techniques, including laparoscopic surgery and robot-assisted laparoscopic surgery.[11–13] Although the latter allows for a more precise and defter operation, and experiences of initial procedures for robotic surgery have been reported even in Mayo III to IV VTT, many institutions still prefer laparoscopes as the major approach for minimally invasive operations.[14–18]

The reasons include the convenience in case of conversion, the flexible choice for the trocar site, and a cheap price compared with robotic surgery.[4] The retroperitoneal laparoscopic approach provides easier access to hilar, shorter operative time, and less bowel irritation compared with the transperitoneal one. Still, the narrow workspace in the retroperitoneum makes the IVC tumor thrombectomy difficult, therefore limiting its use in such surgeries. Making use of the abdominal cavity, PREP-IT is a feasible technique to develop a larger workspace around the IVC for patients with right RCC and Mayo I to III VTT.

As far as we know, no studies have systematically described this technique before. Previous studies had reported the combined retroperitoneal and transperitoneal approach, where the former was applied first for safe vascular control, then the transperitoneal workspace was established to switch the operative route, and the nephrectomy and tumor thrombectomy were finished as with regular transperitoneal laparoscopic procedures.[19–21] The combined approach and PREP-IT share common advantages, including safe hilar control and a large workspace for tumor thrombectomy, while PREP-IT allows for a pure retroperitoneal approach, which is more convenient with fewer surface wounds and bowel irritations. In addition, when compared with the pure retroperitoneal approach, which usually needs an auxiliary arm to hold up the kidney for wider exposure, PREP-IT helps spare this arm for other assistant procedures.

However, this technique also has its limitations compared with the trans-/retroperitoneal approach or the combined technique. First, PREP-IT is not recommended for left RCC, not only because LRN for left RCC with IVC tumor thrombus is more challenging technically, but also because the IVC is not on the side with the expanded workspace.[22] In addition, for large renal masses (generally ≥10 cm), the risk of secondary peritoneum tears increases significantly during PREP-IT. Besides, it is difficult to take it out of the abdominal cavity, and so, the application is limited for such cases.

Vigilance should be raised for patients with a history of abdominal surgery because the postoperative adhesions can increase the risk of bowel damage when incising the peritoneum. Although PREP-IT leads to less bowel irritation when compared with the transperitoneal approach, the potential risks cannot be ignored, and so, patients with a history of abdominal surgery are not suitable for this technique, contrary to the traditional retroperitoneal approach. In our study, two patients had a history of abdominal surgery, which were both appendiceal surgeries exclusively, and the risks of bowel damage were well considered by experienced clinical doctors. Another key point for PREP-IT is to close the peritoneal incision. It is widely believed that the incision will be subsequently reperitonealized, and little solid evidence supports the necessity for closure. However, internal hernia might occur with untreated tears as reported, which is rare but sometimes complicated with severe intestinal obstructions.[9,10] Moreover, sufficient bowel preparations were required for PREP-IT because of the peritoneum operation, despite its retroperitoneal route.

In the PREP-IT group, major complications occurred in 2 (3.5%) postoperative patients. According to a previous study on a cohort of 253 patients with renal tumor and VTT in our center, the perioperative occurrence of pulmonary embolism was 2.6%.[23] In another study on 103 patients who experienced IVC interruption in our center, the occurrence of postoperative major complications (defined as Clavien–Dindo Grade ≥3) was 18.8%.[24] Therefore, we consider the occurrence of the three IV complications not unnatural.

In our cases, some other techniques could be applied together with PREP-IT. Segmental IVC resection or IVC transection was performed for complex VTT, including IVC wall invasion and large bland thrombus.[24] For Mayo II to III tumor thrombus, we used the delayed occlusion of the proximal inferior vena cava technique to simplify IVC dissection and exposure, as described previously.[25]

Admittedly, this study has some limitations. First, this is a retrospective single-center study, so bias in patient populations cannot be excluded. In addition, while standard and overweight cases are applicable for this technique according to our experience, the potential effect of high BMI (especially BMI ≥30) on PREP-IT cannot be well demonstrated here, considering that the BMI in PREP-IT group ranges from 20.6 to 26.2. Added difficulty is possible for high BMI cases, as the increased belly fat may oppress the abdominal cavity, making the kidney placement difficult, therefore affecting the IVC exposure. Hence, we recommend sufficient preoperative communication for high BMI cases, and if the retroperitoneal workspace is severely oppressed, conversion to open surgery should be considered.

Finally, PREP-IT is more likely to cause postoperative peritoneal adhesions compared with the traditional retroperitoneal approach. However, our follow-up was insufficient to investigate the proportions of adhesion in the long term. Further studies are needed to verify this potential complication.

Conclusions

In conclusion, the PREP-IT is relatively safe and feasible in retroperitoneal laparoscopic right nephrectomy and IVC tumor thrombectomy, allowing for a large workspace and wide exposure for IVC operations.

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Authors' Contributions

All authors read and approved the final article. Conception and design: J.C., Z.L., and X.Z. Administrative support: S.Z., L.M., H.Z., and C.L. Acquisition of data: G.W., X.T., Y.T., L.G., K.C., and Y.L. Data analysis and interpretation: X.L., Q.G., Q.Z., and P.H. Article writing: All authors.

Author Disclosure Statement

The authors declare no competing interests.

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Supplementary Material

Supplementary Video S1

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Abbreviations Used

ASA = American Society of Anesthesiologists
BMI = body mass index
CT = computed tomography
IQRs = interquartile ranges
IVC = inferior vena cava
LRN = laparoscopic radical nephrectomy
MRI = magnetic resonance imaging
PREP-IT = Pure Retroperitoneal Laparoscopic Peritoneum Incision Technique
RA = renal artery
RCC = renal-cell carcinoma
RV = renal vein
SD = standard derivation
VTT = venous tumor thrombus

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Robot-Assisted Laparoscopic Prostatectomy Experience and Pathological Quality: Are They Always Linked?

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Abstract

Objective: We investigated whether pathological outcomes improved with experience and surgeon generation after robot-assisted laparoscopic prostatectomy (RALP).

Materials and Methods: The study included 1338 patients who underwent RALP between February 2010 and April 2020. We created learning curves for pelvic lymph node dissection (PLND), number of lymph nodes (LNs) removed, and positive surgical margin (PSM) after adjustment for confounders. We compared the outcomes between the first and second generation of surgeons in regression models.

Results: The learning curve regarding PLND indications showed a significant increase with experience for the first generation, whereas the second generation had a learning curve that remained flat at a higher level (92.3%) and significantly better than the first generation ($p < 0.001$). Similarly, the number of LN removed showed a significant increase with experience in both generations, but the overall median number of LN removed was significantly higher in the second generation compared with the first generation (12 *vs* 10, $p < 0.001$). However, the learning curve for PSM remained flat at $\sim 20\%$ after adjustment and did not show improvement with experience in both generations of surgeons ($p = 0.794$).

Conclusions: Surgeons showed improvement with experience and education with RALP with respect to the indications for PLND and number of LNs removed. However, there was no improvement over time and generations for PSM. Experience based solely on the number of patients operated on is not an intrinsic factor in the pathological quality of RALP. Factors other than experience may also play a role in oncologic improvement.

Keywords: prostate cancer, radical prostatectomy, learning curve, robotics

Introduction

Surgical procedures, particularly radical prostatectomy, require skill and expertise that are acquired with experience. Previous studies of open and laparoscopic surgery have shown that surgeon experience and generation improve perioperative, oncologic, and functional outcomes.[1–7] The term ''experience'' is often used to refer to the number of patients operated on. Our aim is to investigate this claim with respect to pathological outcomes after robot-assisted laparoscopic prostatectomy in our tertiary care academic center.

In the context of prostate cancer surgery, we hypothesize that the learning curves for performing pelvic lymph node dissection (PLND), the number of lymph nodes (LNs) removed, and the rate of positive surgical margins (PSMs) improve progressively with surgeon experience until they reach a plateau. We also hypothesize that surgeon generation

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will impact outcomes, increasing the likelihood of performing PLND, increasing the number of LNs removed, and decreasing the rate of PSM.

Materials and Methods

The retrospective study cohort consisted of 1338 patients who underwent robot-assisted laparoscopic prostatectomy (RALP) between February 2010 and April 2020 at a single tertiary care academic center, Charité University Hospital in Berlin, Germany. Six surgeons performed the operations, three of whom performed RALPs between 2010 and 2014 and the other three between 2015 and 2020. The first-generation surgeons had no prior experience with robot-assisted surgery but had experience with open or conventional laparoscopic radical prostatectomy, whereas the first-generation surgeons for RALP procedures trained the second-generation surgeons. This training took place during their Residency program and more intensively during their Fellowship for 2 years.

All patients gave prospective consent for the recording of preoperative, intraoperative, and postoperative data for retrospective analyses. Institutional Ethics Committee approval was obtained (EA2/022/22).

Preoperative work-up for all patients consisted of a prostate biopsy. MRI scans before surgery were introduced and implemented starting from the year 2014 at our center. All patients who underwent surgery from the second generation onward received an MRI as part of their evaluation. Data collected for each patient included initial prostate-specific antigen (PSA) level, TNM clinical stage, final Gleason score of the prostate specimen, use of a frozen section according to the Neuro-SAFE strategy,[8] completion of PLND, number of LNs removed, and the presence of a PSM. The PLND template followed in this study involved limited dissection of external iliac nodes and obturator fossa for all patients, irrespective of tumor stage or Gleason score.

All patients in the study underwent PLND concurrent with prostatectomy. The surgeries were conducted ∼2 to 3 months after the initial diagnosis for all patients. The time taken to perform the PLND intraoperative was never documented. Dedicated uropathologists analyzed the surgical specimens. In this regard, it is important to mention that as a definition, a PSM in NeuroSAFE analysis is reported when at least one invasive malignant gland comes into contact with the linked surgical margin.[8] The use of Neuro-SAFE in our institution started at the end of 2013.

Statistical analyses

Continuous variables were presented as mean and standard deviation or median (interquartile range), depending on the distribution. Student's t-test or Mann–Whitney U test was used to compare the difference between groups. Categorical variables were presented as frequencies and percentages and compared using the chi-square test.

Learning curves were created for PLND, number of LNs removed, and PSM. Multiple logistic regression models were used to evaluate the association between PLND or PSM and surgical experience (entered as a continuous variable). A linear regression model was performed to assess the association between the number of LNs removed and surgical experience. As the relationship between surgical experience and outcomes is likely nonlinear, surgical experience was modeled using restricted cubic splines with four knots for both models, as mentioned above.[9] Adjustments were made based on the following covariates: preoperative PSA (continuous), pTNM stage (2, 3a, 3b), NeuroSAFE frozen section (yes/no), and Gleason score (continuous). The learning curve for the number of LNs removed was produced by the predicted mean, and the learning curve for PLND and PSM was produced by the predicted probability of PLND and PSM for each level of surgical experience, with all covariates set at the mean. All p-values were two sided, and all statistical tests were performed using Stata IC15 (StataCorp, 2017, College Station, TX).

Results

A total of 1344 patients were included in the study, with 666 (49.5%) operated on by first-generation surgeons and 678 (50.5%) operated on by second-generation surgeons. The three first-generation surgeons operated on 347, 242, and 77 patients, respectively, whereas the three second-generation surgeons operated on 541, 74, and 63 patients, respectively. Table 1 shows the clinical and pathological characteristics of the study cohort. A multivariable prespecified model was used to control case mix by adjusting for clinical and pathological variables.

Initial PSA and pathological stage did not differ significantly between the two generations. However, the Gleason score of specimens operated on by first-generation surgeons

Table 1. Patients' Clinical Characteristics According to Surgeon's Generation

	First generation of surgeon (662 patients)	*Second generation of surgeon (676 patients)*	p
Initial PSA, median (IQR)	7.1 (5.4, 11.4)	7.3 (5.4, 10.6)	0.292
Pathological TNM stage, *n* (%)			0.100
pT2	459 (68.9)	497 (73.3)	
pT3a	119 (17.9)	115 (17.0)	
pT3b	88 (13.2)	66 (9.7)	
Gleason score, *n* (%)			<0.001
6	84 (12.6)	116 (17.1)	
7	481 (72.2)	510 (75.2)	
8 or greater	101 (15.2)	52 (7.7)	
PLND performed, *n* (%)	401 (60.2)	626 (92.3)	<0.001
Number of LN, median (IQR)	10 (7, 13)	12 (8, 15)	<0.001
Positive LN, *n* (%)	33 (5)	48 (7)	0.105
Frozen section, *n* (%)	28 (4.2)	646 (95.28)	<0.001
PSM, *n* (%)	225 (33.8)	165 (24.3)	<0.001

IQR = interquartile range; LN = lymph node; PLND = pelvic lymph node dissection; PSA = prostate-specific antigen; PSM = positive surgical margin; TNM = tumor, nodes, metastasis (globally recognised classifications of malignancies).

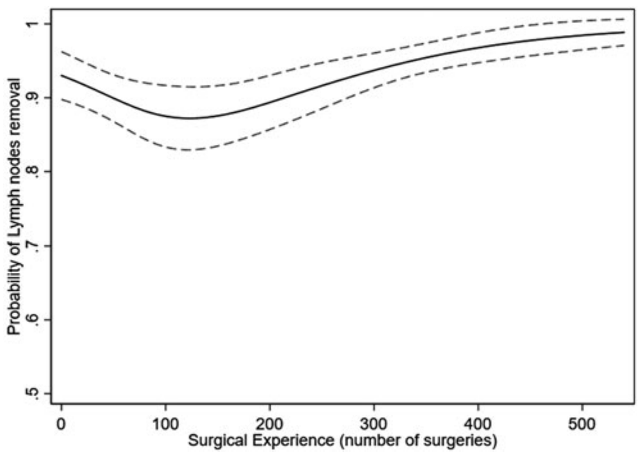

FIG. 1. Overall learning curve for pelvic lymph node dissection performed, controlling for PSA, pathological stage, frozen section, and Gleason score. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) are plotted against increasing surgeon experience. PSA = prostate-specific antigen.

was statistically higher compared with second-generation surgeons ($p < 0.001$).

Initial descriptive analysis showed that PLND was performed in 1027 patients (76.4%). PLND was performed in 401 (60.2%) of the 666 patients operated on by first-generation surgeons and in 626 (92.3%) of the 678 patients operated on by second-generation surgeons (Fig. 1; $p < 0.0019$). A statistically significant improvement in the number of PLNDs performed was observed during the experience of first-generation surgeons. In comparison, second-generation surgeons had a flat learning curve during their experience and overall performed at a significantly higher level than the first generation (Fig. 2; $p < 0.001$).

Similarly, the number of LNs removed increased significantly with experience (Fig. 3). In addition, the median

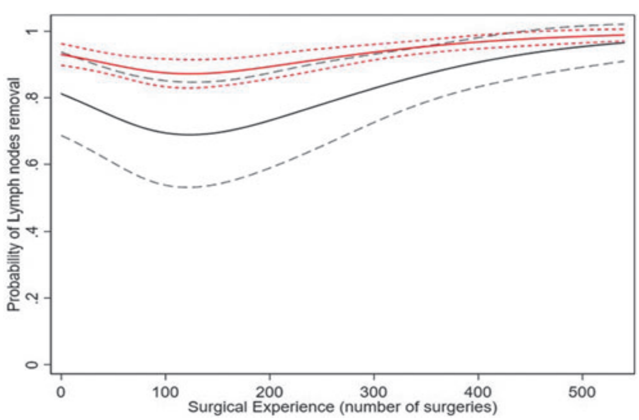

FIG. 2. Learning curve for pelvic lymph node dissection performed according to surgeons' generation, controlling for PSA, pathological stage, frozen section, and Gleason score. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) are plotted against increasing surgeon experience: first-generation surgeon (*black lines*) *vs* second-generation surgeon (*red lines*).

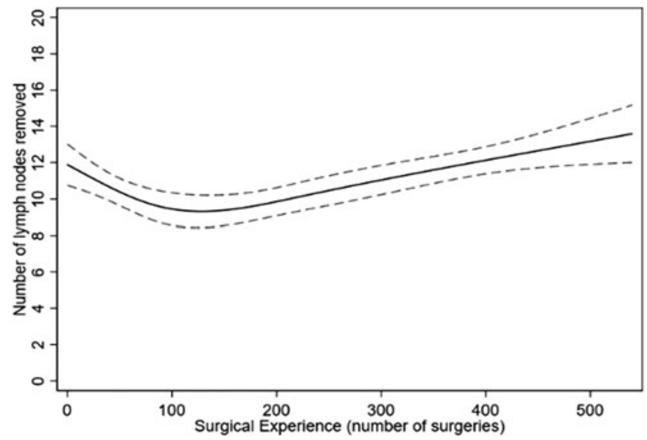

FIG. 3. Overall learning curve for number of lymph nodes removed, controlling for PSA, pathological stage, frozen section, and Gleason score. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) are plotted against increasing surgeon experience.

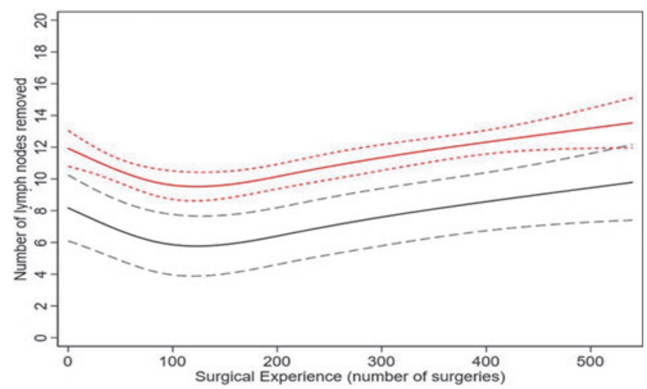

FIG. 4. Learning curve for number of lymph nodes removed according to surgeons' generation, controlling for PSA, pathological stage, frozen section, and Gleason score. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) are plotted against increasing surgeon experience: first-generation surgeon (*black lines*) *vs* second-generation surgeon (*red lines*).

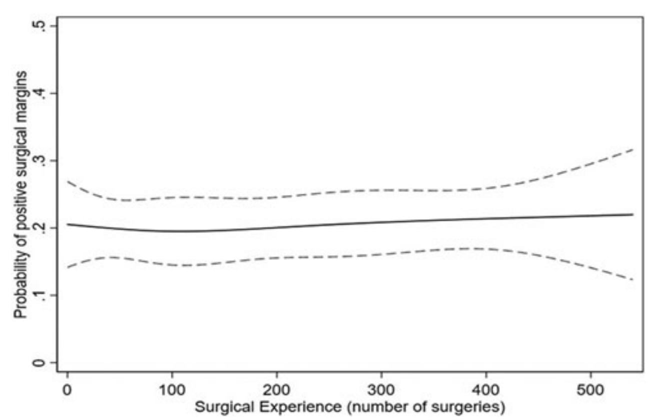

FIG. 5. Overall learning curve for PSMs. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) for PSM, controlling for PSA, pathological stage, frozen section, and Gleason score, are plotted against increasing surgeon experience. PSM = positive surgical margin.

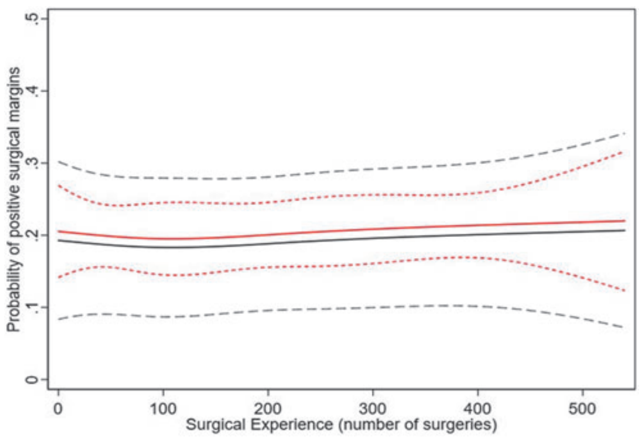

FIG. 6. Learning curve for PSMs according to surgeons' generation. Predicted probability (*solid line*) and 95% confidence intervals (*dashed line*) for PSM, controlling for PSA, pathological stage, frozen section, and Gleason score, are plotted against increasing surgeon experience: first-generation surgeon (*black lines*) *vs* second-generation surgeon (*red lines*).

number of LNs removed was significantly higher in second-generation surgeons than in first-generation surgeons (Fig. 4; 12 *vs* 10, $p < 0.001$).

PSMs were reported in 390 patients (PSM rate: 29%). The first-generation surgeons reported a PSM in 225 patients (33.8%), whereas second-generation surgeons reported a PSM in 165 patients (24.3%). After adjustment for PSA, pathological stage, frozen section, and Gleason score, there was no difference in the learning curve for PSM between the two generations (Fig. 5; $p = 0.79$). The learning curves after adjustment were flat, with a PSM rate of ~20% in both generations of surgeons and showed no improvement with experience (Fig. 6).

Discussion

It is commonly believed that a surgeon with extensive surgical experience will deliver good results to their patients. This often translates into inquiries from patients about the number of procedures a surgeon has performed. Previous studies have shown that in radical prostatectomy, regardless of surgical approach (open, conventional, or robot-assisted laparoscopic), perioperative, oncologic, and functional outcomes improve with surgeon experience and generation.[1–7,10,11] Similar findings have been reported for other urologic cancer surgeries such as radical cystectomy.[12,13]

In this study, we sought to evaluate the statement of robot-assisted radical prostatectomy, which was implemented relatively recently, in 2010, and has since expanded in our tertiary care academic hospital, thus providing a good model for such an evaluation. We analyzed the learning curve of performing PLND as well as the number of LNs removed, which may serve as a good indicator of surgical proficiency. However, this parameter is rarely studied and may be confounded by other factors other than surgical performance, such as the extent of the preoperative work-up. In our study, both learning curves showed improvement over time with an initial decline and over generations of surgeons, in line with previous studies.[14,15] Regarding the decision to perform PLND, we can assume that inexperienced surgeons initially focus on performing radical prostatectomy as the primary goal. As they gain experience and operative times decrease, we assume that the time saved is devoted to PLND.

As reported by Hu and colleagues,[14] the number of removed LNs increases with surgeon's experience. This can be explained by the reduction in operative time, and by the fact that the number of nodes is an easily memorized parameter that can be easily incorporated into a personal surgical assessment. In both generations, the number of LN was first reduced at the beginning of the experience and then increased throughout the experience, with a plateau reached after 200 to 250 operated patients. The fact that the number of PLNDs performed and the LN count started at a higher level for the second generation than for the first may be interpreted as a good transfer of knowledge between the generations of surgeons in the frame of the internal educational program.

Many previous studies have examined the rate of PSM and biochemical recurrence after radical prostatectomy.[1–7,11,16–19] Most have suggested that PSM rate improved with surgeon or institutional experience, underlying the overall progress made through teaching processes and accumulated experience. However, the volume of experience required varied across studies, whether it was a single surgeon,[20] a single surgical group,[2,21] or a multi-institutional study,[1,6,18] and the technique used.[3,5,7] Robot-assisted radical prostatectomy has an indeterminate learning curve, and the shape of the curves varies depending on the parameter selected, such as operative time, transfusion rate, complications, or hospital stay, among others.

For PSM, the volume is not clearly defined, and a recent study suggested that an experience of up to 1600 patients would be required to reach a PSM rate of <10%, and that for pT3 tumors, the curve begins to plateau after 1000 to 1500 cases.[18] In our study, surgeons failed to demonstrate an improvement regarding PSM over time and generations. Different surgeons with the same experience showed differences in PSM rates, suggesting that they tend to repeat the same mistakes throughout the procedures.

Analyzing the data, we observed that patients with T3 disease who did not undergo NeuroSAFE did not benefit from nerve sparing, particularly when advanced abnormalities were detected on MRI. However, nerve sparing was selectively performed for T3 tumors only if there was no obvious nerve invasion on MRI images and when NeuroSAFE results were negative. Therefore, we conclude that nerve sparing was not a confounding factor in this particular cohort.

An important aspect to consider in the preoperative assessment is the inclusion of MRI scans, which could potentially have an impact on the results between the first and second generations. However, despite the utilization of MRI, the results did not show any improvement in PSM rates. This suggests that surgeons may rely more on the NeuroSAFE technique rather than solely on MRI findings. It is important to note that NeuroSAFE focuses on the bilateral peripheral layers of the prostate and does not encompass all aspects of the organ.

Our study demonstrates that ''surgical experience,'' based solely on the number of patients operated on, is not an adequate proxy for oncologic quality. Other factors should play a role in oncological improvement. This raises the question of whether a structured curriculum is an important predictive factor of quality, as suggested by Secin et al.[6] and Vickers et al.[7] In addition, ''Quality Assurance'' concepts may be a key quality factor, as surgical improvement is a continuous process based on learning from previous successes and mistakes, properly analyzed and interpreted.

Another important point to discuss is how surgical and oncologic outcomes improve with generations. When comparing the probability of LN dissection and number of LNs removed, the second generation performed significantly better and immediately higher at the beginning of the experience. This is probably related to the experience the second generation gained when assisting the previous generations. However, assessing its own progresses when comparing continuous numbers, such as number of removed nodes, this method of self-evaluation is not suitable for complex assessments, such as the status of surgical margins in relation to anatomic and pathological complexities.

The main limitation of our study is its single-center retrospective design, but it reflects daily practice in a real-world setting. Our objective was to examine whether the outcomes at a large center are primarily influenced by the volume of cases, particularly concerning PSMs and LN dissection. It was not our intention to generalize these findings to other centers performing robotic prostatectomy. However, this could still be the case at any center performing robotic prostatectomy in high volumes. The main value is that all surgeons performing RALP and all patients without any selection or exclusion were included, and only dedicated uropathologists analyzed all specimens, which eliminates pathological bias. These data are based on pathological findings only and not on long-term biochemical results that could theoretically lead to differences in oncologic outcomes, although it is well documented that pathological and biochemical findings are highly correlated.[17]

Conclusions

With experience and training, surgeons have improved their ability to perform robot-assisted radical prostatectomy, including determining when to perform PLND and increasing the number of LNs removed. However, there has been no improvement in reducing the incidence of PSMs over time and across generations.

Based on these results, we conclude that using the number of patients operated on as the sole metric for assessing the pathological quality after robot-assisted laparoscopic prostatectomy is inadequate. Other factors may also play an important role in achieving better oncologic outcomes. To ensure and validate ongoing surgical improvements, we recommend structured training programs and the implementation of quality assurance processes.

Authors' Contributions

T.A.: Conceptualization, Methodology, and investigation.
P.G.: Statistical analysis.
S.E.: Analysis and interpretation of data.
F.R.: Analysis and interpretation of data.
B.R.: Critical revision of the article.
S.W.: Critical revision of the article.
D.M.: Analysis and interpretation of data.
T.S.: Conceptualization and critical revision of the article.
B.G.: Supervision, Conceptualization, Methodology, and investigation.

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Abbreviations Used

IQR = interquartile range
LN = lymph node
MRI = magnetic resonance imaging
PLND = pelvic lymph node dissection
PSA = prostate-specific antigen
PSM = positive surgical margin
RALP = robot-assisted laparoscopic prostatectomy
TNM = tumor, nodes, metastasis (globally recognised classifications of malignancies)

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Vesicourethral Anastomosis in Transvesical Single-Port Robotic Radical Prostatectomy: A Technical Description and Perioperative Outcomes

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Abstract

Objective: To describe the technical evolution and perioperative outcomes of vesicourethral anastomosis (VUA) in transvesical (TV) single-port robot-assisted radical prostatectomy (SP-RARP).

Materials and Methods: A retrospective review was performed on 189 patients who underwent TV SP-RARP by a single surgeon using the purpose-built SP robotic platform. VUA was completed from within the bladder using two unidirectional V-loc sutures in a continuous, semicircular manner with greater emphasis posteriorly. The most recent 20 cases of TV SP-RARP were selected to evaluate the anastomosis technique and to compare the perioperative outcomes with the first 20 cases of TV SP-RARP performed at our institution. Demographic and clinical data were collected from the prospectively maintained database and statistical analysis was performed.

Results: VUA was effectively completed in all cases using the aforementioned technique without any suture breaks, need for conversion, or evidence of intraoperative complication, including urine leak. Marked improvement in the learning curve was observed, which translated to significant reduction in the number of VUA sutures (median: 13 *vs* 15, $p < 0.05$) and faster anastomosis time (median: 19.1 *vs* 33.5 minutes, $p < 0.05$). The number of anastomotic sutures did not correlate with the prostatectomy specimen weight or volume, especially with both being significantly greater in the latest cases (median weight: 45.1 *vs* 37.6 g, $p < 0.05$; median volume: 40.9 *vs* 36.2 mL, $p < 0.05$). Postoperative outcomes were favorable with immediate continence achieved in 51.3% of our total cohort and with no patients demonstrating evidence of bladder neck contracture.

Conclusion: We provided a detailed technical description of VUA in TV SP-RARP. The improved maneuverability of the SP robotic platform allowed for unique movements to facilitate suture placements from within the confined space of the bladder. The learning curve of a single surgeon was shown in our study, which resulted in notable reduction in the number of sutures, faster anastomosis time, and improved perioperative outcomes.

Keywords: minimally invasive surgery, radical prostatectomy, robotic surgery, single-port, vesicourethral anastomosis

Introduction

Currently, different approaches of single-port robot-assisted radical prostatectomy (SP-RARP) have been introduced with surgical access able to be obtained via transperitoneal (TP), extraperitoneal, transperineal, and transvesical (TV) routes.[1,2] The benefits of the TV approach (TV SP-RARP) in the management of localized prostate cancer have been previously demonstrated, especially in patients with previous abdominal surgeries and in those where regional anesthesia may be preferable.[3–5] The latter can be facilitated as the SP approach no longer required the steep Trendelenburg position that was routinely utilized in the multiport (MP) techniques. The localization of surgical field with direct access into the bladder also provided additional benefits in enhancing postoperative recovery with

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many patients able to be discharged on the same day with minimal analgesia requirements.[3,4,6]

Despite the advantages, the advent of TV SP-RARP also introduced a new challenge for surgeons to determine the best approach to completing vesicourethral anastomosis (VUA) in a small working space from within the bladder. As such, this study sought to describe the refined VUA technique for TV SP-RARP along with the unique articulations of the needle holder using the purpose-built SP robotic platform and to evaluate the early perioperative outcomes.

Materials and Methods

Study design

A retrospective review was performed on 189 patients who underwent TV SP-RARP between November 2020 and March 2023. Demographic and perioperative variables were collected from the prospectively maintained Institutional Review Board (IRB)-approved database. All SP cases were completed using the DaVinci SP robotic surgical system (Intuitive Surgical, Inc., Sunnyvale, CA) by a single experienced robotic surgeon (J.H.K.) with technique as described previously.[3,4] All double-articulating instruments, including the camera and the Remotely Operated Suction Irrigation (ROSI) system (Vascular Technology, Inc. (VTI), Nashua, NH), were passed through a multichannel cannula of the purpose-built SP Access Port (Intuitive Surgical, Inc.). Intraoperative videos recorded by the robotic console were used to review the suture placements, different articulations of the needle holder, as well as the number of sutures used and the suture needle passed for each VUA.

For the purpose of this study, the most recent 20 cases of TV SP-RARP were selected to evaluate the technique and perioperative outcomes of our VUA approach. The group was compared with the first 20 cases of TV-SP and the latest 20 cases of MP TP-RARP performed at our institution to identify any changes along the learning curve of TV SP-RARP and to appreciate the differences in techniques and needle holder articulations between the MP and SP approaches. The TP MP-RARP was used as a comparison given the intraoperative view and working space of the retropubic approach that is familiar to most urologists.

Vesicourethral anastomosis technique

VUA was performed using 15 and 23 cm unidirectional 3-0 Covidien V-Loc 90 (Medtronic, Minneapolis, MN) sutures on RB-1 needles. The sutures came dyed and undyed to distinguish between left- and right-sided anastomoses. Following the placement of Rocco stitch for posterior reconstruction, the left-sided anastomosis was commenced at 5 O'clock in a clockwise manner until 11 O'clock. Sutures at the bladder mucosa were placed outside-in and were closer to each other posteriorly and diverged anteriorly. In contrast, urethral sutures were placed inside-out at approximately equal distances from each other. The bladder and urethral mucosa were approximated after each needle passage. The second suture was started at 5 O'clock in a counterclockwise direction until it meets the other suture at 11 O'clock where the two sutures can be tied together to form a surgical knot.

Examples of different suturing positions, such as right- and left-handed forehand and backhand, for each point in the anastomosis, were summarized in Figure 1. In addition, we presented a novel suturing movement that is unique to the TV SP-RARP approach, called the ''modified backhand,'' where the suture needle was deflected at a more acute angle of approximately 30° with respect to the needle holder, which allowed for additional rotation movement of the needle toward itself.

Following completion of the anastomosis, a Foley catheter was placed under vision and an intraoperative leak test was performed before robot undocking. Urinary postvoid residual (PVR) measurement was obtained at the time of Foley catheter removal. International Prostate Symptom Score (IPSS) and uroflowmetry with PVR were obtained during routine postoperative follow-up to also assess for healing and as a surrogate to investigate for any evidence of bladder neck contracture.

Statistical analysis

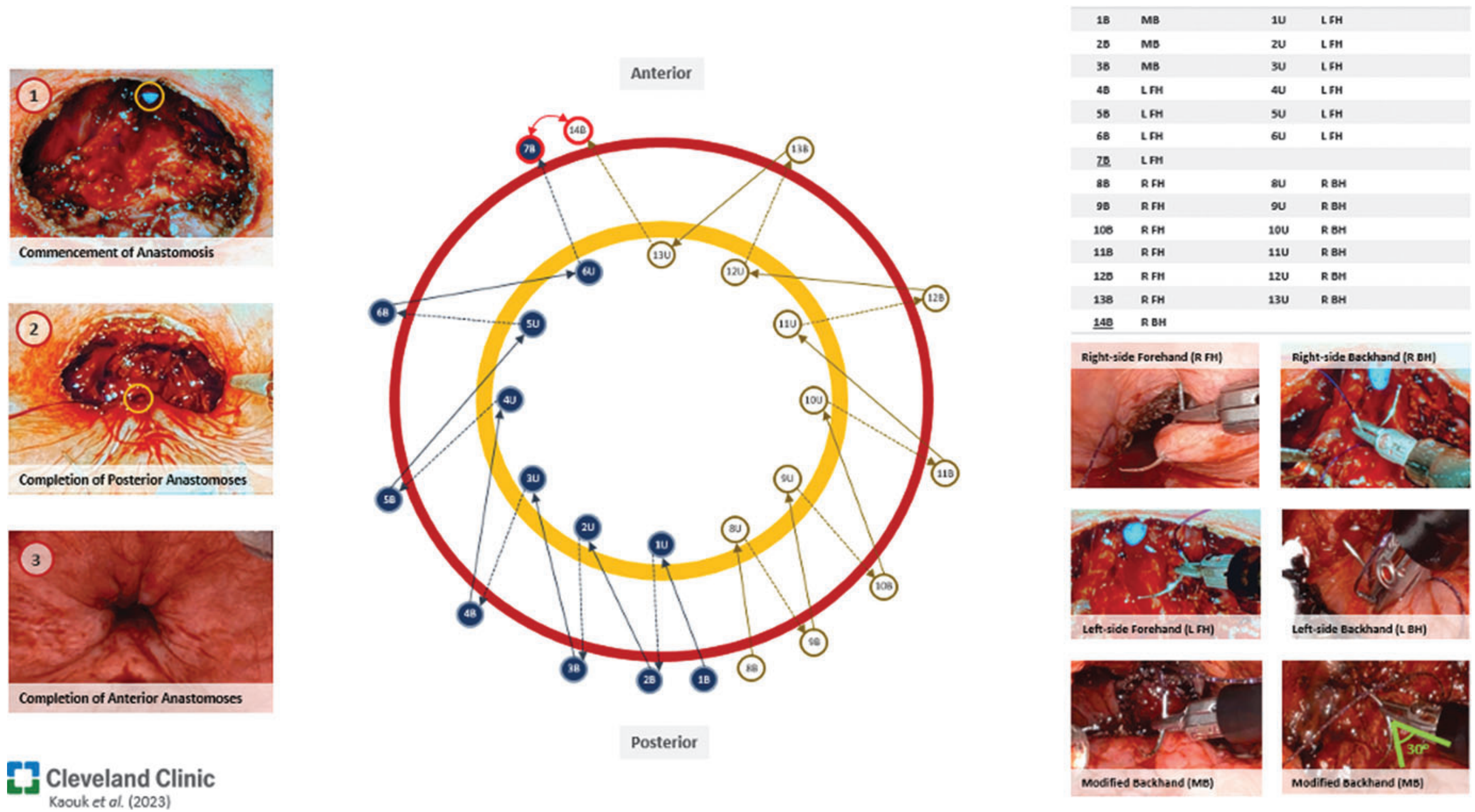
Statistical analysis was performed using IBM SPSS version 29.0. Continuous variables were reported as median and range, while categorical variables were reported as absolute and relative percent frequencies. Statistical significance was determined at a p-value of <0.05 using Chi-square and Fisher's exact tests for categorical variables and t-test for continuous variables.

Results

VUA for the 20 most recent cases of TV SP-RARP were completed effectively using the aforementioned technique (Fig. 1). There were no suture breaks or need for additional sutures throughout the series. All cases were completed without any conversion or additional port. Baseline demographic and clinical characteristics were presented in Table 1. Perioperative and postoperative outcomes were shown in Table 2. The median anastomosis time was 19.1 minutes (range 12.5–43.7 minutes), which constituted 11.5% (range 5.4%–25.3%) of the total operating time. The median number of suture needles passed was 13 (range 10–16). There were more sutures passed on the right, compared to those posteriorly and on the left. There was no statistically significant relationship between the number of anastomotic sutures passed with the weight and volume of the prostate specimens ($p = 0.627$ and 0.415, respectively).

When compared with the first 20 cases of TV SP-RARP, the more recent cases were identified to have a significantly lower number of sutures passed (median 15 *vs* 13, $p \leq 0.05$) and faster anastomosis time (median 33.5 *vs* 19.1 minutes, $p \leq 0.05$), despite having a significantly higher specimen volume (median 36.2 *vs* 40.9 mL, $p \leq 0.05$). These improvements in VUA-related outcomes in the latest 20 cases of TV SP-RARP may reflect the learning curve of an experienced robotic surgeon, which was also evident by the marked reduction in the overall operating and robotic console times between the two groups as depicted in Table 2 (median operating time 207 *vs* 172 minutes, $p \leq 0.05$; median robotic console time 143.3 *vs* 104.8 minutes, $p \leq 0.05$).

In a separate comparison, the number of anastomotic sutures passed was noted to be identical between the latest 20 cases of TV-SP and the most recent 20 cases of TP MP-RARP (median 13 *vs* 14, $p = 0.319$). VUA time, however, was faster in the MP approach (median 19.1 *vs* 13.5



1B	MB	1U	L FH
2B	MB	2U	L FH
3B	MB	3U	L FH
4B	L FH	4U	L FH
5B	L FH	5U	L FH
6B	L FH	6U	L FH
7B	L FH		
8B	R FH	8U	R BH
9B	R FH	9U	R BH
10B	R FH	10U	R BH
11B	R FH	11U	R BH
12B	R FH	12U	R BH
13B	R FH	13U	R BH
14B	R BH		

FIG. 1. Detailed technical description of VUA for TV SP-RARP. *Left*: (1) *top-down view* at the bladder neck defect at the commencement of VUA (*orange circle* represents the urethra); (2) *top-down view* following completion of posterior anastomosis (*orange circle* represents the urethra); (3) *top-down view* at the completed VUA. *Middle*: VUA suture placements at the bladder mucosa (*red circle*) and the urethral mucosa (*orange* circle). Each throw location was numbered in sequence and labeled based on its bladder (''B'') or urethral locations (''U''). *Top right*: descriptive table outlining the hand movements for each suture location. *Bottom right*: intraoperative images for each hand movement for suture placements, namely R FH and R BH, L FH, and L BH, as well as the novel MB. L BH = left-side backhand; L FH = left-side forehand; MB = modified backhand; R BH = right-side backhand; R FH = right-side forehand; SP-RARP = single-port robot-assisted radical prostatectomy; TV = transvesical; VUA = vesicourethral anastomosis.

Table 1. Baseline Demographic and Clinical Characteristics for the First 20 Cases of Transvesical (TV) Single-Port Robot-Assisted Radical Prostatectomy (SP-RARP), the Most Recent 20 Cases of TV SP-RARP, and the Latest 20 Cases of Transperitoneal Multiport-RARP

	TV SP-RARP (first 20 cases)	*TV SP-RARP (latest 20 cases)*	*TP MP-RARP (latest 20 cases)*	p
Age (years), median (range)	62.3 (52.3–71.3)	62.7 (48.5–73.8)	69 (51–80)	**<0.05** A *vs* B: 0.760 B *vs* C: <0.05
BMI (kg/m^2), median (range)	27.4 (22.4–39.9)	28.7 (23.1–41.9)	29 (24–47)	0.154
ASA, *n* (%)				0.786
ASA 2	6/20 (30)	4/20 (20)	5/20 (25)	
ASA 3	13/20 (65)	3/20 (80)	14/20 (70)	
ASA 4	1/20 (5)	0/20 (0)	1/20 (5)	
CCI, median (range)	4 (3–5)	4 (1–7)	5 (3–7)	**<0.05** A *vs* B: 0.892 B *vs* C: <0.05
Preoperative PSA (ng/mL), median (range)	4.7 (2–9.1)	5.5 (3.9–19.1)	10.7 (4.8–29.9)	**<0.05** A *vs* B: 0.514 B *vs* C: <0.05
Biopsy Gleason Grade Group, *n* (%)				**<0.05** A *vs* B: 0.721 B *vs* C: <0.05
Group 1	6/20 (30)	5/20 (25)	2/20 (10)	
Group 2	11/20 (55)	12/20 (60)	5/20 (25)	
Group 3	3/20 (15)	2/20 (10)	2/20 (10)	
Group 4	0/20 (0)	0/20 (0)	5/20 (25)	
Group 5	0/20 (0)	1/20 (5)	6/20 (30)	
cT stage, *n* (%)				0.595
cT1c	19/20 (95)	18/20 (90)	17/20 (85)	
cT2a	1/20 (5)	2/20 (10)	1/20 (5)	
cT3a	0/20 (0)	0/20 (0)	1/20 (5)	
cT3b	0/20 (0)	0/20 (0)	1/20 (5)	
NCCN risk categories, *n* (%)				**<0.05** A *vs* B: 0.488 B *vs* C: <0.05
Extremely low	0/20 (0)	0/20 (0)	1/20 (5)	
Low	6/20 (30)	4/20 (20)	0/20 (0)	
Intermediate	14/20 (70)	15/20 (75)	6/20 (30)	
High	0/20 (0)	1/20 (5)	8/20 (40)	
Extremely high	0/20 (0)	0/20 (0)	5/20 (25)	
Prostate volume (mL), median (range)	31 (22–34.75)	37 (31.35–43.5)	53 (20–184)	**<0.05** A *vs* B: 0.455 B *vs* C: <0.05
Preoperative IPSS, median (range)	8 (1–26)	8 (1–28)	16 (1–30)	0.089

ASA = American Society of Anesthesiologists; BMI = body mass index; CCI = Charlson Comorbidity Index; cT = clinical T; IPSS = International Prostate Symptom Score; MP = multiport; NCCN = National Comprehensive Cancer Network; PSA = prostate-specific antigen; RARP = robot-assisted radical prostatectomy; SP = single port; TP = transperitoneal; TV = transvesical.

minutes, $p \leq 0.05$). Interestingly, the TP-MP cohort was noted to have larger prostate volume and greater specimen weight (median prostate volume 37 *vs* 53 mL, $p \leq 0.05$; median specimen weight 45.1 *vs* 65.9 g, $p \leq 0.05$), which further stressed the lack of relationship between VUA and the prostatic dimensions.

In addition to the sutures passed during VUA, we identified that additional sutures were often required to close the bladder defect in the TP-MP approach (50% *vs* 80%, $p \leq 0.05$). For the purpose of this study, these extra threads were not included in our analysis as they did not contribute to the anastomosis.

There was no evidence of any intraoperative complication in all three groups, including for positive intraoperative leak test. Foley catheter duration was significantly shorter following TV SP-RARP, compared to those who had TP-MP (median 5 *vs* 7, $p \leq 0.05$). One patient who underwent TV SP-RARP developed acute urinary retention (AUR) 1 day following Foley catheter removal on postoperative day (POD) 3. The patient was a 60-year-old with intermediate-risk prostate cancer and a resected specimen volume of 50.5 mL. On reviewing the VUA, the patient was found to have the highest number of sutures compared to the rest of the group (16 *vs* median 13). The patient had an effective trial of void with zero PVR following subsequent removal of Foley catheter.

In the remaining patients, urinary PVR outcomes were comparable across the three groups with most patients able

Table 2. Perioperative and Postoperative Outcomes for the First 20 Cases of Transvesical (TV) Single-Port Robot-Assisted Radical Prostatectomy (SP-RARP), the Most Recent 20 Cases of TV SP-RARP, and the Latest 20 Cases of Transperitoneal Multiport-RARP

	TV SP-RARP (first 20 cases)	*TV SP-RARP (latest 20 cases)*	*TP MP-RARP (latest 20 cases)*	p
Perioperative outcomes				
Operating time (minutes), median (range)	207 (159–248)	172 (142–232)	215.5 (161–291)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
Console time (minutes), median (range)	143.3 (103.7–194.6)	104.8 (50–149.9)	164.7 (115.8–223.1)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
Anastomosis time (minutes), median (range)	33.5 (20.3–45.5)	19.1 (12.5–43.7)	13.5 (7.2–22.6)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
% of operating time, median (range)	14.7 (9.3–21.5)	11.5 (5.4–25.3)	6.2 (3.4–8.6)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
% of console time, median (range)	23.2 (11.8–32.1)	18.7 (9.9–41)	7.4 (4.9–14.7)	**<0.05** A *vs* B: 0.706 B *vs* C: <0.05
Number of sutures, median (range)	15 (12–22)	13 (10–16)	14 (12–16)	**<0.05** A *vs* B: <0.05 B *vs* C: 0.178
Posterior sutures, median (range)	3 (2–6)	2 (2–3)	3 (2–4)	**<0.05** A *vs* B: <0.05 B *vs* C: 0.094
Right-sided sutures, median (range)	6 (4–9)	6 (4–8)	6 (3–8)	0.433
Left-sided sutures, median (range)	5 (4–11)	5 (4–7)	6 (4–7)	0.167
Specimen weight (g), median (range)	37.6 (22.7–52.7)	45.1 (29.3–116.4)	65.9 (27.4–265.8)	**<0.05** A *vs* B: 0.460 B *vs* C: <0.05
Specimen volume (mL), median (range)	36.2 (23.7–62.2)	40.9 (27.2–112.2)	65.5 (22.8–231.9)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
Number of suture per mL of specimen volume, median (range)	0.440 (0.249–0.626)	0.339 (0.097–0.478)	0.219 (0.065–0.571)	**<0.05** A *vs* B: <0.05 B *vs* C: 0.051
Bladder neck reconstruction, *n* (%)	1/20 (5)	1/20 (5)	6/20 (30)	**<0.05** A *vs* B: <0.05 B *vs* C: <0.05
Positive intraoperative leak test, *n* (%)	0/20 (0)	0/20 (0)	0/20 (0)	**—**
Histopathology				
Pathology Gleason Grade Group, *n* (%)				**<0.05** A *vs* B: 0.086 B *vs* C: <0.05
Group 1	2/19 (10.5)	0/20 (0)	0/20 (0)	
Group 2	13/19 (68.4)	19/20 (95)	7/20 (35)	
Group 3	4/19 (21.1)	1/20 (5)	7/20 (35)	
Group 4	0/19 (0)	0/20 (0)	0/20 (0)	
Group 5	0/19 (0)	0/20 (0)	6/20 (30)	
pT stage, *n* (%)				0.182
pT2	11/20 (55)	8/20 (40)	7/20 (35)	
pT3a	8/20 (40)	11/20 (55)	7/20 (35)	
pT3b	1/20 (5)	1/20 (5)	6/20 (30)	
pN stage, *n* (%)				**<0.05** A *vs* B: 0.151 B *vs* C: <0.05
pNx	16/20 (80)	19/20 (95)	2/20 (10)	
pN0	4/20 (20)	1/20 (5)	14/20 (70)	
pN1	0/20 (0)	0/20 (0)	4/20 (20)	

(*continued*)

TABLE 2. (CONTINUED)

	TV SP-RARP (first 20 cases)	*TV SP-RARP (latest 20 cases)*	*TP MP-RARP (latest 20 cases)*	p
Postoperative outcomes				
Foley catheter duration, median (range)	5 (3–9)	5 (3–9)	7 (6–12)	**<0.05** A *vs* B: 0.250 A *vs* C: <0.05
Urinary PVR (mL), median (range)	0 (0–20)	0 (0–20)	0 (0–20)	0.759
Urine leak, *n* (%)	0/20 (0)	0/20 (0)	0/20 (0)	—
Immediate continence, *n* (%)	8/20 (40)	8/18 (44.4)	5/17 (29.4)	0.644
IPSS at 6 weeks, median (range)	3 (0–15)	3 (0–12)	9 (5–23)	<0.05 A *vs* B: 0.669 A *vs* C: 0.055

pN = pathology N; pT = pathology T; PVR = postvoid residual.

to empty their bladder completely following Foley catheter removal. Continence outcomes were found to be better following TV SP-RARP with immediate continence achieved in 44.4% of the most recent cases, compared to 29.4% in patients following TP-MP. Despite this superior outcome, the immediate continence rate in this select group of patients was lower than the 51.7% rate in the overall cohort of 189 TV SP-RARP patients. At the routine 6 weeks postoperative follow-up, IPSS score was significantly better in patients who underwent TV SP-RARP compared to the MP cohort (median 3 *vs* 9, $p \leq 0.05$). Nevertheless, both approaches demonstrated marked improvements in the IPSS scores compared to the median preoperative values of 8 and 16 in the TV-SP and TP-MP, respectively.

Discussion

The formation of a watertight VUA represents one of the final and most crucial steps in RP. With the rising popularity of TV SP-RARP, this present study provided the first detailed description of creating VUA from within the bladder using the purpose-built SP robotic system, along with the learning curve of an experienced robotic surgeon. Our technique utilized two unidirectional barbed sutures, commenced at 5 O'clock in clockwise and counterclockwise directions until they met and knotted together at 11 O'clock (Fig. 1). Based on our experience, we recommend against starting and finishing at the midline to improve the visibility during each consecutive suture placement and the subsequent surgical knot.

In terms of suture distributions, our technique put a heavier emphasis on the posterior anastomosis, with posterior sutures placed on the bladder mucosa being more closely located to each other, as opposed to the more anteriorly placed sutures. The benefits of posterior fixation have been previously demonstrated, such as by Rocco et al., to promote earlier return of urinary continence.[7,8] The addition of anterior fixation may provide some benefits in the early postoperative phase but without significant additional value in long-term continence outcomes.[9–11]

For all cases of TV SP-RARP, resection was started by first marking the vesicoprostatic junction at the bladder mucosa with electrocautery (Fig. 2). We postulate that a greater prostate specimen contributes to a larger bladder defect, which can influence the number of VUA sutures. Such correlation between specimen volume and anastomotic sutures, however, was not demonstrated in our series. Instead, the number of sutures passed in the more recent 20 cases of TV SP-RARP were shown to be significantly lower despite the larger specimen volumes compared to the first 20 cases. Intraoperatively, the reduced number of suture needles passed in recent cases contributed to a significantly faster operating time.

The marked improvement can also be credited to the learning curve of an experienced surgeon after performing more than 100 cases of TV SP-RARP. When compared to TP MP-RARP, the TV SP-RARP approach offered the unique advantage of providing a clear visualization of each suture placement as it pulls the urethral stump proximally toward the bladder neck, therefore improving the economy of movement and reducing the need for additional sutures to close bladder defects following VUA.

On review of the literature, previous studies on VUA in RARP predominantly focused on the different outcomes with varying suture materials, favoring barbed sutures as utilized in our present study.[10,12–24] Despite some heterogeneities in the study design and follow-up, the incidence of anastomotic complications, such as urine leak, urinary retention, and strictures, was relatively low (Table 3).[10,12–17,19–25] We report one case of AUR in our series. The incidence of AUR following RARP was relatively uncommon with risk previously estimated to be <5%.[26–28] Different risk factors have been proposed with the most important determinant being an early Foley catheter removal of <4–5 days considering the risk of postoperative edema.[26]

Despite our patient having his Foley catheter removed on POD3, this was not a deviation from our routine clinical practice with most patients who underwent TV SP-RARP having their Foley removed between POD3–7. It is important to appreciate, however, that this patient had the highest number of anastomotic sutures in the group. There remains a paucity of evidence in the literature surrounding the correlation between the number of VUA sutures with the risk of various complications, including postoperative edema and AUR.

The number of anastomotic sutures passed in our cohort was considerably higher when compared to prior studies on open retropubic radical prostatectomy (ORP) and laparoscopic RP (LRP). Gallo et al. compared the outcomes in

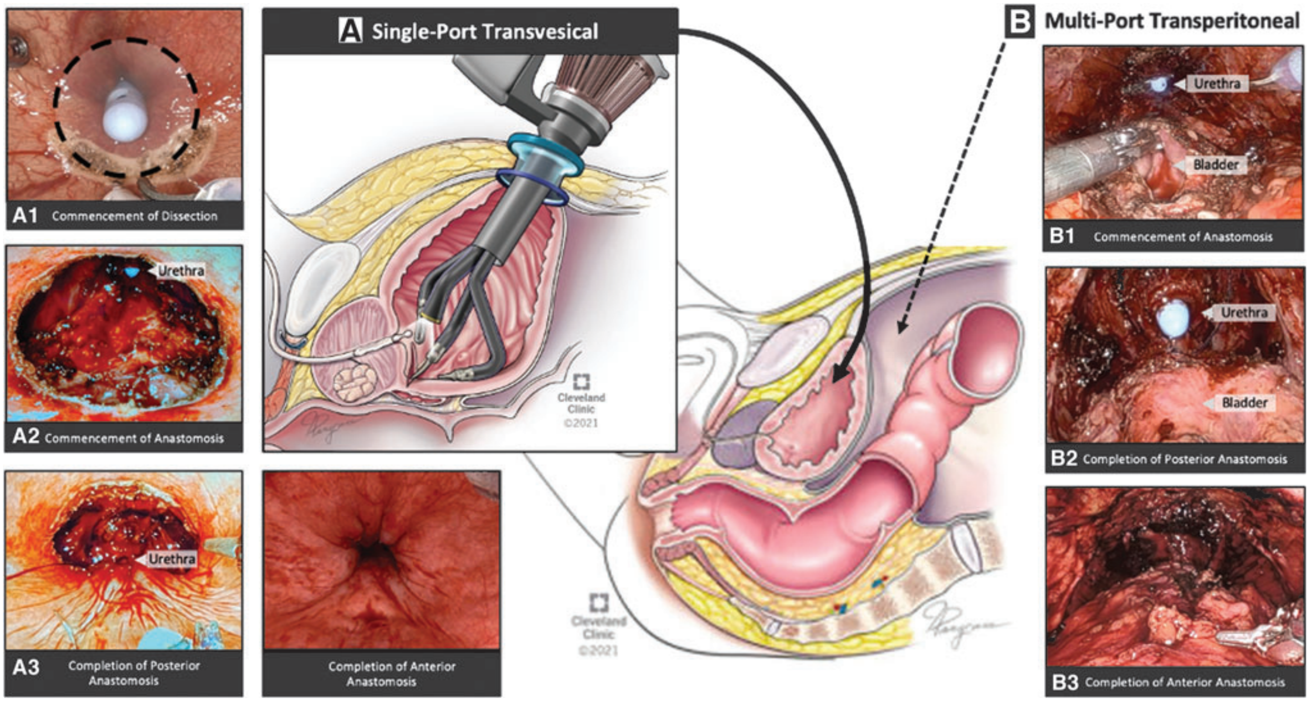


FIG. 2. **(A)** Illustration detailing the intraoperative approach for TV SP-RARP; **(A1)** intraoperative *top-down view* at the commencement of prostate dissection; **(A2)** *top-down view* at the commencement of VUA; **(A3)** *top-down view* following the completion of posterior anastomosis; and **(A4)** *top-down view* at the completed VUA and reconstructed bladder neck. **(B1)** Intraoperative view during a TP MP-RARP with the urethral lumen and bladder mucosa exposed, at the commencement of VUA; **(A2)** *pelvic view* at the completion of the posterior anastomosis; and **(A3)** at the completion of anterior anastomosis. MP = multiport; TP = transperitoneal.

ORP patients who underwent VUA with just two, four, and six monocryl sutures. Although intraoperative leaks were initially demonstrated in up to 10% of patients who had a two-suture anastomosis, no leaks were identified on cystogram on POD14 before Foley catheter removal. The intraoperative leaks were managed with fibrin sealant, rather than necessitating placements of additional sutures.[29] A later study comparing a two-suture and four-suture VUA in ORP identified an 8% incidence of postoperative urine leak in both groups that resolved spontaneously and with other perioperative and functional outcomes remaining identical.[30] For LRP, at least two main approaches of VUA have been described.

Traditionally, VUA was constructed using 6–10 interrupted sutures with intracorporeal knots.[31] In 2003, van Velthoven et al. popularized the single-knot running anastomosis technique starting at the posterior aspect of the bladder with approximately five throws on each side until they meet at the midline anteriorly.[32] Subsequent evaluation of the technique based on 391 responding urologists showed the rarity of early and late complications with them being observed in <2% of cases.[33]

It is important to appreciate that there has been an increasing role of the TV approach in patients with previous abdominal surgery. Hence, throughout our experience, we have encountered several circumstances where approximating the bladder neck to the urethral stump during VUA can be proven to be difficult. To troubleshoot, we would first recommend decreasing the pneumovesical pressure, which can be reduced to 5 mmHg. Should the operating field need to be collapsed further, surgeons can consider engaging the suction using the ROSI. Alternatively, stay sutures that were used for cystostomy at the start of the operation can be released. In the event that tissue approximation remained difficult, dissections can be extended laterally to detach the lateral attachments of the bladder and release the tension of the anastomosis between 9 and 3 O'clock.

For the remaining area of the anastomosis, if required, flap configuration with or without the 6 O'clock floor plate of the rectourethralis muscle may be pursued. Following the aforementioned steps, any remaining gaps on the anterior aspect of the VUA can be closed with a reverse tennis racquet suture configuration.

Our study is not without its limitations. The first pertained to the retrospective nature and the small number of cases in our series. Twenty cases were selected for each group given our preliminary finding on the learning curve of TV SP-RARP with perioperative improvements identified following 20 cases. Given our focus on the description of our refined technique based on the most recent cases of TV-SP, our follow-up data were relatively short and limited. Hence, it may be too early to capture long-term complications, such as bladder neck or anastomotic strictures. In addition, cystoscopic evaluation was not routinely performed on all patients following RARP. Hence, we relied on other proxies such as changes in IPSS or uroflowmetry parameters that may raise suspicion toward the presence of such complications, which can then be investigated with cystoscopy.

Similarly, retrograde cystogram was not routinely done to investigate urine extravasation. Nevertheless, despite the shorter duration of indwelling Foley catheter duration in our SP TV-RARP series and with all patients linked to

Table 3. Previously Published Studies on Vesicourethral Anastomosis in Robot-Assisted Radical Prostatectomy

Authors (year)	*Study type*	n	*Suture type*	*Follow-up duration*	*Urine leak*	*Urinary retention*	*Continence*	*Strictures*[a]
Qi et al. (2023)[18]	Retrospective	38	Unidirectional; 3-0 V-Loc™; periurethral approximation	3 months	—	—	Immediate: 71.1% 1 month: 76.3% 3 months: 94.7%	—
		37	Unidirectional; 3-0 V-Loc; standard approach, NOS	3 months	—	—	Immediate: 37.8% 1 month: 43.2% 3 months: 78.4%	—
Rajih et al. (2020)[19]	Prospective	141	Bidirectional; 3-0 Monocryl®	24 months	0%	—	1 month: 56% 3 months: 73% 6 months: 84% 12 months: 91%	0%
		181	Bidirectional; V-Loc 180	24 months	0%	—	1 month: 26% 3 months: 46% 6 months: 60% 12 months: 72%	0%
Porreca et al. (2018)[17]	Prospective	121	Bidirectional; 3-0 barbed Filblock®	3 months	0%	—	3 days: 45% 7 days: 75% 1 month: 88% 3 months: 94%	—
Haga et al. (2018)[12]	Prospective	50	Bidirectional; 3-0 V-Loc 180	6 months	0%	—	More common at 1 and 3 months	—
		38	Bidirectional; 3-0 polydioxanone (PDS II) suture	6 months	0%	—		—
Chen et al. (2015)[25]	Prospective	350	Unidirectional; 3-0 Monocryl	2 weeks	1.4%	—	—	5.7%
Zorn et al. (2012)[23]	Prospective RCT	33	Unidirectional; 3-0 Monocryl	Mean: 6.2 months	0%	0%	1 month: 64% 3 months: 76% 6 months: 88%	0%
		33	Unidirectional; 3-0 V-Loc 180	Mean: 6.2 months	0%	0%	1 month: 69% 3 months: 81% 6 months: 92%	0%
Manganiello et al. (2012)[14]	Prospective	35	Unidirectional; 3-0 V-Loc	5 months	8.6%[b]	—	2 months: 76% 5 months: 88%	0%
		35	Unidirectional; 3-0 Monocryl	5 months	5.7%[b]	—	2 months: 56% 5 months: 88%	0%
Massoud et al. (2013)[15]	Prospective	40	Unidirectional; 3-0 V-Loc	12 months	—	—	97.5%	2.5%
		40	Unidirectional; 2-0 braided coated polyglactin (Vicryl)	12 months	—	—	95%	2.5%
Hemal et al. (2012)[13]	Prospective	25	Unidirectional; 3-0 Monocryl	6 months	0%	0%	—	0%
		25	Unidirectional; 3-0 V-Loc 180	6 months	0%	0%	—	0%
		5	Unidirectional; 3-0 Quill SRS™	6 months	0%	0%	—	0%
Polland et al. (2011)[16]	Prospective	42	Unidirectional; 3-0 Monocryl	Mean 9.4 months	0%	—	6 weeks: 48% 6 months: 84%	0%
		42	Unidirectional; 3-0 V-Loc	Mean 9.4 months	0%	—	6 weeks: 52% 6 months: 88%	0%
Sammon et al. (2011)[20]	Prospective RCT	31	Unidirectional; 3-0 Monocryl	Median 44.5 months	3.2%	0%	6 weeks: 25%	0%
		33	Unidirectional; 3-0 V-Loc	Median 43 months	0%	0%	6 weeks: 38.7%	0%

(*continued*)

Table 3. (Continued)

Authors (year)	*Study type*	n	*Suture type*	*Follow-up duration*	*Urine leak*	*Urinary retention*	*Continence*	*Strictures*[a]
Zorn et al. (2011)[24]	Prospective	30	Unidirectional; 3-0 V-Loc 180	Mean: 3.3 months	0%	0%	1 month: 47% 3 months: 65%	0%
Tewari et al. (2010)[21]	Prospective	50	Unidirectional; 3-0 V-Loc 180	—	2%[b]	0%	—	—
		50	Unidirectional; 3-0 poliglecaprone 25	—	0%	0%	—	—
Williams et al. (2010)[22]	Prospective RCT	36	Bidirectional; 3-0 polyglactin 910 (Vicryl)	—	20%[b]	—	—	—
		45	Bidirectional; 3-0 V-Loc	—	2.8%[b]	—	—	—
Koliakos et al. (2010)[10]	Prospective	23	Unidirectional; 3-0 Monocryl; posterior and anterior fixation	7 weeks	0%	—	Mean time to continence: 23.6 days	0%
		24	Unidirectional; 3-0 Monocryl; Van Velthoven	7 weeks	0%	—	Mean time to continence: 37.9 days	0%

[a]Includes bladder neck and anastomotic strictures.
[b]Evaluated with cystogram.
RCT = randomized controlled trial.

postoperative care services at our institution, we have yet to identify any case of symptomatic urine leak that warranted the need to extend Foley catheter duration or other types of management.

Conclusion

We provided the first description of the VUA technique for TV SP-RARP. Despite the small working space within the confines of the bladder, the maneuverability of the SP robotic platform allowed for uncomplicated completion of each VUA. The number of anastomotic sutures passed was not influenced by the size of the intraoperative specimen. The learning curve of an experienced robotic surgeon was evident in our series as demonstrated by the reduced number of sutures and faster anastomosis times while maintaining favorable perioperative and early functional outcomes.

Authors' Contributions

Conceptualization and design: N.A.S. and J.H.K.

Data acquisition: N.A.S., E.L.F., R.R.-C., J.S.C., and A.G. Statistical analysis and data interpretation: N.A.S. Drafting of the article: N.A.S. Critical revision of article: J.H.K. and E.L.F.

Author Disclosure Statement

J.H.K. is a speaker for Intuitive Surgical, Inc., and is a consultant for EndoQuest Robotics, Method AI, and VTI. The remaining authors have no conflicts of interest to disclose.

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Abbreviations Used

ASA = American Society of Anesthesiologist
AUR = acute urinary retention
BMI = body mass index
CCI = Charlson Comorbidity Index
cT = clinical T
IPSS = International Prostate Symptoms Score
IRB = Institutional Review Board
L BH = left-side backhand
L FH = left-side forehand
LRP = laparoscopic radical prostatectomy
LUTS = lower urinary tract symptoms
MB = modified backhand
MP = multiport
NCCN = National Comprehensive Cancer Network
ORP = open retropubic radical prostatectomy
PSA = prostate specific antigen
PVR = postvoid residual
RARP = robot-assisted radical prostatectomy
R BH = right-side backhand
RCT = randomized controlled trial
R FH = right-side forehand
ROSI = Remotely Operated Suction Irrigation
RP = radical prostatectomy
SP = single port
TP = transperitoneal
TV = transvesical
VUA = vesicourethral anastomosis

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Comment on: "Vesicourethral Anastomosis in Transvesical Single-Port Robotic Radical Prostatectomy: A Technical Description and Perioperative Outcomes" by Soputro *et al.*

Aditya Sathe, MD,[1] Luke A. Shumaker, MD,[1] and Soroush Rais-Bahrami, MD, MBA[1–3]

We commend the authors on their exemplary demonstration of an elegant surgical approach that may improve postoperative recovery and quality-of-life for patients undergoing radical prostatectomy. This technique demonstrates the general progress resulting from advances in surgical platforms and increasingly adept robotic surgeons. The result is a spectrum of new approaches to well-established surgical procedures including radical prostatectomy, a procedure that has evolved for over a century. The transvesical single-port robotic-assisted radical prostatectomy (RARP) and anastomotic technique detailed in this issue of the *Journal of Endourology*, is an excellent example of how previously limiting anatomic spaces can now be used with excellent results and patient benefit.[1] This new landscape allowing for multiple surgical approaches has made the publishing of these techniques and associated outcomes imperative.

Although the efficacy of single-port transperitoneal RARP and single-port extraperitoneal RARP have been reported on previously, this study is the first detailed technical illustration of a transvesical vesicourethral anastomosis using the single-port robotic device.[2,3] By directly comparing the first 20 cases performed by a single-surgeon to the most recent 20 cases in a total series of 189 patients, the authors define an expected learning curve for surgeons beginning to employ this technique. The experimental group and multiport comparator groups are limited in numbers, but the improved immediate continence rates and higher International Prostate Symptom Score observed with the transvesical approach are encouraging and certainly warrant further study with larger patient series in the future.

The defining feature of single-site, minimally invasive robotic surgery is the ability to perform complex movements in highly confined, deep anatomic spaces such as the approach to the bladder neck. The transvesical vesicourethral anastomosis technique described here is a perfect example of what is now possible with the purpose-built single-port robotic platform. The implications of this technical description and reported clinical experience extend beyond prostate cancer management to a broad spectrum of urologic and nonurologic surgeries. Cancer survivorship and transgender care have advanced significantly in the era of single-site, minimally invasive surgery, and these advances will almost certainly continue as techniques are shared and outcomes published.[4,5] Robotic surgeons and trainees have much to be excited about as the skills for operating in previously limiting anatomic spaces via remote console will likely be transferrable to platforms on the horizon that will allow even smaller incisions or completely orthotopic surgeries.[6] Again, we congratulate the authors on this well-described, well-illustrated technique and count it as another data point corroborating the expanding capabilities of minimally invasive surgical techniques.

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Effect of Peritoneal Interposition Flap to Prevent Symptomatic Lymphoceles in Robot-Assisted Radical Prostatectomy with Pelvic Lymphadenectomy: A Meta-Analysis and Systematic Review

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Abstract

Background: This systematic review and meta-analysis investigated whether peritoneal interposition flap (PIF) prevent lymphocele formation after robot-assisted radical prostatectomy with extended pelvic lymph node dissection.
Materials and Methods: We performed a systematic review and cumulative meta-analysis of the primary outcomes according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, Assessing the Methodological Quality of Systematic Reviews guidelines and risk-of-bias tool. Five databases, including Medline, PubMed, Cochrane Library, Scopus, and Web of Science, were systematically searched. The time frame of the search was set from the creation of the database to February 2023.
Results: Meta-analysis of symptomatic lymphoceles (sLCs) rates revealed significant difference between PIF and no PIF group (eight studies pooled; $p = 0.005$), The sLCs rates account for 2.6% (28/1074) and 7.1% (85/1186) in the PIF and no PIF group, respectively. The resulting odds ratio was 0.34 (95% confidence interval: 0.16–0.73), taking into account the heterogeneity of these studies ($Q = 14.32$, $p = 0.05$; $I^2 = 51\%$).
Conclusion: PIF is an effective intraoperative modification on the prevention or reduction of sLC, which is worthy of further clinical promotion.
Systematic Review Registration: National Institute for Health and Care Research, identifier CRD42022364461

Keywords: peritoneal rotation flap, peritoneal interpolated flap, peritoneal reapproximation, pelvic lymphadenectomy, meta-analysis, systematic review

Introduction

Prostate cancer is one of the most prevalent malignant tumors affecting the urogenital system. According to the Global Cancer Statistics Report 2020, which was published by the International Agency for Research on Cancer in February 2021, prostate cancer accounted for 7.3% of all malignant tumors worldwide, with 1,414,259 new cases in 2020, making it the third most common cancer after breast and lung cancer. In addition, there were 375,304 prostate cancer deaths in 2020, which accounted for 3.8% of all malignant tumors and ranked eighth in terms of mortality rate.[1] Since the introduction of robot-assisted laparoscopic prostatectomy (RALP) in the United States in 2000, it has rapidly become the preferred surgical approach for prostate cancer, favored by many doctors and patients. In particular, RALP has been widely accepted by young doctors.[2]

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Robot-assisted radical prostatectomy (RARP) combined with pelvic lymph node dissection is a major cause of symptomatic lymphoceles (sLCs), with a prevalence ranging from 2% to 10%.[3] Large cysts can compress the bladder, causing or exacerbating voiding irritation syndrome.[4] Furthermore, compression of the external iliac vessels can result in deep vein thrombosis in the lower extremities and secondary lymphatic inflammation.

We investigated the impact of various intraoperative modifications on the prevention or reduction of sLCs.[4,5] In 2015, Lebeis et al. introduced the peritoneal interposition flap (PIF) as a simple intraoperative modification to reduce sLCs in patients undergoing RALP.[6] Based on follow-up studies,[7–13] PIF currently appears to be the most promising method for reducing or preventing robotic pelvic lymph node dissection (PLND)-related sLCs. Various surgical techniques have been proposed by different authors with the aim of reducing the incidence of lymphocele formation during RARP. These techniques and methods involve manipulation of the peritoneum, including dissection, fixation, and suturing.

Authors differ in their specific approach to the surgical procedure. Lebeis et al. suggested creating a peritoneal window during the pelvic lymph node dissection.[6] Dal Moro and Zattoni employed the Preventing Lymphocele Ensuring Absorption Transperitoneally (P.L.E.A.T.) technique, which includes lymphatic vessel clearance, reanastomosis, and suturing of a triangular flap onto the peritoneum.[9] Stolzenburg et al. described the technique of four-point peritoneal flap fixation (4PPFF).[12] Lee et al. inverted and sutured the peritoneum inward to cover the area of lymph node dissection.[11] Bründl et al. followed Lebeis' original method.[8] Student Jr et al. performed peritoneal separation and fixation onto the pubic bone.[13] Gloger et al. utilized bilateral peritoneal flap technique.[10]

Although there are differences in the specific procedural steps, the common goal of all these techniques and methods is to prevent lymphatic fluid accumulation and lymphocele formation. In addition, the timing of these surgeries is consistent, as they are performed during RARP, usually concurrent with pelvic lymph node dissection. However, a comprehensive analysis of existing studies is lacking. As a result, we conducted further studies on PIF and performed a meta-analysis comparing sLC rates between PIF and no PIF groups after PLND in RALP.

Materials and Methods

Literature search

This meta-analysis has been reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards and is fully compliant with the PRISMA 2020 statement.[14] The quality assessment was performed according to Assessing the Methodological Quality of Systematic Reviews 2 and risk-of-bias tool (RoB2), which was rigorously described and was fully consistent for each question.[15,16] This systematic review has been registered with PROSPERO (CRD42022364461).

The literature search and selection process were performed independently by two authors, with disagreements between authors resolved by negotiation of a third reviewer (T.W.) when an agreement could not be reached. We systematically and comprehensively searched five databases, PubMed, Embase, Scopus, Medline, and Cochrane, for published trials up to February 2023. The following MeSH and main keywords were used: ''prostate cancer,'' ''robot-assisted radical prostatectomy'' ''pelvic lymph node dissection,'' ''symptomatic lymphoceles,'' ''peritoneal flap'' (or) ''peritoneal interposition flap'' (or) ''P.L.E.A.T.,'' and associated terms. The language was not restricted. Also, manual searches of the reference lists in the selected studies to retrieve all relevant data have been implemented.

Eligibility criteria

We included only retrospective, prospective, and randomized controlled trials (RCTs) study designs. The inclusion criteria of the meta-analysis were defined as follows: retrospective, prospective, or RCTs studies on RARP attributable to localized prostate cancer, in which the influence of a PIF on the formation of sLCs was analyzed comparatively. The following exclusion criteria were considered for our study: (1) All non-RCTs, nonretrospective studies, nonprospective studies, case series, and case reports will be excluded. (2) Studies (any RCTs) that could not provide available outcome data for extraction will be excluded. (3) Trials not reported in English. (4) Editorials, conference abstracts, letters, or expert opinions. (5) Laboratory or animal studies.

Two authors (J.Z. and L.Z.) independently assessed the identified studies and reviewed the abstracts to select full articles.

Discussion was performed among all authors to resolve any disagreements. The study endpoint of sLCs was identical in the selected studies ([fever as a symptom of an infected lymphocele, lower abdominal pain, lower extremity swelling, and/or deep vein thrombosis] in combination with a pelvic fluid formation).

Study quality assessment

Based on the initial search results, the Newcastle-Ottawa Scale (NOS) was used to assess the quality of the retrospective and prospective studies.[17] This scale includes the three domains of selection, comparability, and exposure, with scores above six stars identifying high-quality studies. Student Jr. et al.[13] and Gloger et al.[10] were RCTs, therefore, RoB2 was used for assessing the quality too.[15]

Data extraction

Two review authors (Junjie Zhou and Lin Zhou) independently extracted the data from the included studies using an Excel spread sheet/previously designed data extraction form. Extracted data will be then cross-checked between the two authors, and any discrepancy resolved by consensus discussion. Data were to be extracted from the studies, comprising study characteristics (first author, year of publication, country, study design, study settings, study period, participants of RARP+PLND, participants of RARP+PLND+PIF), participants' characteristics [age, body mass index (BMI) and lymph nodes count], and perioperative (including fever as a symptom of an infected lymphocele, lower abdominal pain, lower extremity swelling, and/or deep vein thrombosis in combination with a pelvic fluid formation) outcomes.

Statistical analysis

The primary endpoint of this meta-analysis was the sLC rate and assessed using odds ratios (ORs). We divided patients into intervention groups (PIF), control groups (no PIF) based on whether PIF was performed. We conducted this systematic review according to the suggested present protocol and the recommendations by The Cochrane Reviewers' Handbook.[18] The statistical analysis was performed by me Dr. Junjie and was further confirmed by another reviewer. We did the meta-analysis using Review Manager Software (RevMan version 5.4; Cochrane Collaboration, Oxford, UK). I reported 95% confidence intervals (95% CIs) and *p*-values for all outcome indicators.

The q and χ^2 tests were used to verify the level of heterogeneity among the included studies. Differences were considered significant if $I^2 > 50\%$. Based on the results of the heterogeneity test, $I^2 \geq 50\%$ or $p < 0.1$, a random-effects model was used to pool the estimates. Conversely, a fixed-effects model was utilized. Meta-analyses of continuous

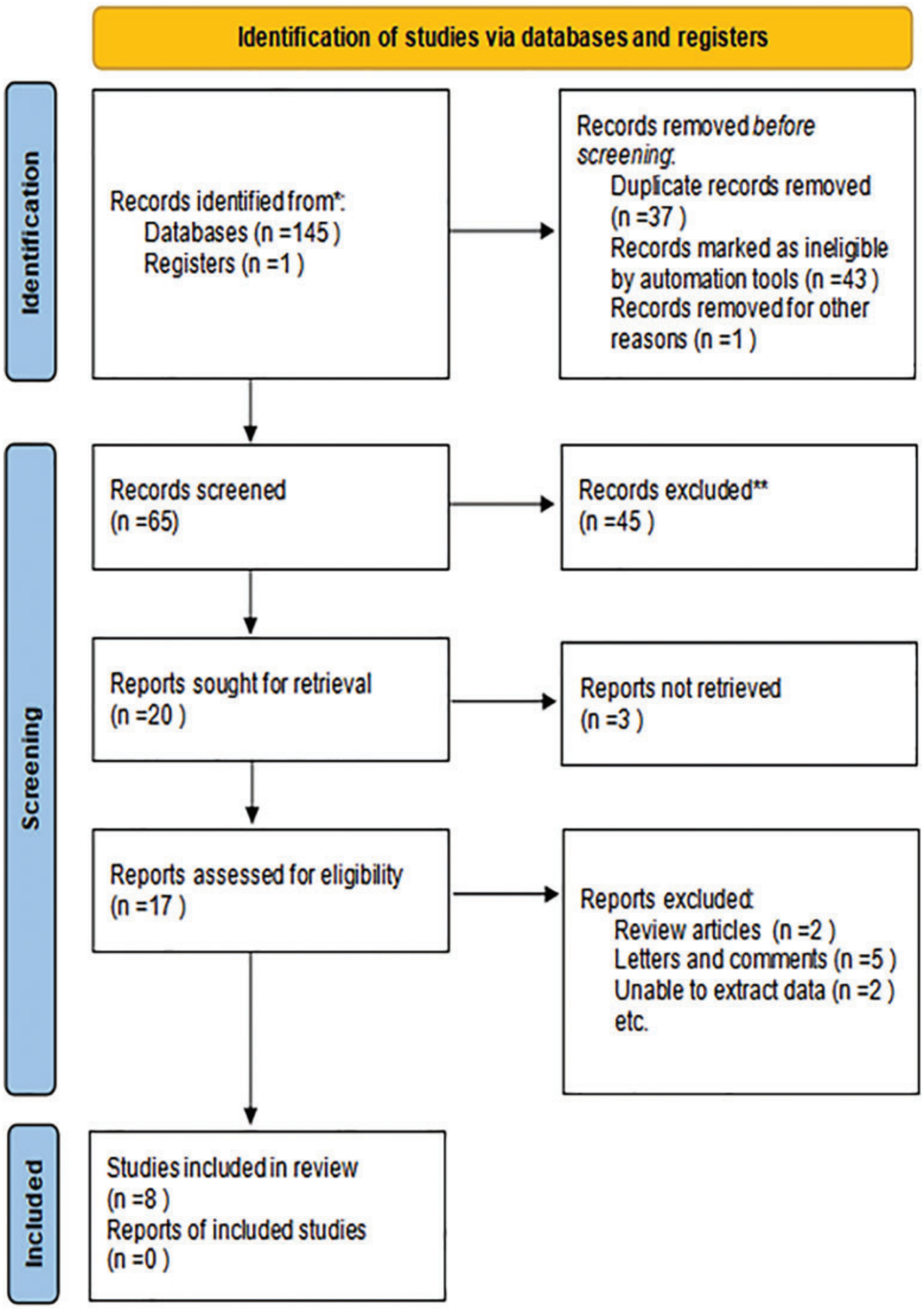

FIG. 1. Flow diagram of the study selection process. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Color images are available online.

Table 1. Baseline Data for Studies Included in the Meta-Analysis

References	Year	Study	Center	Procedure	Sample (n)	LN count (median with IQR or mean ± SD)	p	BMI, kg/m² (median with IQR or mean ± SD)	p
Lebeis et al.[6]	2015	Retrospective	Single center	PIF	77	4.2 ± na	0.420	28.9 ± na	0.520
				No PIF	77	3.8 ± na		29.3 ± na	
Dal Moro and Zattoni[9]	2017	Retrospective	Single center	PIF	176	10 (6.5–15)	<0.001	NA	NA
				No PIF	195	5 (0–11)		NA	
Stolzenburg et al.[12]	2018	Retrospective	Single center	PIF	193	15 (range: 5–33)	0.908	26.9 (range: 20.8–42.3)	0.815
				No PIF	193	15 (range: 6–32)		27.2 (range: 19.9–41.8)	
Boğa et al.[7]	2020	Retrospective	Single center	PIF	41	15.2 ± 7.9	0.070	26.4 ± 7.4	0.290
				No PIF	38	19 ± 10.7		27.4 ± 5.0	
Lee et al.[11]	2020	Retrospective	Single center	PIF	117	19 ± 8.5	0.999	28.6 ± 4.5	0.314
				No PIF	201	14.7 ± 8.9		29.4 ± 5.0	
Bründl et al.[8]	2020	Prospective	Multicenter	PIF	108	15 (10–22)	0.946	27.4 (25.6–29.7)	0.449
				No PIF	124	16 (11–21)		27.2 (25–29.9)	
Student Jr. et al.[13]	2022	RCT	Single center	PIF	123	17 (6–19)	0.962	28.1 (19.72–43.28)	0.275
				No PIF	122	17 (7–56)		28.9 (20.57–43.94)	
Gloger et al.[10]	2022	RCT	Multicenter	PIF	239	14 (11–18)	0.4	26 (25–29)	NA
				No PIF	236	14 (11–19)		27 (25–30)	

BMI = body mass index; IQR = interquartile range; LN = lymph nodes; NA = not available; PIF = peritoneal interposition flap; RCT = randomized controlled trial; SD = standard deviation.

variables was performed using the inverse variance method, and dichotomous variables were pooled using the Mantel–Haenszel method. In addition, further sensitivity analyses were performed for those studies with a high degree of heterogeneity ($I^2 \geq 50\%$ or $p < 0.1$)

Results

Description of studies

The researchers retrieved 146 records from five databases. After reading titles and author names, 37 duplicate studies were excluded. When study topics, abstracts, and keywords were considered, 45 records unrelated to the study topic were excluded, and the remaining 17 studies were reviewed for completeness. Complete information could not be extracted for two articles, there were also seven reviews and letters, so we excluded them.

Finally, five retrospective studies, one prospective study, and two RCTs studies including 2260 patients were included in the review (Fig. 1). Table 1 provides the baseline data extracted from each of the included studies. This includes the author's name, year of publication, study center, type, sample, procedure, BMI, and other records.

Quality assessment

Table 2 shows the NOS study quality rating scores for the included studies. All studies were high-quality, with ratings of more than six stars. Figure 2 shows the conclusions of the quality assessment based on the RoB2.[17]

Outcomes

Meta-analysis of sLCs rates revealed significant difference between PIF and no PIF group (eight studies pooled; $p = 0.005$), The sLCs rates account for 2.6% (28/1074) and 7.1% (85/1186) in the PIF and no PIF group, respectively (Fig. 3). The resulting OR was 0.34 (95% CI:

Table 2. Quality Score of Included Studies Bases on the Newcastle-Ottawa Scale

Study	Selection			Comparability			Exposure			Total stars
	REC	SNEC	AE	DO	SC	AF	AO	FU	AFU	
Lebeis et al.[6]	1	1	1		1	1		1	1	7
Dal Moro and Zattoni[9]	1	1	1	1	1			1	1	7
Stolzenburg et al.[12]	1	1	1	1	1	1	1	1	1	9
Boğa et al.[7]	1	1	1	1	1			1	1	7
Lee et al.[11]	1	1	1	1	1		1	1	1	8
Bründl et al.[8]	1	1	1	1	1	1		1	1	8

AE = ascertainment of exposure; AF = study controls for other important factors; AFU = adequacy of follow-up of cohort (≥80%); AO = assessment of outcome; DO = demonstration that outcome of interest was not present at start of study; FU = follow-up long enough for outcomes to occur; REC = representativeness of the cohort; SC = study controls most important factors; SNEC = selection of the none posed cohort.

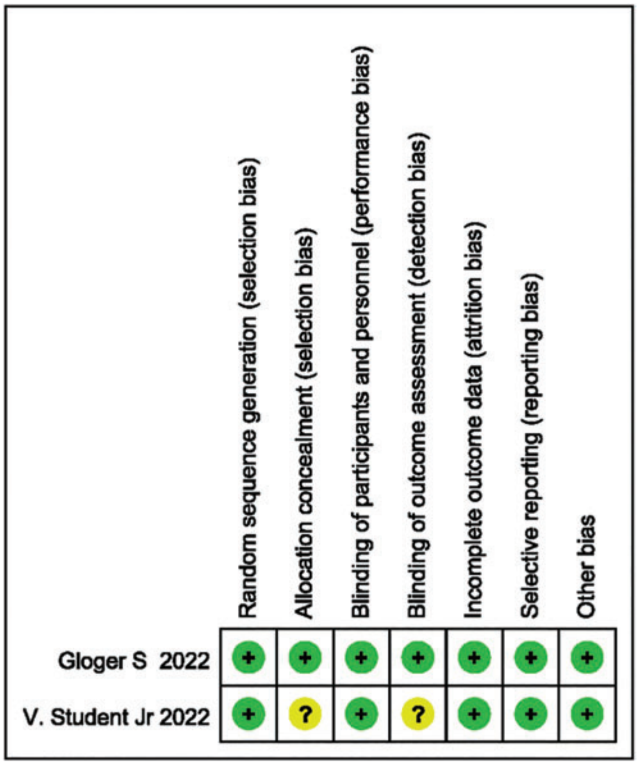

FIG. 2. Risk of bias for included randomized controlled trials. Color images are available online.

0.16–0.73), taking into account the heterogeneity of these studies ($Q=14.32$, $p=0.05$; $I^2=51\%$; Fig. 3).

Discussion

The results of the meta-analysis of the eight studies mentioned earlier showed that the sLC rate was reduced 66% (95% CI: 1%–99%) in the PIF group. In all studies, the rationale for PIF to reduce or prevent sLCs is the same: to ensure that lymphatic fluid can enter the peritoneal cavity from the pelvis and to increase the area of peritoneal absorption.

In 2015, Lebeis et al. first proposed and implemented PIF,[6] a procedure performed by two surgeons in a single center who used the existing peritoneum covering the bladder to create a peritoneal window that allowed lymphatic fluid to continue into the peritoneal cavity to be reabsorbed in the event of a lymphatic fistula, thereby reducing the incidence of symptomatic lymphatic cysts. A total of 154 eligible patients were included in this study, and 77 patients who underwent PIF were compared with 77 patients who did not, suggesting that PIF is beneficial in reducing the incidence of postoperative symptomatic lymph node cysts.

Dal Moro and Zattoni proposed P.L.E.A.T.[9] performed by the same surgeon (Fabrizio Dal Moro) in a single center, which to some extent avoids bias arising from differences in the proficiency or skill of multiple surgeons. One hundred seventy-six patients with PIF compared with 195 patients without PIF, the P.L.E.A.T. technique is a rapid, cost-effective, easy-to-perform, and safe method to reduce the risk of sLC after transabdominal robotic PLND.

Stolzenburg et al.[12] modified the method proposed by Lebeis et al.[6] All four surgeons sutured the peritoneal abdominal wall incision ends (anterior and lateral pelvic walls on both sides) at four points after extended pelvic lymph node dissection (ePLND), exposing the peritoneal surface to the iliac vessels and closed fossa, called 4PPFF, the larger peritoneal exposure area of 4PPFF facilitates more fluid absorption compared with the two-point fixation method of Lebeis et al.[6] Also, peritoneal fixation prevents excessive bladder flexion, thus reducing postoperative urinary problems in patients. 4PPFF is a safe and effective method to prevent lymphatic cysts in patients with radical prostatectomy combined with PLND.

In the study by Lee et al. in which a single surgeon (Daniel D Eun) performed trans-anterior peritoneal RARP and PLND in all patients,[11] they retrospectively compared 117 PIF patients with 201 no PIF patients, and the procedure and outcomes were similar to Lebeis et al.[6] suggesting that the risk of symptomatic lymphoceles after RARP and bilateral PLND can be significantly reduced.

However, some scholars have argued that PIF does not provide any benefit to patients, but rather increases the operative time and the risk of lymphatic cyst formation.

Study or Subgroup	PIF Events	PIF Total	NO PIF Events	NO PIF Total	Weight	Odds Ratio M-H, Random, 95% CI
Boğa et al.[7]	5	41	2	38	11.5%	2.50 [0.46, 13.73]
Bründl et al.[8]	9	108	12	124	19.7%	0.85 [0.34, 2.10]
Dal Moro and Zattoni[9]	1	176	8	195	8.9%	0.13 [0.02, 1.08]
Gloger et al.[10]	8	239	19	236	20.5%	0.40 [0.17, 0.92]
Lebeis et al.[6]	0	77	9	77	5.6%	0.05 [0.00, 0.81]
Lee et al.[11]	0	117	12	201	5.6%	0.06 [0.00, 1.10]
Stolzenburg et al.[12]	2	193	9	193	12.8%	0.21 [0.05, 1.00]
Student Jr. et al.[13]	3	123	14	122	15.5%	0.19 [0.05, 0.69]
Total (95% CI)		**1074**		**1186**	**100.0%**	**0.34 [0.16, 0.73]**
Total events	28		85			

Heterogeneity: Tau² = 0.54; Chi² = 14.32, df = 7 (P = 0.05); I² = 51%
Test for overall effect: Z = 2.78 (P = 0.005)

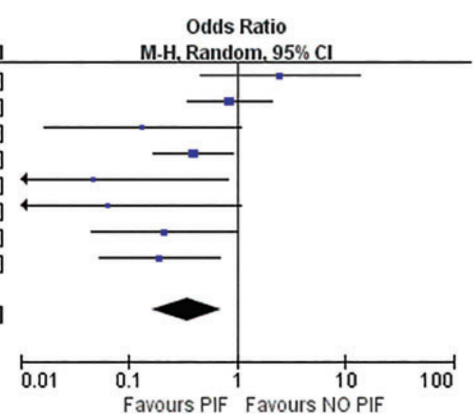

FIG. 3. Forest plot from the results of the eight studies available assessing cumulative incidence of the endpoint sLCs after RARP and PLND in the groups PIF *vs* no PIF. CI = confidence interval; M–H = Mantel–Haenszel; PIF = peritoneal interposition flap; PLND = pelvic lymph node dissection; RARP = robot-assisted radical prostatectomy; sLC = symptomatic lymphocele. Color images are available online.

In the study by Boğa et al.,[7] transperitoneal robot-assisted radical prostatectomy and ePLND were performed by two surgeons in a single center on 79 patients, respectively, and postoperatively 41 patients had PIF performed by one of the doctors, whereas the other 38 patients did not. This study was the main source of heterogeneity differences in this meta-analysis, and if the study of Boğa et al. was excluded,[7] the heterogeneity of this meta-analysis would have been greatly reduced, with I^2 dropping to 38%. We believe that this may be related to the small sample size of the single center and the proficiency and experience of the surgeon's surgical skills.

Bründl et al.[8] came to similar conclusions as Boğa et al.[7] In this single-blind multicenter prospective study, 108 patients who received PIF compared with 124 patients who did not receive PIF found that the use of PIF was not statistically significantly associated with the development of symptomatic lymphatic cysts, the reduction in the volume of lymphatic cysts, and notably, they did not significantly affect the PIF patients' postoperative urinary function in a favorable opinion.

In addition, we included two new studies in which 123 patients underwent PIF and 122 patients did not in the prospective randomized single-center unilateral blinded study of Student Jr et al. performed by two experienced surgeons,[13] who further modified the approach of Lebeis et al. by fixing a peritoneal free flap (PerFix) to the pubic bone to reduce the occurrence of lymphatic cysts.[6] Unusually, they used CT to assess for the presence of lymphatic cysts.

This is more accurate than cystography and ultrasound detection, which may also have contributed to the lower overall incidence of lymphatic cysts in patients with PerFix (24%) than in those without PerFix in the study by Student Jr et al.[13] (36%) (PerFix) significantly reduced the incidence of symptomatic lymphatic cysts. In another multicenter prospective RCT by Gloger et al.,[10] 239 patients received bilateral PIF, and 217 patients did not. Fixation of bilateral cystoperitoneal flaps to the endopelvic fascia significantly reduced the overall incidence of lymphatic cysts and the incidence of symptomatic lymphatic cysts in the treatment group.

Conclusion

Our meta-analysis showed that PIF was effective in preventing the incidence of sLCs. For patients undergoing RARP with pelvic lymphadenectomy, compared with no PIF group, the sLC rate was reduced 66% (95% CI: 1%–99%) in the PIF group. It was statistically significant ($p = 0.005$). PIF is an effective intraoperative modification on the prevention or reduction of sLC, which is worthy of further clinical promotion.

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Authors' Contributions

T.W. and X.D. conceived and designed the experiments. J.Z., L.Z., and Y.T. analyzed the data. H.S., Q.X., and X.M. contributed reagents/materials/analysis. J.Z. and S.W. wrote the article. All the authors have read and approved the final article.

Provenance and Peer Review

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Author Disclosure Statement

All the authors have nothing to declare.

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Abbreviations Used

4PPFF = four-point peritoneal flap fixation
AE = ascertainment of exposure
AF = study controls for other important factors
AFU = adequacy of follow-up of cohort (≥80%)
AO = assessment of outcome
BMI = body mass index
CI = confidence interval
CT = computed tomography
DO = demonstration that outcome of interest was not present at start of study
ePLND = extended pelvic lymph node dissection
FU = follow-up long enough for outcomes to occur
IQR = interquartile range
M–H = Mantel–Haenszel
NA = not available
NOS = Newcastle-Ottawa Scale
OR = odds ratio
PerFix = fixing a peritoneal free flap
PIF = peritoneal interposition flap
PLND = pelvic lymph node dissection
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RALP = robot-assisted laparoscopic prostatectomy
RARP = robot-assisted radical prostatectomy
RCT = randomized controlled trial
REC = representativeness of the cohort
RoB2 = risk-of-bias tool
SC = study controls most important factors
SD = standard deviation
sLCs = symptomatic lymphoceles
SNEC = selection of the none posed cohort

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Initial Experience of Robot-Assisted Simple Prostatectomy with Hugo Robot-Assisted Surgery System: Step-by-Step Description of Two Different Techniques

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Abstract

Introduction: There are only a few clinical data on nononcologic procedures performed with the new Hugo™ robot-assisted surgery (RAS) system. Robot-assisted simple prostatectomy (RASP) is a minimally invasive treatment option for benign prostatic hyperplasia, and it demonstrated equal early functional and better perioperative outcomes as compared with open simple prostatectomy. In this article, we reported the first large series of RASP performed with Hugo RAS system.
Methods: This Supplementary Video S1 is a step-by-step description of two different techniques for RASP. We analyzed the data of 20 consecutive patients who underwent RASP at OLV Hospital (Belgium) between February 2022 and March 2023. Patients baseline characteristics, perioperative and pathologic, and 1-month postoperative outcomes were reported, using the median (interquartile range [IQR]) and frequencies, as appropriate.
Results: Median age (IQR) and preoperative prostate specific antigen (PSA) were 72 (67–76) years, and 7.7 (5.0–13.4) ng/mL, respectively. A total of 11 patients experienced an episode of preoperative acute urinary retention, and 8 men had an indwelling bladder catheter at the time of the surgery. No intraoperative complication occurred, and there was no need for conversion to open surgery. Median operative and console time were 165 (121–180) and 125 (101–148) minutes. On the first postoperative day the urethral catheter was removed in 80% of the patients. Median length of stay was 3 (3–4) days. Three patients had minor postoperative complications. On final pathology report, median prostate volume was 120 (101–154) g. On postoperative uroflowmetry, median Qmax and postvoid residual were 16 (13–26) mL/s and 15 (0–34) mL, respectively.
Conclusions: This series represents the first report of surgical outcomes of RASP executed with Hugo RAS system. Awaiting study with longer follow-up, our study suggests that Hugo RAS has multiple applications, and it can ensure optimal outcomes in nononcologic procedures.

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Keywords: robotics, robot-assisted simple prostatectomy, benign prostatic hyperplasia, Medtronic Hugo RAS system, surgical technique

Introduction

Simple prostatectomy is indicated in patients with enlarged glands (>80 g) who present with recurrent or persistent lower urinary tract symptoms, acute urinary retention, significant symptoms from bladder outlet obstruction (BPO) not responsive to medical therapy, recurrent gross hematuria of prostatic origin, bladder calculi secondary to obstruction or pathophysiologic changes of the kidneys, ureters, or bladder secondary to prostatic obstruction.[1]

Robot-assisted simple prostatectomy (RASP) is a minimally invasive surgical technique first described by Sotelo et al. in 2008 as an alternative to open simple prostatectomy (OSP) for treating benign prostatic hyperplasia.[2] Instead of traditional open surgery, RASP employs a robotic system to remove the enlarged prostate gland through small abdominal incisions.

Studies have shown that RASP offers better perioperative outcomes and equal early functional outcomes compared with OSP, including shorter hospital stay, reduced blood loss, lower risk of blood transfusion, and shorter learning curve.[3,4]

RASP is particularly well suited for patients with large prostate glands or for those who have concomitant bladder diverticulum and/or bladder stones.[5,6]

Despite these potential benefits, the widespread adoption of RASP is currently limited by a few factors. First, the availability of robotic surgery platforms is still limited in some regions. In addition, the cost-effectiveness of RASP is one of the most important factors involved in the application of this surgical technique. However, recent studies demonstrated that, in the past decade, with the innovation of robotic surgery and the introduction of dedicated robotic training programs, the related costs for robotic surgery might be reduced because of the significantly decreased length of stay, rate of complications, and readmissions.[6–9]

Furthermore, in the coming years the global market for surgical robots is expected to grow, with new companies entering the market, and leading to potential cost savings thanks to less expensive devices and an increased competition between companies.[7,8] In this context, on February 2022, the Medtronic modular multiport robotic system, HUGO robot-assisted surgery (RAS) system, has received the CE Mark approval for urologic, gynecologic, and general surgical procedures in adults. The new HUGO™ RAS consists of a system tower, an open console with innovative hand controllers with a ‘‘pistol-like'' design and four independent arm carts.

There are limited clinical data on nononcologic procedures performed with the new HUGO RAS system in urology. In this Supplementary Video S1, we describe two surgical techniques of RASP and report the first series of RASP performed with this new robotic platform.

Materials and Methods

Patient population and study outcomes

We analyzed data of 20 consecutive patients who underwent RASP at OLV Hospital (Aalst, Belgium) between February 2022 and March 2023. Procedures were performed by four experienced robotic surgeons using the novel HUGO RAS surgical platform.

Our main goal was to describe step-by-step two different surgical techniques for RASP (anterior and posterior approach). Patients' baseline characteristics, perioperative outcomes, pathologic outcomes, and 1-month postoperative outcomes were reported. Before surgery, all patients with elevated prostate specific antigen levels underwent MRI to exclude the presence of area with Prostate Imaging Reporting and Data System score ≥3 and the need for a prostate biopsy. Complications were prospectively recorded according to the Dindo–Clavien classification.[9] All data are reported using the median (interquartile range [IQR]) and frequencies (proportions), as appropriate. Owing to the low number of procedures, we were not able to compare surgical outcomes between the two different techniques described in the Supplementary Video S1.

Surgical techniques

After general anesthesia, the patients were placed in a supine 25° to 30° Trendelenburg position. The 11-mm endoscope port was placed on the midline above the umbilicus, ~16 to 18 cm from the target anatomy, as previously described.[10,11] Other two 8-mm robotic ports were placed under vision on a transversal line 5 cm below the optical port and at least 8 cm between each other, and 2 cm away from bony prominences. Then, the fourth arm port is placed on the same plane of the endoscope port, at least 8 cm from the surgeon's left-hand port.

Finally, one 5-mm laparoscopic trocar and one 12-mm AirSeal© system port were positioned in the right hemiabdomen for the bedside assistant (Fig. 1).[12]

To guarantee enough space and maneuverability for the bedside assistant, three carts were docked from the left side of

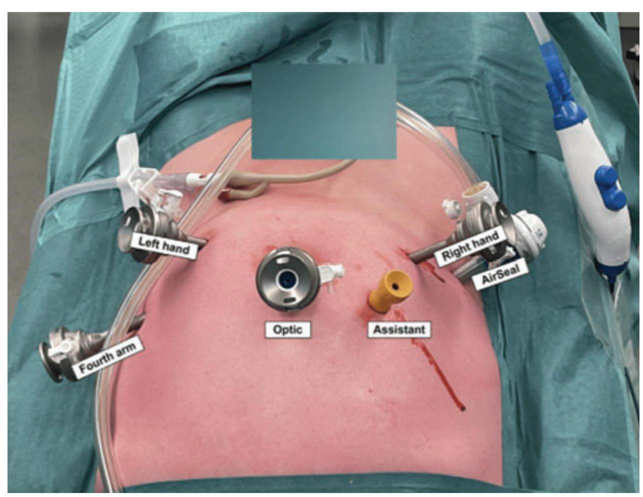

FIG. 1. Trocar placement for RASP. The optic trocar is an 11-mm trocar, whereas all the other robotic trocars are 8 mm. The assistant trocars are 5 and a 12 mm AirSeal. RASP, robot-assisted simple prostatectomy. Color images available online.

the patient and one from the right side. The tilt and docking angles of each cart were already described and are illustrated in Figure 2.[13,14]

All procedures were performed with a 0° lens using three robotic instruments: monopolar curved scissors, Maryland bipolar forceps, or Cadiere forceps and needle driver. For both techniques, the procedures were concluded by removing the specimens from the camera port and closing the robotic ports.

Anterior approach. The first procedure shown in the Supplementary Video S1 is performed using an anterior transperitoneal approach. The medial umbilical ligament is medialized with the nondominant hand, and the peritoneum is then incised where the ligament and vas deferent cross. The paravesical space is carefully dissected until the endopelvic fascia is exposed. This procedure is repeated bilaterally, and finally, the urachus is coagulated and cut. The bladder is opened with a longitudinal cystostomy starting at the level of the prostate-vesical junction. Eventual concomitant bladder stones are removed in this phase through the cystostomy. For better exposure, the two edges of the bladder can be fixed to the abdominal wall using two extracorporeal straight needles. A traction stitch can be placed in the middle lobe to increase exposure. The bilateral ureteral orifices must be identified to avoid injury.

The plane between the prostatic adenoma and the pseudocapsule is developed using sharp and blunt dissection, starting from the 6 O'clock position to the right lobe and then repeating the same procedure to the left lobe. Finally, the prostatic urethra is transected at the apex, and the adenoma is completely dissected. Then the prostatic fossa is carefully inspected for hemostasis, obtained with bipolar or monopolar electrocoagulation, and for any remaining adenoma nodules. A single-layer 3-0 V-loc running suture is utilized to retrigonize the prostatic fossa, running from the urethra to the bladder neck.

At the end of the procedure, a three-way catheter with continuous irrigation is placed, and the cystotomy is closed using a double-layer 3-0 V-loc running sutures, the first layer incorporates the bladder mucosa, whereas the second layer incorporates all the detrusor muscle. To ensure the integrity of the cystorrhaphy, a watertight closure test is performed at the end with 180 mL of saline.

Posterior approach. The second procedure is performed with a posterior approach. The procedure begins with a posterior midline cystostomy of $\sim$3 cm. Bladder retraction is achieved using three stay stitches: two for the edges of the bladder and the last one for retraction of the catheter. Before beginning the enucleation phase, bilateral ureteral orifices must be identified to prevent injury.

The bladder neck is incised at the 6 O'clock position to expose the prostatic adenoma. The plane between the prostatic adenoma and the pseudocapsule is developed using both sharp and blunt dissection. The plane is developed circumferentially on both the right and left sides until the apex is reached. After complete dissection of the prostatic adenoma, the prostatic fossa is carefully inspected for hemostasis, and four to six single stitches are placed to prevent postoperative bleeding. A three-way catheter with 30 to 40 mL in the balloon and continuous irrigation is positioned in the prostatic

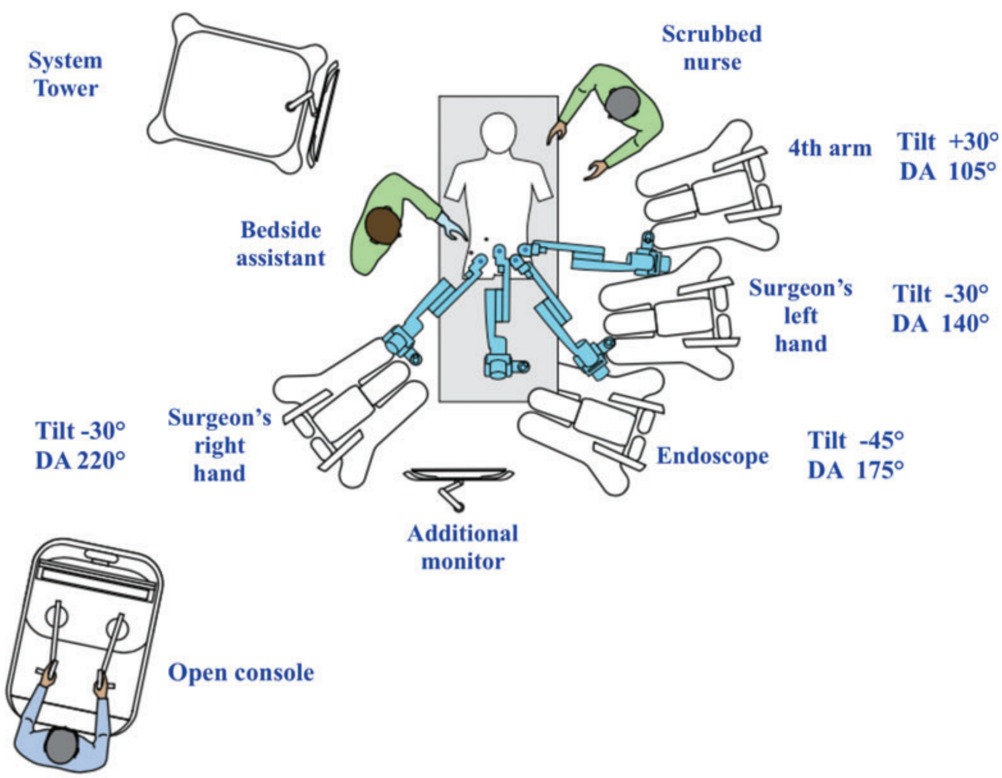

FIG. 2. Operating room setting with the positioning, each tilt and DA (Docking Angle) of the four separate cart. DA, docking angle. Color images available online.

fossa. Finally, the cystotomy incision is closed with a single layer of separate full thickness stitches, and a watertight closure test is performed to ensure the integrity of the cystorrhaphy.

Results

The demographic characteristics of our cohort are shown in Table 1. Overall, 17 (85%) procedures were performed with the anterior approach; median age and body mass index were 72 (IQR: 67–76) years and 29 (IQR: 25–31) Kg/m^2, respectively. Median preoperative PSA level was 7.7 (IQR: 5.0–13.4) ng/mL.

On the preoperative uroflowmetry, the median Qmax and postvoid residual (PVR) were 9.7 (IQR: 6.0–11.8) mL/s and 95 (IQR: 11–334) mL. A total of 11 (55%) patients had an episode of preoperative acute urinary retention, and 5 and 3 men had an indwelling urethral and suprapubic bladder catheter at the time of the surgery, respectively. Four patients had a concomitant bladder stone, and two men had a bladder diverticulum, which were removed in the same procedure. Three out of four patients (75%, $n = 15$) underwent previous unsuccessful pharmacologic treatments.

Perioperative data and postoperative outcomes are shown in Table 2. Median docking, operative, and console times were 7 (IQR: 5–9), 165 (IQR: 121–180), and 125 (IQR: 101–148) minutes, respectively. No intraoperative complication occurred, and there was no need for conversion to an open or laparoscopic procedure and/or additional ports placement. Median estimated blood loss was 400 (IQR: 313–875) mL. No drainage was placed, and the urethral catheter was removed on the first postoperative day in 80% of the patients. Median length of stay was 3 (IQR: 3–4) days. According to the Clavien–Dindo classification, only minor (grade I and grade II) postoperative complications were observed in three patients (15%).

Table 1. Patients' Baseline Characteristics

Baseline characteristics	
Media age, median (IQR), years	72 (67–76)
Body mass index, median (IQR), Kg/m^2	29 (25–31)
ASA, median (IQR)	2 (2–3)
Prior abdominal surgery, *n* (%)	6 (30)
Preoperative PSA level, median (IQR), ng/mL	7.7 (5.0–13.4)
Preoperative uroflowmetry, median (IQR)	
Qmax, mL/s	9.7 (6.0–11.8)
PVR, mL	95 (11–334)
Episode of preoperative acute urinary retention, *n* (%)	11 (55)
Previous unsuccessful pharmacologic treatments, *n* (%)	15 (75)
Indwelling urethral and suprapubic bladder catheter, *n* (%)	
Urethral bladder catheter	5 (25)
Suprapubic bladder catheter	3 (15)
Concomitant bladder stone or diverticulum, *n* (%)	
Bladder stone	4 (20)
Bladder diverticulum	2 (10)

ASA = American Society of Anesthesiology; IQR = interquartile range; PSA = prostate specific antigen; PVR = postvoid residual.

Table 2. Perioperative Data and Postoperative Outcomes

Perioperative data and postoperative outcomes	
Procedure time, median (IQR), minutes	
Docking	7 (5–9)
Operative	165 (121–180)
Console	125 (101–148)
Estimated blood loss, median (IQR), mL	400 (313–875)
Intraoperative complications, *n* (%)	0 (0)
Surgical technique, *n* (%)	
Anterior approach	17 (85)
Posterior approach	3 (15)
Length of stay, median (IQR), days	3 (3–4)
Catheter removal, *n* (%), day	
1	16 (80)
2	3 (15)
3	1 (5)
Postoperative complications, *n* (%)	
Clavien Grade 1	1 (5)
Clavien Grade 2	2 (10)
Clavien Grade >2	0 (0)
30 day readmission, *n* (%)	0 (0)
Prostate volume on final pathology report, median (IQR), g	120 (101–154)
Prostate cancer diagnosis, *n* (%)	1 (5)
Postoperative uroflowmetry, median (IQR)	
Qmax, mL/s	16 (13–26)
PVR, mL	15 (0–34)

On final pathology report, the median prostate volume was 120 (IQR: 101–154) g and one patient was found with an International Society of Urological Pathology (ISUP) group 1 prostatic cancer, pT stage of T1a. The first postoperative follow-up was at 35 (IQR: 27–45) days and the median follow-up was 3 (IQR: 1–6) months. On the postoperative uroflowmetry, the median Qmax and PVR were 16 (IQR: 13–26) mL/s and 15 (IQR: 0–34) mL, respectively.

Discussion

In this article, we report the surgical outcomes of the first large series of RASP using the novel Hugo RAS system.

All the procedures were concluded without technical problems, including conflict among the robotic arms or major issues, in fact our port placement and operating room setting, already described for RASP and radical prostatectomy, allow optimal working space between the robotic arms.[13,14] Moreover, this setting provided more space both on the right and left side of the patient allowing the bedside assistant and scrubbed nurse to easily access all robotic instruments.

One of the main differences between the HUGO RAS system and other robot surgical platforms is the presence of four separate arm carts that must be docked individually. For this reason, longer docking times may be a concern, but literature reports indicate that the docking time for the HUGO RAS system, after the initial cases, is ∼9 minutes,[15–17] which is similar to the time reported by Broeders and others for the da Vinci system.[18]

RASP is becoming a size-independent treatment for the management of BPO caused by a large prostate gland.[4] It is, also, a demanding procedure when done in a minimally invasive manner, as it includes challenging enucleation steps (adenoma dissection) and reconstructive steps (hemostasis of the adenoma fossa and the re-trigonization). However, it allows both short hospital stay and lower blood loss rate, with a low incidence of perioperative complications.[4] Concerning these fundamental aspects, we reported no intraoperative and no major postoperative complications. The reported estimated blood loss for OSP seems to be higher than for RASP[4,19,20]; this situation is also reflected in the no need of intraoperative transfusion, which compared favorably with the rates seen for laser techniques for similar-sized glands.[21]

Compared with data reported in the literature, we reported a shorter length of stay and catheterization time. In our series, in 80% of the patients, the catheter was removed on postoperative day 1, whereas different literature series reported a median time of 5 up to 10 days.[21–23] This might be attributed both to surgical technique (such as the expertise of all the surgeons, meticulous hemostasis during enucleation, and re-trigonization of the prostatic fossa) and to the hospital postoperative management. The efficacy of RASP is also confirmed, in most researchers, with a significant improvement of the postoperative outcomes in comparison with preoperative values, such as Qmax and PVR, about 18.9 mL/s and 13.3 mL, respectively.[21–23]

Randomized controlled trials have been conducted to compare the effectiveness of RASP with other surgical techniques used to treat benign prostatic hyperplasia. These techniques include holmium laser enucleation prostate (HoLEP) and OSP. The results of these trials have shown that RASP produces similar outcomes to HoLEP and OSP in terms of Qmax, International Prostate Symptom Score, and reoperation rate.[4,22,24] However, it is important to consider certain characteristics associated with each surgical procedure. For example, both HoLEP and OSP carry a risk of bleeding, with an estimated transfusion rate of about 7% to 14%.[25] In addition, OSP may lead to transient postoperative urinary incontinence (up to 10%) and urethral stricture (up to 6%).[26] In contrast, HoLEP is associated with disadvantages such as prolonged urethral instrumentation, a steep learning curve, and longer operative times.[27]

In this Supplementary Video S1, we also describe two different surgical techniques for RASP: anterior and posterior approaches. The anterior approach, similar to robot-assisted radical prostatectomy, involves technical phases such as bladder drop and development of the Retzius plane, so it can be preferred in most of the center. However, this approach permits a limited observation of the ureteral orifices and the trigone, and the steep angle of the instrument can make accurate hemostasis and re-trigonization of the prostatic fossa more difficult.[28]

In addition, the development of the Retzius plane and bladder detachment can cause the formation of suprapubic adhesions with consequent postoperative complications.[29] In contrast, the posterior approach requires limited pelvic dissection and at the same time allows a broader view inside the prostatic fossa, easier re-trigonization, because of the urethra position with the instruments, and a better hemostasis on the anterior prostatic capsule.[30] Although as described by Mirvald and others in their comparative analysis there are no significant differences between the two RASP approaches in terms of complication rates and postoperative outcomes in the treatment of large prostatic adenomas.[28]

The main limitations of this study are the short follow-up time and the limited number of cases, which prevented us from making a meaningful comparison of outcomes between the two different techniques. Further research with larger sample sizes may be necessary to fully evaluate the eventual difference in outcomes of these techniques. In addition, we believe that more studies are needed to compare the surgical outcomes and the cost analysis of RASP between the different new robotic platforms.

Conclusions

This series represents the first report of surgical outcomes of RASP executed with the novel HUGO RAS system. Awaiting further comparative evidence with long-term follow-up, these preliminary results are comparable with those described in the literature for RASP performed with other robotic systems, suggesting that HUGO RAS has multiple potential applications, and it ensures optimal outcomes also in nononcologic procedures.

Authors' Contributions

Methodology, investigation, data collection, formal analysis, and writing—original draft by A.P. Investigation, writing—review and editing, and data curation by M.P. Conceptualization investigation, writing—review and editing, data curation, and visualization by C.A.B. Investigation, validation, writing—review and editing, and visualization by F.P. Investigation, validation, and writing—review and editing by G.S. and M.T. Investigation and validation by M.P.L., E.B., N.F., S.R., and C.C.-R. Supervision and validation by A.I., R.D.G., and A.M. Conceptualization, supervision, and validation by F.G. Review and editing, data curation, visualization, and supervision by G.D.N. All authors read and approved the final version of the article.

Author Disclosure Statement

No competing financial interests exist.

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Supplementary Material

Supplementary Video S1

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Abbreviations Used

ASA = American Society of Anesthesiology
BPO = bladder prostatic obstruction
DA = docking angle
HoLEP = holmium laser enucleation prostate
IQR = interquartile range
ISUP = International Society of Urological Pathology
MRI = magnetic resonance imaging
OSP = open simple prostatectomy
PSA = prostate specific antigen
PVR = postvoid residual
RAS = robot-assisted surgery
RASP = robot-assisted simple prostatectomy

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Comparisons of the Safety and Effectiveness of Robot-Assisted *vs* Laparoscopic Partial Nephrectomy for Central Renal Angiomyolipomas: A Propensity Score-Matched Analysis Study

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Abstract

Objective: To compare the safety and effectiveness of robot-assisted partial nephrectomy (RAPN) *vs* laparoscopic partial nephrectomy (LPN) in the treatment of central renal angiomyolipomas (AMLs).
Methods: We retrospectively analyzed the clinical data of 103 patients who were treated with either RAPN or LPN for central AMLs between January 2017 and June 2022. Propensity scores were matched according to sex, age, laterality, body mass index, symptoms, diameter of tumor, location of tumor distribution, R.E.N.A.L score, preoperative hemoglobin, preoperative serum creatinine, preoperative estimated glomerular filtration rate, chronic disease, previous abdominal surgery, preoperative selective arterial embolization, American Society of Anesthesiologists scale, and duration of follow-up, and after matching, perioperative and prognostic data of the two groups were compared.
Results: A total of 57 patients underwent RAPN, and 46 patients underwent LPN. Before matching, there were more complex AMLs in the RAPN group, and R.E.N.A.L scores differed between the two groups (10 *vs* 9, $p < 0.001$). After matching, the median warm ischemic time in the RAPN group was significantly shorter than that in the LPN group (21.5 minutes *vs* 28 minutes, $p = 0.034$), as well as the median time of postoperative mobilization (1 day *vs* 2 days, $p < 0.001$). The other indicators were not significantly different between the groups.
Conclusions: For central AMLs, both RAPN and LPN were safe and feasible surgical treatments, but RAPN might be associated with shorter warm ischemia time and earlier postoperative mobilization.

Keywords: retroperitoneal approach, central renal angiomyolipomas, robot-assisted laparoscopy, partial nephrectomy, propensity score

Introduction

Renal angiomyolipoma (AML), representing a family of tumors that originate from perivascular epithelioid cells, is composed of varying proportions of abnormal blood vessels, smooth muscle, and adipose tissue.[1] AMLs are the most prevalent benign renal tumors, but it accounts for only 0.3% to 3% of all renal neoplasms.[2,3] Around 80% to 90% of AMLs are clinically sporadic, whereas only 10% to 20% of AMLs are associated with tuberous sclerosis (TSC) and occur mainly in women.[4,5] Owing to the widespread use of imaging techniques, most patients are diagnosed incidentally as asymptomatic.[6] The

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main complication of renal AML is tumor rupture and bleeding, which can be life-threatening in severe cases.[7]

Surgical management of benign renal tumors remains somewhat controversial. In particular, low-risk AMLs detected early in the clinical setting are usually managed with observation and follow-up and do not require any treatment. However, surgical intervention is the generally accepted treatment option for AML patients who have tumors >4 cm in diameter; these patients are at risk of cancer as well as rupture and bleeding and present with clinical symptoms such as hematuria and low-back pain.[8–11]

The greatest advantage of surgery is that it can remove the lesion completely and has good long-term efficacy.[12–14] When the condition permits, even if there is a possibility of recurrence or metastasis after radical resection, all patients should consider the feasibility of nephron-sparing surgery, which is of great significance for the protection of renal function, especially in AML patients with anatomical or functional isolated kidney, impaired renal function, multiple tumors in both kidneys, or AML combined with TSC.[15–17]

Central renal AML generally refers to AMLs near to the renal hilum.[18] Because of proximity to the renal arterioles and collecting system, it is much more difficult to preserve the renal unit and reconstruct the kidney when resecting central renal AML. In addition, the surgical procedure has a high complication rate, which is a challenge for urologists. Compared with traditional open surgery, laparoscopic surgery is less traumatic and has a better prognosis for patients.[19] Among the laparoscopic surgery approaches, the robot-assisted laparoscopic technique, with its unique 3D field of view and flexible robotic arm operation, has led to the further development of minimally invasive surgery, which is increasingly important in partial nephrectomy, especially for reconstructive surgery requiring repeated suturing.[20,21]

In conjunction with the relevant literature, clinical studies have now found that laparoscopic partial nephrectomy (LPN) is safe and effective for the treatment of hilar tumors,[22] and a case involving the use of a robot-assisted laparoscopic retroperitoneal approach for the removal of large hilar AML has been reported.[23] However, studies comparing the safety and effectiveness of LPN and robot-assisted partial nephrectomy (RAPN) for central AMLs have not been reported.

In addition, compared with renal malignancies, AML, as a benign tumor with relatively lower tumor-free requirements, can be combined with aspiration to remove tumor tissue during PN, further shortening warm ischemic time (WIT), reducing intraoperative bleeding, and allowing more preservation of renal units. Therefore, whether RAPN is significantly superior to LPN in the management of AMLs is controversial and deserves further exploration. The aim of this study was to compare the safety and effectiveness of LPN and RAPN for central AMLs and to provide some reference and help in the clinical selection of surgical approaches for the treatment of central AMLs.

Materials and Methods

We retrospectively analyzed the clinical data of 103 patients with central AMLs, who were clinically seen between January 2017 and June 2022, and the study was approved by the Institutional Review Board and the Ethics Committee. Inclusion criteria were as follows: (1) CT or MRI suggested that the lesion was located in and around the renal hilum; (2) absence of important contraindications to surgery and ability to tolerate surgery; (3) surgical procedure was LPN or RAPN by using a retroperitoneal approach; (4) diagnosis of AMLs confirmed by postoperative pathology; and (5) no acute or chronic renal insufficiency.

Exclusion criteria were as follows: (1) Inability to tolerate surgery because of co-occurrence of cardiac, pulmonary, and other important organ diseases; (2) severe coagulation dysfunction; (3) presence of pathology of renal epithelioid AML or malignant biological behavior such as invasion and venous invasion; (4) AML occurrence combined with malignancy; (5) anatomical or functional isolated kidney; (6) confirmed diagnosis of TSC; and (7) missing clinical data.

A total of 103 patient data points were obtained, and all patients provided informed consent. All patients underwent preoperative CT or MRI of the abdomen (Fig. 1 shows the preoperative CT images of a 38-year-old female patient with central renal AML). Patients' baseline indicators included sex, age, laterality, body mass index (BMI), symptoms, diameter of tumor, location of tumor distribution, R.E.N.A.L score, preoperative hemoglobin, preoperative serum creatinine, preoperative estimated glomerular filtration rate (eGFR), chronic disease, previous abdominal surgery, preoperative selective arterial embolization (SAE), American Society of Anesthesiologists (ASA) scale, and duration of follow-up.

Perioperative as well as prognosis-related indicators included postoperative hemoglobin, change in hemoglobin, postoperative serum creatinine, change in serum creatinine, postoperative eGFR, change in eGFR, no hilar clamping, WIT, operating time, intraoperative blood transfusion, estimated blood loss (EBL), time to oral food, postoperative mobilization, time to removal of catheter, time to removal of drainage, postoperative hospitalization, postoperative complications, and recurrence. R.E.N.A.L scores were calculated from preoperative images (preferred CT), and all scores were completed by the same clinically experienced surgeon.

Surgery

All procedures were conducted using a retroperitoneal approach and were performed by experienced urologists. (Figs. 2 and 3 show the intraoperative operation and postoperative pathological results, respectively, of RAPN in a 38-year-old female patient with central renal AML). The general procedure is as follows: (1) Patient Position: Completely healthy lateral position; (2) Establishment of surgical access: RAPN: A 12 mm trocar for the da Vinci laparoscopic trocar is inserted 2 cm above the iliac crest.

A da Vinci 8 mm trocar for the da Vinci bipolar electrocoagulation forceps is placed in the posterior axillary line, and then the following trocar is placed under direct view of the da Vinci laparoscope, respectively: a da Vinci 8 mm trocar is inserted in the anterior axillary line under the ribs for the da Vinci electrical scissors, and the assistant's 12 mm trocar was placed ~8 cm below this trocar; LPN: A 10 mm trocar is inserted 2 cm above the iliac crest, a 5 mm incision is made below the rib margin in the anterior axillary line and a 5 mm trocar is inserted if the area is on the left side of the lumbar region, a 10 mm trocar is inserted below the rib margin in the anterior axillary line if the area is on the right side of the lumbar region, and finally a 10 mm trocar is left in

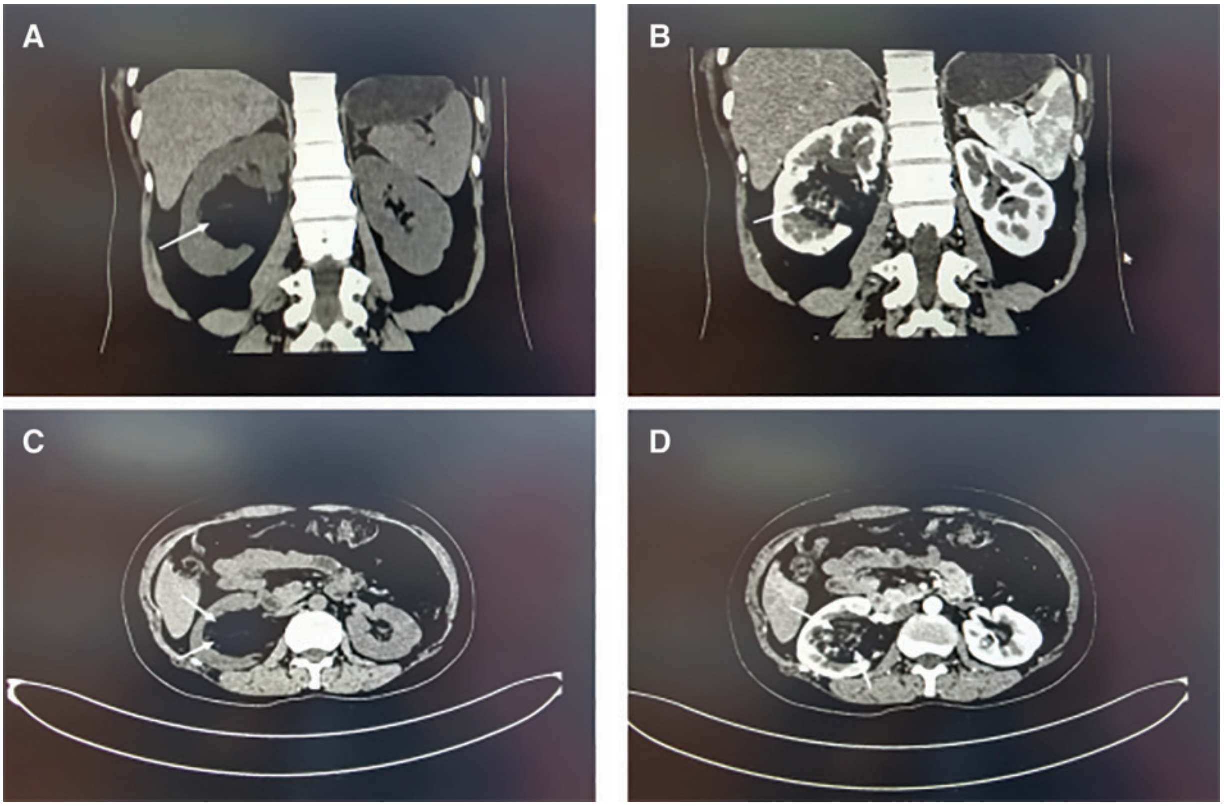

FIG. 1. Preoperative CT image of the patient's abdomen (central tumor size $\sim 5.8 \times 3.8$ cm). **(A, B)** Cross-sectional CT scan+contrast. **(C, D)** Coronal CT scan+contrast. The *white arrow* points to the site of the tumor. Color images are available online.

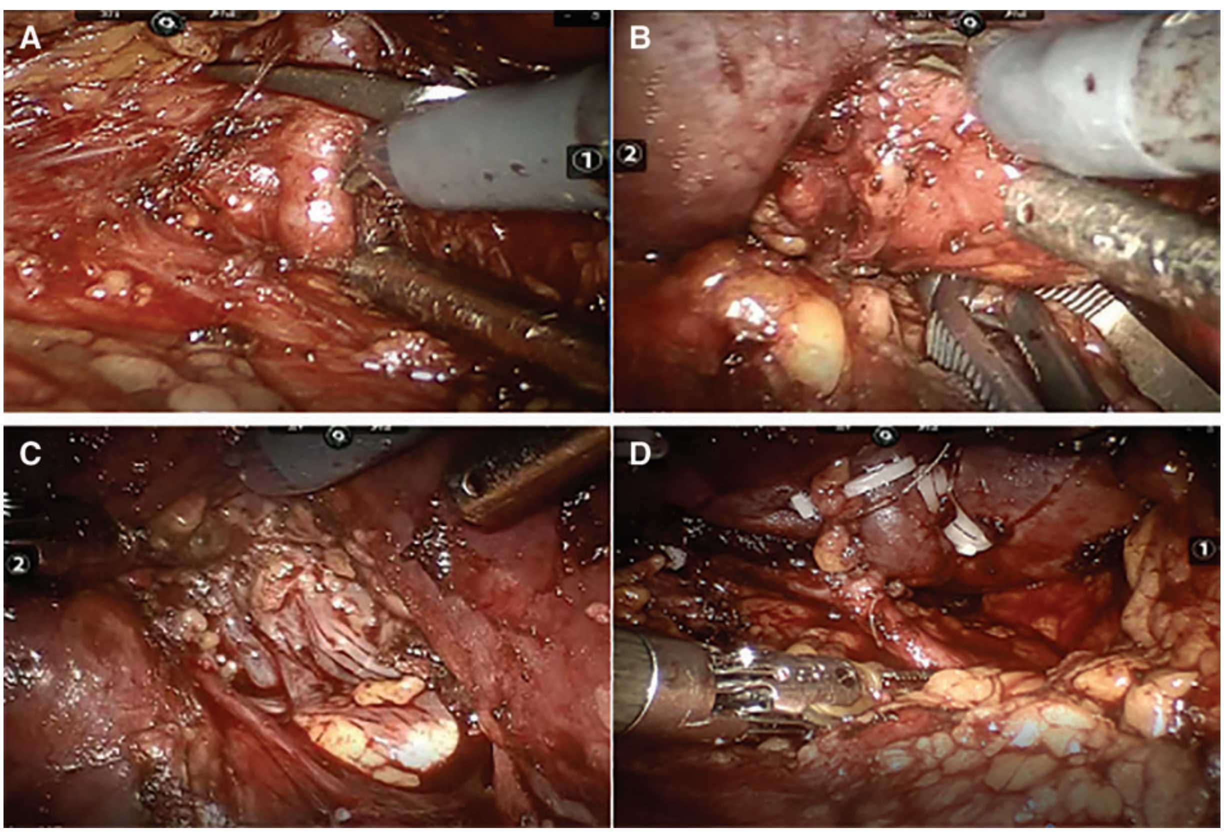

FIG. 2. A 38-year-old female with central renal angiomyolipoma underwent RAPN. **(A)** Blocking the renal artery. **(B)** Separating the angiomyolipoma. **(C)** Deep cavity-shaped trauma. **(D)** After layered sutures. RAPN = robot-assisted partial nephrectomy. Color images are available online.

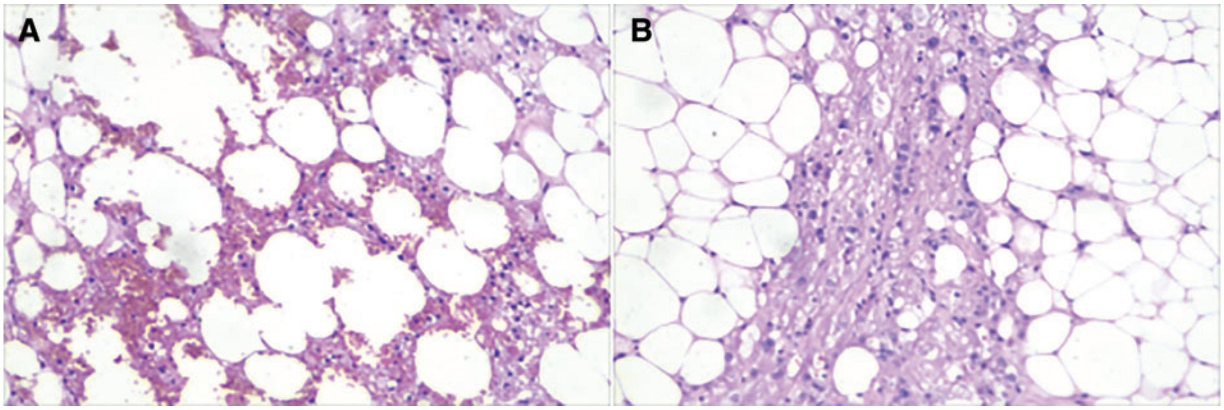

FIG. 3. Postoperative pathological findings of the patient in Figure 1. **(A, B)** Microscopic lesion was nodular, clearly defined relative to the surrounding tissue, with mature adipocytes intertwined with spindle-shaped smooth muscle cells and encircling blood vessels. The nuclei of the smooth muscle cells were short and spindle shaped, and there was abundant, red staining cytoplasm; a large number of foam-like tissue and foam-like cells were intermixed with the cells (HE staining, magnification $\times$100). HE = hematoxylin-eosin. Color images are available online.

the posterior axillary line, the laparoscope is inserted over the iliac crest, and the ultrasonic knife and detachment forceps are inserted from the remaining trocar; (3) tumor removal: The lateral peritoneum was incised and the extraperitoneal fat was separated and then the kidney was fully freed, first to confirm the location of the tumor, and then to locate the renal artery and to close it with a vascular clamp.

After that, the peritoneal membrane of the kidney was cut open and the tumor tissue was seen at this time. According to the intraoperative situation, the tumor was cut along the edge of the tumor 0.5 cm or suctioned off fully with an oversized suction device until it was washed out, and if the tumor was closely adhered to the peritoneum, part of the peritoneum was removed and finally checked that no tumor remained; and (4) renorrhaphy technique: The renal collecting system was closed with 3-0 barbed sutures and the renal parenchymal trauma was closed with 2-0 barbed sutures in succession, ensuring that each stitch was pulled tight and secured with a Hem-o-lok clip. The vascular clamp was then removed and the renal warm ischemia time was recorded. Patients who experienced a SAE preoperatively were required to wait 3 months or longer before their procedures.

Outcome measures and statistical analysis

Propensity score matching analysis was used in this study to minimize selection bias and confounding factors. Logistic regression models were constructed by examining variables such as baseline indicators to estimate propensity scores; patients who received RAPN were matched 1:1 to those who received LPN. The two groups of patients were then compared for perioperative and prognostic-related indicators. Continuous variables were first tested for normality, and if they satisfied normal distribution criteria, they were described by the mean and standard deviation using the *t* test for two independent samples, whereas those for which data did not have a normal distribution were described by the median and interquartile ranges using the Mann–Whitney test. Categorical variables were reported using proportions and tested using the chi-square test. Statistical tests were two sided and were considered statistically significant when $p < 0.05$. Statistical analyses were conducted using SPSS 26.0 software (SPSS, Chicago, IL).

Results

In total, 57 patients underwent RAPN, 46 patients underwent LPN, and postoperative specimens from all patients were pathologically confirmed as renal AMLs and all surgical margins were negative. None of the AML patients we included received everolimus. Table 1 presents a comparison of preoperative information before and after propensity score matching in the RAPN and LPN groups. After matching at 1:1, the baseline variables were better balanced across groups. The number of patients after propensity score matching was 27 in both the RAPN and LPN groups.

The perioperative and prognostic indicators are shown in Table 2. There were three cases in the LPN group without intraoperative renal artery block and four similar cases in the RAPN group, with no statistically significant difference ($p = 1$). After removing zero ischemic cases, the median renal warm ischemia time was 28 minutes in the LPN group, the shortest was 9 minutes, and the longest was 36 minutes.

In contrast, the median renal warm ischemia time in the RAPN group was 21.5 minutes, the shortest was 10 minutes and the longest was 40 minutes, with statistically significant differences between the two groups ($p = 0.034$). The median time of postoperative mobilization in the RAPN group was significantly shorter than that in the LPN group (1 day *vs* 2 days, $p < 0.001$). The median operating time was 160 minutes in the LPN group, the shortest was 75 minutes, the longest was 370 minutes, and the median operating time was 156 minutes in the RAPN group, the shortest was 95 minutes and the longest was 265 minutes; there was no statistically significant difference ($p = 0.788$). There were three cases of intraoperative blood transfusion in the LPN group and one case in the RAPN group with no statistically significant difference ($p = 0.603$).

The median EBL in the LPN group was 150 mL, with a minimum of 50 mL and a maximum of 1500 mL, and the median EBL in the RAPN group was 150 mL, with a

Table 1. Comparison of Preoperative Data Between the Two Groups of Patients Before and After Propensity Score Matching

	Before propensity score matching			*After propensity score matching*		
Variables	*LPN* (n=46)	*RAPN* (n=57)	p	*LPN* (n=27)	*RAPN* (n=27)	p
Gender						
Male, *n* (%)	10 (21.7)	15 (26.3)	0.590	6 (22.2)	6 (22.2)	1
Female, *n* (%)	36 (78.3)	42 (73.7)		21 (77.8)	21 (77.8)	
Age (years), mean (SD)	46.11 (11.83)	47.12 (10.17)	0.641	47.04 (11.81)	48.67 (11.02)	0.602
BMI (kg/m^2)	21.79 (19.55, 24.16)[a]	23.07 (20.69, 24.85)[a]	0.094	22.51 (3.52)[b]	22.01 (2.90)[b]	0.572
Laterality						
Left, *n* (%)	23 (50)	27 (47.4)	0.791	13 (48.1)	12 (44.4)	0.785
Right, *n* (%)	23 (50)	30 (52.6)		14 (51.9)	15 (55.6)	
Symptoms						
None, *n* (%)	16 (34.8)	19 (33.3)	0.753	8 (29.6)	11 (40.7)	0.479
Abdominal pain, *n* (%)	29 (63.0)	34 (59.6)		18 (66.7)	15 (55.6)	
Hematuria, *n* (%)	0	2 (3.5)		0	1 (3.7)	
Both, *n* (%)	1 (2.2)	2 (3.5)		1 (3.7)	0	
Diameter of tumor (cm), median (IQR)	4.95 (4.00, 6.43)	5.30 (4.20, 6.80)	0.401	4.80 (4.30, 6.30)	5.20 (4.10, 6.40)	0.897
Location of tumor distribution						
A, *n* (%)	24 (52.2)	22 (38.6)	0.372	15 (55.6)	12 (44.4)	0.562
P, *n* (%)	9 (19.6)	13 (22.8)		4 (14.8)	7 (25.9)	
X, *n* (%)	13 (28.3)	22 (38.6)		8 (29.6)	8 (29.6)	
R.E.N.A.L score, median (IQR)	9 (8, 9)	10 (9, 10)	<0.001	9 (9, 10)	9 (9, 10)	0.451
Preoperative SAE, *n* (%)	4 (8.7)	5 (8.8)	1	0	1 (3.7)	1
Chronic disease						
None, *n* (%)	38 (82.6)	47 (82.5)	0.949	24 (88.9)	26 (96.3)	0.740
Hypertension, *n* (%)	7 (15.2)	7 (12.3)		2 (7.4)	0	
Diabetes, *n* (%)	0	1 (1.8)		0	0	
Both, *n* (%)	1 (2.2)	2 (3.5)		1 (3.7)	1 (3.7)	
Previous abdominal surgery, *n* (%)	11 (23.9)	13 (22.8)	0.895	5 (18.5)	8 (29.6)	0.340
ASA scale						
I, II, *n* (%)	18 (39.1)	15 (26.3)	0.166	8 (29.6)	7 (25.9)	0.761
III, IV, *n* (%)	28 (60.9)	42 (73.7)		19 (70.4)	20 (74.1)	
Preoperative hemoglobin (g/L)	130.63 (15.50)[b]	130.93 (12.66)[b]	0.914	135 (127, 140)[a]	128 (121, 140)[a]	0.268
Preoperative serum creatinine (μmol/L), median (IQR)	56.60 (53.43, 65.20)	59.30 (53.15, 71.35)	0.341	57.90 (52.60, 64.80)	57.30 (51.70, 68.90)	0.986
Preoperative eGFR (mL/min/1.73 m^2)	106.92 (15.05)[b]	104.29 (15.13)[b]	0.382	103.05 (95.18, 112.64)[a]	104.01 (97.23, 117.96)[a]	0.755
Duration of follow-up (months), median (IQR)	46.50 (35.00, 56.75)	41.00 (19.00, 60.00)	0.328	50.00 (36.00, 59.00)	45.00 (31.00, 63.00)	0.849

[a]Median (IQR).
[b]Mean (SD).

Location of tumor distribution: Mass assigned a descriptor of A (Anterior), P (Posterior), or X; eGFR, calculated by CKD-EPI (① female: Scr ≤0.7 mg/dL, eGFR = 144 × (Scr/0.7)$^{-0.329}$ × 0.933^{age}; Scr >0.7 mg/dL, eGFR = 144 × (Scr/0.7)$^{-1.209}$ × 0.933^{age}; ② male: Scr ≤0.9 mg/dL, eGFR = 141 × (Scr/0.9)$^{-0.411}$ × 0.933^{age}; Scr >0.9 mg/dL, eGFR = 141 × (Scr/0.9)$^{-1.209}$ × 0.933^{age}).

ASA = American Society of Anesthesiologists; BMI = body mass index; CKD-EPI = chronic kidney disease epidemiology collaboration; eGFR = estimated glomerular filtration rate; LPN = laparoscopic partial nephrectomy; RAPN = robot-assisted partial nephrectomy; SAE = selective arterial embolization; Scr = serum creatinine.

Table 2. Perioperative and Prognostic Outcomes of Patients in Both Groups After Propensity Score Matching

Variables	*LPN* (n = *27)*	*RAPN* (n = *27)*	p
Postoperative hemoglobin (g/L), mean (SD)	112.70 (12.02)	111.93 (12.93)	0.820
Change in hemoglobin (g/L), mean (SD)	20.04 (11.83)	17.78 (10.57)	0.463
Postoperative serum creatinine (μmol/L), median (IQR)	71.3 (62.0, 79.4)	68.6 (58.0, 81.5)	0.484
Change in serum creatinine (μmol/L), median (IQR)	10.7 (5.9, 21.5)	9.8 (2.9, 14.5)	0.257
postoperative eGFR (mL/min/1.73 m^2), median (IQR)	93.28 (72.59, 105.04)	94.31 (79.15, 107.86)	0.622
Change in eGFR (mL/min/1.73 m^2), median (IQR)	8.71 (5.33, 27.20)	8.59 (4.97, 19.03)	0.539
No hilar clamping, *n* (%)	3 (11.1)	4 (14.8)	1
WIT (minutes), median (IQR)	28.00 (20.00, 29.00)	21.50 (15.00, 24.75)	0.034
Operating time (minutes), median (IQR)	160 (120, 190)	156 (145, 180)	0.788
Intraoperative blood transfusion, *n* (%)	3 (11.1)	1 (3.7)	0.603
EBL (mL), median (IQR)	150 (100, 300)	150 (100, 250)	0.522
Time to oral food (days), median (IQR)	1 (1, 2)	1 (1, 2)	0.315
Postoperative mobilization (days), median (IQR)	2 (2, 3)	1 (1, 2)	<0.001
Time to removal of catheter (days), median (IQR)	4 (3, 5)	4 (2, 6)	0.623
Time to removal of drainage (days), median (IQR)	5 (3, 7)	5 (3, 6)	0.592
Postoperative hospitalization (days), median (IQR)	6 (5, 8)	6 (6, 7)	0.916
Postoperative complications, *n* (%)	1 (3.7)	1 (3.7)	1
Recurrence, *n* (%)	1 (3.7)	1 (3.7)	1

EBL = estimated blood loss; WIT = warm ischemic time.

minimum of 30 mL and a maximum of 1500 mL; there was no statistically significant difference ($p = 0.522$). In both groups, the surgical approach was not changed intraoperatively. After surgery and for clinical improvement, one patient in the LPN group was treated with blood transfusion because of excessive bloody drainage, and one patient in the RAPN group was treated with medication for incisional infection. And there was one case of tumor recurrence during the follow-up period in both groups.

Discussion

Renal AML is a common clinical disease encountered by urologists, and the choice of related surgical treatment modality is always controversial according to the type of tumor as well as the experience of the surgeon. More studies have reported surgical interventions for AMLs involving RAPN, LPN, SAE, laparoscopic aspiration, microwave ablation, radiofrequency ablation, and traditional open surgery; they have also included a variety of patients as study subjects, such as patients with giant and bleeding types, but the conclusions reached vary and need to be verified by more studies.[24–30]

In addition, SAE has been considered a less invasive treatment in recent years and may be a better option for sporadic AMLs, but is more prone to tumor recurrence, incomplete treatment, and the possible need for secondary surgery compared with surgical treatment.[31,32] Central AML is complicated to handle because of the extreme complex location near the renal hilum.[18] Currently, performing partial nephrectomy for central AMLs is one of the difficult urological procedures, and there is controversy about which surgical approach to prioritize, and it is necessary to study the effectiveness and safety of RAPN and LPN in the treatment of the tumor.

In this study, we used propensity score matching analysis. The mean age at presentation in the matched LPN and RAPN groups in this study was 47.04 and 48.67 years, respectively, with a male-to-female ratio of 1:3.5, which is similar to that reported in the literature.[33,34] Because epithelioid AMLs is also an uncommon type of AML and is characterized by malignant potential,[35] it was included in the exclusion criteria to avoid influencing the study results. All study subjects with central tumors <4 cm in diameter or with high comorbidity were treated surgically for the following three reasons: (1) The possibility of renal cell carcinoma was suspected on preoperative imaging; (2) the tumor grew in a poor location and untimely management would seriously affect the patient's renal function; and (3) the patient strongly requested surgical treatment.

The surgical approach in this study adopted a retroperitoneal approach, which is attributable to the fact that retroperitoneal approach has long been used in laparoscopic techniques in China, which makes most urologists more familiar with retroperitoneal anatomy and can directly access the operative field, which has less influence on the operative process and facilitates the control of intraoperative complications by the primary surgeon. In addition, patients with a history of previous abdominal surgery will increase the risk of postoperative adhesive bowel obstruction and it is not conducive to the control of postoperative complications.

The median time to oral food was 1 day in both groups, which can be assumed to be a result of the lesser intestinal impact of retroperitoneal approach, and therefore faster recovery of gastrointestinal function in both groups. Harke et al.[36] compared and analyzed both robotic transabdominal and retroperitoneal approaches for partial nephrectomy. The median length of stay was 9 (4–50) days in the transabdominal group and 8 (2–22) days in the retroperitoneal group, with a statistically significant difference ($p < 0.001$). In this study, the median time of postoperative hospitalization was 6 (6–7) days in the RAPN group and 6 (5–8) days in the LPN group.

Both groups had markedly shorter time than that reported in the above study for the transabdominal approach, and it can be concluded that the retroperitoneal approach can shorten the time of postoperative hospitalization and reduce the total cost of hospitalization for patients compared to the transabdominal approach. In addition, the median time of postoperative mobilization in the RAPN group was significantly shorter than that in the LPN group (1 day *vs* 2 days, $p < 0.001$); this can be considered a result of the fine robotic surgical manipulation, which enables better suturing of the wound and thus reconstruction of the kidney.

WIT is an important index for evaluating partial nephrectomy, and its duration is controversial in terms of its effect on postoperative renal function. Some studies have reported that WIT >30 minutes has a substantial influence on postoperative eGFR.[37] Thompson et al.[38] studied the relationship between WIT and chronic kidney disease after partial nephrectomy in 362 patients with isolated kidneys and finally arrived at 25 minutes as the ideal cutoff value for WIT.

However, an analysis of a prospective study showed that a 30- to 60-minute duration of renal warm ischemia does not cause severe functional loss in the kidney.[39] Overall, excessive prolongation of WIT may seriously affect the postoperative renal function of patients, so it is important to first ensure complete removal of the tumor during partial nephrectomy, and then to keep the WIT below 30 minutes, as much as possible. In our study, with the removal of cases with no ischemia, the median WIT of the RAPN group was 21.5 minutes, which was significantly shorter compared with the LPN group at 28 minutes ($p = 0.034$); we believe that this is mainly attributable to the unique 3D field of view and flexible robotic arm operation of the da Vinci robot.

A previous clinical comparison study[34] reported that the median WIT of LPN in the treatment of giant AMLs (62 patients with a mean tumor size of 8 cm and a mean renal score of 8) was 22 minutes, compared with only 17 minutes in the RAPN group (62 patients with a mean tumor size of 8 cm and a mean renal score of 9); this result is somewhat shorter than the WIT we reported, but our results are similar to those reported by Xiong et al.[25] (21.02 minutes in the RAPN group and 27.73 minutes in the LPN group).

In addition, the operating time is one of the indicators used to evaluate the surgery and can reflect the smoothness of the whole procedure. In our study, the median operating time was 160 minutes in the LPN group, and the median operating time was 156 minutes in the RAPN group; there was no statistically significant difference ($p = 0.788$). The operating time in the RAPN group in this study includes the intraoperative robot arm change time, perhaps robotic surgery takes less time.

However, the operating time in both groups was longer compared with conventional partial nephrectomy,[28] which we believe is a reflection of the high surgical difficulty in cases of central AML, and the median renal score of 9 in both groups confirms the complexity of this type of tumor.[40] In addition, Pu et al.[41] performed retroperitoneal LPN in 30 complex renal tumors (R.E.N.A.L score ≥7) and showed a mean operating time of 252 ± 58.3 minutes; Roushias et al.[42] performed transperitoneal LPN in 44 moderately complex renal tumors (R.E.N.A.L score of 7–9) and showed a mean operating time of 151 ± 5.56 minutes; therefore, our results are relatively acceptable.

Compared with laparoscopic surgery, robot-assisted surgery has been considered to be more delicate and less invasive and should be superior to laparoscopic surgery in terms of controlling intraoperative bleeding and protecting kidney function.[43,44] However, the results of this study showed no statistically significant difference between the two groups in terms of postoperative hemoglobin, postoperative serum creatinine, postoperative eGFR, change in hemoglobin, change in serum creatinine, or change in eGFR, EBL, and intraoperative blood transfusion (one case in the RAPN group and three cases in the LPN group).

The reason for this result may be related to the following two factors: (1) laparoscopic surgery was performed earlier in our hospital and partial nephrectomy occurred at a very mature stage; (2) the sample size of this study was small, so the data were not sufficient to show the difference between the two groups. However, there was still a significant change in those indicators. This may be closely related to the complex anatomical location of central AMLs, which inevitably leads to damaging blood vessels when dealing with this type of tumor; further consequences are increased bleeding, increased ischemia of the renal parenchyma, and the inevitable removal of part of the normal renal parenchyma to ensure complete resection of the tumor, resulting in postoperative decrease in hemoglobin and levels of renal function.

It has been reported in the literature that the quality and quantity of intraoperatively preserved normal renal parenchyma is the main factor affecting postoperative renal function in PN, whereas WIT is a secondary factor.[45] Therefore, preserving as much normal renal parenchyma as possible, whereas shortening WIT is the key to preserving renal function.

Overall, choosing either the RAPN or LPN surgical approach is safe and feasible for patients with central AMLs. However, this study has some limitations, including its status as a retrospective clinical study with some confounding bias. Although we matched for variables such as sex, age, BMI, laterality, tumor diameter, and R.E.N.A.L score, there may still have been some potential selection bias or confounding factors. In addition, the data in this study were from a single center, and the procedures were performed by different primary surgeons. Despite these limitations, this study is the first study conducted to date on central renal AMLs, and large-sample, multicenter, prospective, randomized studies are needed to validate our findings in the future.

Conclusions

For central AMLs, both RAPN and LPN were safe and feasible surgical treatments, but RAPN might be associated with shorter warm ischemia time and earlier postoperative mobilization.

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Authors' Contributions

Q.-Q.Z. designed the study. Q.-Q.Z., Z.-W.L., and Y.L. wrote the article. B.-B.G. and T.S. reviewed the article. Y.-F.L. analyzed the data and created the tables and graphs. Z.-C.Z. collected and organized the patient data. Q.-Q.Z., Z.-W.L., and Y.L. contributed equally to the study. All the authors read and approved the final article.

Availability of Data and Materials

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to participate

This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Nanchang University. Written informed consent was obtained from every patient included in this study before execution of this study.

Consent for Publication

All authors agree to submit this article.

Author Disclosure Statement

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Abbreviations Used

AML = angiomyolipoma
ASA = American society of anesthesiologists
CT = computed tomography
EBL = estimated blood loss
eGFR = estimated glomerular filtration rate.
HE = hematoxylin-eosin
LPN = laparoscopic partial nephrectomy
MRI = magnetic resonance imaging
PN = partial nephrectomy
RAPN = robot-assisted partial nephrectomy
SAE = selective arterial embolization
Scr = serum creatinine
WIT = warm ischemic time

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Short-Term Clinical Outcomes of Bladder Neck Incision at Time of Holmium Laser Enucleation of the Prostate

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Abstract

Introduction: The effect of prophylactic bladder neck incision (BNI) at time of holmium laser enucleation of the prostate (HoLEP) is unknown. The aim of our study was to examine HoLEP outcomes with a specific focus on rates of bladder neck contractures (BNCs), with and without utilizing prophylactic BNI.
Materials and Methods: We performed a retrospective review of HoLEP patients from January 2021 until January 2022. Outcomes of patients who underwent BNI at time of HoLEP were compared with those who underwent standard HoLEP alone. Student's *t*-tests, chi-square tests, and logistic regressions were performed using SAS Studio.
Results: In total, 421 patients underwent HoLEP. BNI was concurrently performed in 74 (17.6%) HoLEP patients. BNI patients were younger (67.5 ± 9.0 years *vs* 71.1 ± 8.2 years, $p = 0.00007$) and had smaller prostates (60.7 ± 30.3 cc *vs* 133.2 ± 64.5 cc, $p < 0.0001$). Procedure, enucleation, and morcellation times were shorter in the BNI group (all $p < 0.0001$). There was no statistical difference in same-day discharge rates (90.4% *vs* 87.7%, $p = 0.5$), short-term functional outcomes, emergency department (ED) visits, or readmission rates between the two groups. At 14 months mean follow-up, two BNCs occurred in patients in the control group (0.6%), and no BNCs occurred in patients who underwent BNI (0.0%, $p = 0.5$).
Conclusions: BNI at time of HoLEP did not decrease the ability to achieve same-day discharge or increase 90-day complications, ED visits, or readmission rates. No BNCs occurred in patients who underwent prophylactic BNI (0.0%) despite a smaller gland size and lower specimen weight in this cohort. Further prospective studies are required to conclude if concurrent BNI at time of HoLEP is protective against BNC.

Keywords: benign prostatic hypertrophy, bladder neck incisions, bladder neck contracture, HoLEP

Introduction

Holmium laser enucleation of the prostate (HoLEP) is a size-independent surgical treatment option for benign prostatic hyperplasia (BPH).[1] One main advantage of HoLEP is the ability to treat patients with very large prostates, with low rates of morbidity relative to simple prostatectomy.[1] In addition to treating patients with very large prostates, HoLEP can also be offered to patients with ''small'' prostates (<30 g).[1] In a series of more than 1000 HoLEPs, a correlation was identified between small gland sizes and postoperative bladder neck contracture (BNC) development.[2] The authors identified that patients who developed a BNC had a mean enucleated specimen weight of 38.5 g. In an attempt to prevent postoperative BNC, the authors began routinely performing prophylactic bladder neck incision (BNI) during HoLEP on patients with glands less than 40 cc in size.[2]

It has been previously demonstrated that prophylactic BNI after transurethral resection of the prostate (TURP) in glands <20 cc decreased the BNC rate from 7.5% (12/161) to 0.87%

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($n = 1/114$).[3] Unfortunately, examining rates of BNC after HoLEP is more difficult than after TURP due to a lower incidence of postoperative BNC. Previous retrospective HoLEP series have demonstrated BNC rates of 1.6% to 2.1% with approximately half occurring within the first year of follow-up.[4,5]

Our current practice is to perform prophylactic BNI at the time of HoLEP in patients who have a narrow bladder neck opening after laser enucleation. BNIs are performed in an attempt to decrease rates of postoperative BNCs. We currently do not utilize an exact prostate size cutoff to decide when to perform BNI after HoLEP. Instead, it is a judgment decision on the part of the surgeon based on the appearance of the post-enucleation bladder neck. The aim of our study was to describe contemporary HoLEP postoperative outcomes of patients, with a focus on rates of BNC, in high-volume practice with and without utilization of prophylactic BNI.

Materials and Methods

Overview

Patients undergoing HoLEP at Northwestern University are consented to enroll into a prospectively maintained database with institutional review board approval. We retrospectively reviewed patients in our database who underwent HoLEP between January 2021 and January 2022 (to allow for sufficient follow-up to detect BNCs). Patients who received concurrent BNI at time of HoLEP were compared with those that did not. All HoLEPs were performed by one expert surgeon at a single center using a 120 W Moses™ 2.0 Laser and technique previously described.[6] BNIs were performed at the surgeon's discretion for a narrow appearing bladder neck after prostate enucleation. BNIs were performed with the holmium laser using the laser settings 2.0 J and 50 Hz and incising at the 3-, 6-, and 9-o'clock bladder neck positions. BNIs were started proximally from the bladder neck and carried distally to the mid-prostatic fossa. The BNIs were deepened with multiple passes of the laser until the bladder neck fibers were visibly incised and the bladder neck adequately opened. Postoperatively, same-day discharge HoLEP was performed as previously reported by our group.[6]

Preoperative variables included age, body mass index, American Society of Anesthesiology (ASA) score as a surrogate for comorbidity, anticoagulation use, history of BPH surgery, prostate size, and prostate serum antigen. Intraoperative variables included: procedure, enucleation, and morcellation time, total energy, and operating room (OR) specimen weight. Postoperative variables included same-day discharge rate and 90-day complications, emergency department (ED) visits, and readmission rates.

Outcomes

The primary outcomes of our study were to assess the rate of postoperative BNC and the rate of successful same-day discharge. The secondary outcome was to assess the 90-day complication rates, ED visits, and readmissions. We defined BNCs as a bladder neck stenosis/contracture visualized on follow-up cystoscopy or obstructive symptoms requiring a secondary BNI procedure. To better characterize the BNI group, we performed additional subgroup analyses by examining a limited cohort with preoperative prostate size <55 cc and another limited cohort with OR specimen weights <55 g (cutoffs were based on prior studies;[4,7] Supplementary Tables S1 and S2).

Statistical analyses

The means of continuous variables were compared using Student's *t*-tests. Categorical variables were compared using chi-square tests. Variables that were statistically significant on univariate analysis were then incorporated into a multivariate logistic regression model. All statistical tests were two-sided, and a p-value of <0.05 was predetermined to be statistically significant. All analyses were performed using SAS Studio (SAS institute, 2021).

Results

A total of 421 patients underwent HoLEP during the study period; 74 patients were in the BNI group, and 347 patients were in the control group. Patients undergoing BNI were younger (67.5 ± 9.0 years *vs* 71.1 ± 8.2 years, $p = 0.0007$), higher preoperative American Urological Association Symptom Score (AUASS) (21.8 ± 7.2 *vs* 18.5 ± 8.0, $p = 0.01$), had lower ASA scores (48.7% were ASA 3 *vs* 54.6%, $p = 0.027$), and had smaller preoperatively assessed prostate size (60.7 ± 30.3 cc *vs* 133.2 ± 64.5 cc, $p < 0.0001$) compared with patients who did not undergo BNI (Table 1).

The procedure, enucleation, and morcellation times were shorter in the BNI group ($p < 0.0001$ for all variables, respectively; Table 1). Furthermore, the total energy used was lower (83.6 ± 58.1 kJ *vs* 160.0 ± 463.8 kJ, $p = 0.004$), and the OR enucleated specimen weight was also less (24.3 ± 25.1 g *vs* 82.6 ± 52.5 g, $p < 0.0001$) for the BNI group compared with the control group, respectively.

To further characterize the BNI cohort, we restricted the cohort by prostate size only, which resulted in similar mean prostate sizes for the BNI and control groups: 42.0 ± 10.9 cc *vs* 38.7 ± 15.8 cc, $p = 0.4$, but OR specimen weight remained significantly different: 17.9 ± 12.0 g *vs* 53.5 ± 44.1 g, $p < 0.0001$ (Supplementary Table S1). Restricting the cohort by OR specimen weight only, resulted in significantly different mean prostate sizes: 54.8 ± 18.3 cc *vs* 84.9 ± 37.1 cc, $p < 0.0001$, as well as significantly different mean OR specimen weights: 19.0 ± 11.8 g *vs* 33.9 ± 12.8 g, $p < 0.0001$ (Supplementary Table S2).

Primary outcomes

There was no difference in same-day discharge rates between the BNI and control groups (90.4% *vs* 87.7%, $p = 0.5$; Table 1). The mean follow-up was 13.8 ± 2.8 months *vs* 14.1 ± 2.9 months ($p = 0.4$) for the BNI and control groups, respectively (Table 2). Only two patients in the entire cohort developed a BNC, both from the control group (0.0% *vs* 0.6%, $p = 0.5$; Table 2). The BNCs manifested as symptomatic recurrence of weak stream ~7.5 months after HoLEP. Both BNC patients required secondary laser BNI procedures under a general anesthesia, with no subsequent recurrences to date.

Secondary outcomes

There was no difference in the 90-day complication rate (15.7% *vs* 13.5%, $p = 0.7$) or 90-day readmission rate (4.0%

Table 1. Perioperative Characteristics of the Bladder Neck Incision and Control groups

Variable	*BNI group* (n = 74)	*Control group* (n = 347)	*Odds ratio*	*95% CI*	p
Mean age (years)	67.5 (9.0)	71.1 (8.2)			**0.0007**
Mean body mass index (kg/m^2)	27.8 (4.6)	27.5 (4.7)			0.63
ASA					
1	2 (2.7)	0 (0.0)			**0.03**
2	36 (48.7)	155 (44.3)			
3	36 (48.7)	191 (54.6)			
4	0 (0.0)	4 (1.1)			
Anticoagulation (yes/no)	18 (24.3)	74 (21.1)	0.83	0.46–1.50	0.50
Prior BPH surgery (yes/no)	9 (14.1)	55 (15.7)	1.34	0.63–2.86	0.40
Preoperative prostate size (g)	60.7 (30.3)	133.2 (64.5)			**<0.0001**
Preoperative AUASS	21.8	18.5			**0.01**
Preoperative MISI	6.1	6.0			0.46
Preoperative MISI bother	1.8	1.5			0.72
Prostate serum antigen (ng/mL)	4.47 (14.0)	7.44 (9.30)			0.11
Procedure time (minutes)	50.6 (32.2)	76.4 (30.7)			**<0.0001**
Enucleation time (minutes)	23.3 (21.1)	37.9 (14.7)			**<0.0001**
Morcellation time (minutes)	3.26 (3.34)	11.1 (10.2)			**<0.0001**
Total energy (kJ)	83.6 (58.1)	160.0 (463.8)			**0.004**
OR specimen weight (g)	24.3 (25.1)	82.6 (52.5)			**<0.0001**

Standard deviations of means are shown in parentheses. Percentages of categorical variables are shown in parentheses. Anticoagulation is routinely held before holmium laser enucleation of the prostate after consultation with the prescribing physician.

ASA = American Society of Anesthesiology score; AUASS = American Urological Association Symptom Score; BNI = bladder neck incision; BPH = benign prostatic hyperplasia; CI = confidence interval; MISI = Michigan Incontinence Symptom Index; OR = operating room.

vs 2.9%, $p = 0.6$; Table 2) between the BNI and control groups, respectively. Almost all 90-day complications were Clavien–Dindo grade II or less (40/41, 97.5%), and there were no statistically significant differences comparing the grades of complications between groups (Table 2). The 90-day ED visit rate was higher for the BNI group (12.2% *vs* 6.3%, $p = 0.08$; Table 2), but this difference did not meet a level of statistical significance. Reasons for 90-day ED visits are reported in Table 3. There was no statistical difference between the control group and the BNI group in regard to postoperative AUASS (7.6 *vs* 7.7, $p = 0.89$), postoperative Michigan Incontinence Symptom Index (MISI) score (6.0 *vs* 5.1, $p = 0.46$), or MISI bother score (1.1 *vs* 0.9, $p = 0.72$).

Multivariate analysis

Significant variables on univariate analysis (age, ASA, prostate size, procedure/enucleation/morcellation time, total energy, and OR specimen weight) were then incorporated into a

Table 2. Postoperative Outcomes of the Bladder Neck Incision and Control Groups

Variable	*BNI group* (n = 74)	*Control group* (n = 347)	*Odds ratio*	*95% CI*	p
Mean follow-up (months)	13.8 (2.8)	14.1 (2.9)			0.4
Bladder neck contracture (yes/no)	0 (0.0)	2 (0.6)	1.00	0.99–1.02	0.5
Same-day discharge (yes/no)	66 (90.4)	307 (87.7)	1.32	0.57–3.06	0.5
90-Day complications (yes/no)	8 (15.7)	33 (13.5)	0.86	0.38–1.94	0.7
Grade I	6 (75.0)	19 (57.6)			0.4
Grade II	2 (25.0)	13 (39.4)			0.5
Grade III	0 (0.0)	0			—
Grade IVa	0 (0.0)	1 (3.0)			0.7
Grade IVb	0 (0.0)	0			—
Grade V	0 (0.0)	0			—
90-Day ED visits (yes/no)	9 (12.2)	22 (6.3)	0.48	0.21–1.10	0.08
90-Day readmissions (yes/no)	3 (4.0)	10 (2.9)	0.7	0.19–2.59	0.6
Functional outcomes (last follow-up)					
Postoperative AUASS	7.7	7.6			0.89
Postoperative MISI	4.6	3.4			0.46
Postoperative MISI bother	0.7	0.7			0.72
Time from OR to last follow-up (months)	3.4	3.7			0.37

Standard deviations of means are shown in parentheses. Percentages of categorical variables are shown in parentheses.

ED = emergency department.

TABLE 3. MULTIVARIATE LOGISTIC REGRESSION MODEL COMPARING CHARACTERISTICS BETWEEN THE BLADDER NECK INCISION AND CONTROL GROUPS

Variable	*Odds ratio*	*95% CI*	p
Age (years)	0.99	0.95–1.04	0.7
ASA			0.9
Procedure time (minutes)	0.99	0.97–1.01	0.3
Enucleation time (minutes)	0.99	0.93–1.06	0.9
Morcellation time (minutes)	1.05	0.89–1.24	0.6
Total energy (kJ)	0.99	0.89–1.24	0.2
Prostate size (cc)	0.98	0.96–0.99	0.037
OR specimen weight (g)	0.97	0.94–0.99	0.042

multivariate logistic regression model. Only prostate size and specimen weight remained significantly different on multivariate analysis ($p = 0.042$ and $p = 0.037$, respectively; Table 3).

Discussion

In this retrospective review of 421 patients undergoing HoLEP at a high-volume academic center using Moses 2.0 laser technology, 74 patients underwent prophylactic BNI after HoLEP. The overall BNC rate was low (2/421, 0.5%), and no patients developed a BNC in the BNI (0%, 0/74) group. The BNI group on multivariate analysis was found to have smaller prostate size and OR specimen weight. Based on low rates of BNC events and our study design, we cannot imply that prophylactic BNI is protective, but a 0.0% rate of BNC in the prophylactic BNI arm (smaller prostates, lower specimen weight, and younger age) is reassuring and should prompt further prospective investigation. Patients who underwent a prophylactic BNI did not appear to be negatively impacted by the additional maneuver in any measurable way.

BNCs after HoLEP are usually diagnosed when a patient presents with a recurrence of bothersome lower urinary tract symptoms. In our experience, these men are relatively easy to identify. The patients clinically are initially satisfied by the voiding results of their HoLEP, and subsequently present months afterward with a disappointing reduction in their urinary stream. Although post-HoLEP BNCs can be treated with transurethral laser incision, preventing their development is preferred from a patient, provider, and overall system standpoint.[4] BNI has been previously shown to prevent BNC development in patients undergoing BPH surgery.[3] BNCs after TURP were hypothesized to occur because of extensive resection of the bladder neck, excessive fulguration, or exposure to excess heat energy.[3] Kulb et al. reduced the BNC rate from 4.7% to 0.72% ($p < 0.05$) by incising the bladder neck fibers at the 6-o'clock position from the trigone to the verumontanum after TURP.[3] To the best of our knowledge, although BNI has been reported after HoLEP, the outcomes and characteristics of patients undergoing prophylactic BNI have not been reported in detail.

BNC after HoLEP is a relatively uncommon complication, which makes it difficult to study. Krambeck et al. previously noted a mean specimen weight of 38.5 g in men developing BNCs and began incorporating BNI in prostate sizes <40 cc.[2] In another study of 1476 HoLEP patients with up to 18 years of follow-up, Ibrahim et al. reported a BNC rate of 2.1%.[4] The authors noted that BNCs only developed in patients with prostate size <55 cc and suggested that prophylactic BNI may be beneficial for these individuals.[4] In another study of 1216 HoLEP patients with up to 14 years of follow-up, Elkoushy et al. assessed risk factors for reoperation after HoLEP.[7] Their group identified a BNC rate of 1.15% ($n = 14$). Younger age ($p = 0.02$) and smaller gland size (54.2 cc *vs* 94.6 cc, $p = 0.004$) were associated with BNC.[7] On multivariate analysis, only smaller gland size remained significantly associated with BNC (odds ratio 1.84, $p = 0.02$). However, in a study of 127 patients undergoing HoLEP with 5-year follow-up, Enikeev et al. conflictingly did not identify an association between prostate size and BNC ($p = 0.16$).[8]

Similar to Elkoushy et al., we also identified that patients undergoing prophylactic BNI were younger ($p = 0.0007$), had a smaller prostate size ($p < 0.0001$), and had a lower specimen weight ($p < 0.0001$). On multivariate analysis, only prostate size and OR specimen weight remained significant. Both prostate size and specimen weight have been used to recommend prophylactic BNI. To better characterize the BNI group, we performed additional subgroup analyses by examining a limited cohort with prostate size <55 cc (no restriction on OR specimen weight) and another limited cohort with OR specimen weights <55 g (no size restrictions). These cutoffs were based on prior studies.[4,7]

Restricting the cohort by prostate size only, resulted in similar mean prostate sizes for both groups, but OR specimen weight remained significantly different (Supplementary Table S1). Restricting the cohort by OR specimen weight only, resulted in significantly different mean prostate sizes and OR specimen weights (Supplementary Table S2). The discrepancy between the two subcohorts suggests that occasionally the preoperative prostate size may be inaccurate, which might explain why the limited prostate size cohort had similar prostate sizes, but significantly different OR specimen weights (Supplementary Table S1).

Ibrahim et al. found that BNCs occur within 2 years of follow-up and 46.7% of BNCs (14/30) occur within the first year.[4] Enikeev et al. reported an overall BNC rate of 3.9% (5/127) and 60% of these occur within the first 3 years of follow-up ($n = 3/5$).[8] Krambeck et al. reported an increasing BNC rate with longer follow-up.[2] However, fewer patients were available at extended follow-up periods, which may have introduced bias, as patients with postoperative concerns continue to follow-up for longer durations after surgery. The mean follow-up in our study was 14 months (range 9–20 months), which is shorter than the previously mentioned studies, but should be adequate to assess for most BNC cases. Most patients included in this study completed 1 year or longer of follow-up after HoLEP ($n = 326/430$, 75.8%).

Only two BNCs developed throughout the entire study period (2/421, 0.5%), which were treated with laser incision of BNC. At the time of analysis, both patients were free from BNC recurrence at 3 and 8 months after their laser BNI. No association between BNI and BNC was identified, but this could be due to limited power of this study. Interestingly, the patients who developed a BNC had a preoperative prostate size of 160 and 73 cc. Neither patient had a preoperative risk factor for BNC formation (small preoperative prostate volume, intravesical Bacillus Calmette-Guerin therapy, or prior pelvic radiation). Both patients presented with straining, urgency, and slow urinary stream ~7.5 months after HoLEP. The results of

Table 4. Etiologies for 90-Day Emergency Department Visits Among the Bladder Neck Incision and Control Groups

Etiology	*BNI group* (n = *74*)	*Control group* (n = *347*)
Neurological		
Bell's Palsy	1 (1.4)	
Foot drop		1 (0.3)
Stroke		1 (0.3)
Seizure	1 (1.4)	
Cardiovascular		
Heart failure	1 (1.4)	
Respiratory		1 (0.3)
Gastrointestinal		
Gastrointestinal bleed		1 (0.3)
Genitourinary		
Hematuria	3 (4.1)	8 (2.3)
Urinary retention	1 (1.4)	5 (1.4)
Dysuria	1 (1.4)	
Flank pain		1 (0.3)
Hematologic		
Deep vein thrombosis/ Pulmonary Emboli		1 (0.3)
Infectious		
Urinary tract infection	1 (1.4)	3 (0.9)
Total	9 (12.1)	22 (6.3)

Percentages are shown in parentheses (proportion of the overall complications).

our study suggest that factors outside of prostate size may play a role in formation of BNC after HoLEP.

We did not identify that prophylactic BNI increased 90-day complication, readmission rates, or influenced postoperative functional outcomes. The rate of ED visits was increased in the BNI group, but this did not reach a level of statistical significance. It remains unclear why the ED visit rate was higher in the BNI group. In both cohorts, hematuria was the most common reason for ED visit, and each cohort had a similar proportion of these visits (4.1% *vs* 2.3%, Table 4).

This study has several limitations including its retrospective design and duration of follow-up. Predictors of BNC could not be further examined due to a low rate of events ($n = 2$). Ultimately, a randomized controlled trial (RCT) matching patients with prostates of similar gland sizes would be required to determine if BNI at time of HoLEP definitively reduced rates of BNC. Given low rates of BNC in our contemporary study, an RCT would require multiple years of follow-up. Assuming a BNC incidence of 1.5%, to detect if BNI could reduce the BNC incidence to 0.75%, at a power of 0.80 and an alpha of 0.05, 6206 patients would be required. Designing and executing this trial would be difficult. We believe that our study provides novel insight as no prior studies have described the characteristics and outcomes of patients undergoing BNI after HoLEP in detail.

Conclusions

In this retrospective study of 421 patients who underwent HoLEP with Moses 2.0 technology, 74 patients had a prophylactic BNI performed after enucleation. Patients undergoing BNI at time of HoLEP had a smaller prostate size and lower OR specimen weight. BNI did not decrease the ability for patients to achieve same-day discharge or increase 90-day complications, ED visits, or readmission rates. At a mean follow-up of 14 months, two BNCs occurred in patients in the control group (0.6%), and no BNCs occurred in patients who underwent prophylactic BNI (0%). Further prospective studies with longer follow-up are necessary to confidently conclude that prophylactic BNI at time of HoLEP is protective against BNC. An adequately powered randomized follow-up study is likely not feasible given the low rates of BNC within this retrospective contemporary HoLEP study.

Authors' Contributions

N.S.D.: Data curation, formal analysis, writing. M.S.L.: Conceptualization, formal analysis, writing. M.G.: Data curation, writing—revision. M.A.A.: Conceptualization, writing—revision. J.Ha.: Data curation. J.G.: Data curation, writing—revision J.He.: Data curation. A.E.K.: Conceptualization, supervision, writing—revision.

Author Disclosure Statement

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Supplementary Material

Supplementary Table S1
Supplementary Table S2

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Abbreviations Used

ASA = American Society of Anesthesiology
AUASS = American Urological Association Symptom Score
BNC = bladder neck contracture
BNI = bladder neck incision
BPH = benign prostatic hyperplasia
CI = confidence interval
ED = emergency department
HoLEP = holmium laser enucleation of the prostate
MISI = Michigan Incontinence Symptom Index
OR = operating room
RCT = randomized controlled trial
TURP = transurethral resection of the prostate

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A Propensity Score-Matched Analysis of Perioperative Outcomes of Holmium Laser Enucleation of the Prostate Between Lumenis Pulse 120H and VersaPulse Select 80W

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Abstract

Objectives: Holmium laser enucleation of the prostate (HoLEP) is a valid and safe procedure for the treatment of benign prostatic hyperplasia. This study aimed to examine the perioperative outcomes of HoLEP using a new laser platform, Lumenis Pulse™ 120H, and a previous laser platform, VersaPulse Select 80W.

Methods: A total of 612 patients who underwent holmium laser enucleation were enrolled, including 188 and 424 patients who underwent enucleation using Lumenis Pulse 120H and VersaPulse Select 80W, respectively. They were matched using propensity scores with preoperative patient characteristics, and the differences between the two groups, including operative time, enucleated specimen, transfusion rate, and complication rate, were examined.

Results: Propensity score-matched cohort comprised 364 patients with 182 in the Lumenis Pulse 120H group (50.0%) and 182 in the VersaPulse Select 80W group (50.0%). Operative time was significantly shorter with Lumenis Pulse 120H (55.2 ± 34.4 *vs* 101.4 ± 54.3 minutes, $p < 0.001$). In contrast, no significant differences were seen in resected specimen weight (43.8 ± 29.8 *vs* 39.6 ± 22.6 g, $p = 0.36$), rate of incidental prostate cancer (7.7% *vs* 10.4%, $p = 0.36$), transfusion rate (0.6% *vs* 1.1%, $p = 0.56$), and perioperative complication rates, including urinary tract infection, hematuria, urinary retention, and capsular perforation (5.0% *vs* 5.0%, 4.4% *vs* 2.7%, 0.5% *vs* 4.4%, 0.5% *vs* 0%, respectively, $p = 0.13$).

Conclusions: Lumenis Pulse 120H improved the operative time significantly, which is regarded as one of the disadvantages of HoLEP.

Keywords: prostatic hyperplasia, urologic surgery procedures, urology

Introduction

Benign prostatic hyperplasia (BPH) is a progressive disease caused by hyperplasia of the prostatic transition zone in middle-aged and older men. The prevalence of BPH in the age groups of 60 and 70 years in Japan is 6% and 12%, respectively.[1] Lower urinary tract symptoms are first treated by behavioral therapy or pharmacotherapy; however, surgery is indicated for insufficient effectiveness for the treatments or complications including urinary retention, hematuria, bladder stones, renal dysfunction, or urinary tract infection.

Several surgical procedures are available, such as prostate resection, vaporization, and enucleation. Gilling and colleagues first described holmium laser enucleation of the prostate (HoLEP) in 1996.[2] It is a relatively bloodless procedure that immediately improves urinary symptoms.[3] Several technological and procedural developments have been made over the past years to improve the efficacy of the procedure, including comprehensible technical aspects, types of lasers, and new devices.[4–7] Recently, a new laser platform has been introduced, Lumenis Pulse™ 120H (Lumenis Ltd., Yokneam, Israel).

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The platform allows the change of pulse frequency and setting of high energy up to 120 watts, and the surgeon can easily switch between the two laser energy settings with a dual foot pedal. The lower energy setting is used for hemostasis, whereas the higher energy setting is used for enucleation, which allows the surgeon to perform the procedure more efficiently.

This study retrospectively compared the perioperative outcomes of HoLEP between Lumenis Pulse 120H without MOSES technology (dividing the laser wave into two phases: the first phase separates the water by creating a bubble cavity, and the second phase transfers the laser energy to the target) and a previous holmium laser platform, VersaPulse Select 80W (Lumenis Ltd.).

Materials and Methods

Setting

This study was carried out at Jyoban Hospital, which performs ~1000 urologic surgeries including ~100 HoLEP procedures per year and is one of the highest volume centers for urologic surgery in Japan.

Participants

A total of 612 patients who underwent HoLEP for BPH between July 2013 and October 2021 at our hospital were included, with 424 and 188 patients who underwent HoLEP using VersaPulse Select 80W and Lumenis Pulse 120H, respectively.

Surgical procedure

An experienced surgeon performed HoLEP with VersaPulse Select 80W between July 2013 and September 2019 and with Lumenis Pulse 120H between September 2019 and October 2021. The energy setting of VersaPulse Select 80W was 80 watts, and that of Lumenis Pulse 120H was 96 watts for enucleation and 30 watts for hemostasis, which could be switched easily with a dual-foot pedal. A 28F continuous cycle flow Storz laser resectoscope was used and laser energy was delivered with a 550 μm fiber. The procedure for HoLEP was performed as described by Kuo et al.[8]

A morcellator system, Lumenis VersaCut™ (Lumenis Ltd.), was used to remove the enucleated prostatic lobes. At the end of the surgery, a 22F three-way catheter was detained and flow irrigation was continued until the following day. On the second postoperative day, the catheter was usually removed.

Data collection

We collected patients' data from medical records, including age, preoperative prostate-specific antigen (PSA) level, presence of previous biopsy history, operative time, resected specimen weight, presence of incidental prostate cancer, perioperative complications, and presence of postoperative transfusion.

The total prostate volume (TPV) and transitional zone volume (TZV) were calculated using the ellipsoid formula (length $\times$ width $\times$ height $\times$ 0.52), which were measured with axial and sagittal slices on T2-weighed imaging (T2WI) of MRI. Moreover, radiologists evaluated whether there were malignant findings. MRI was conducted using a 1.5 T whole-body scanner (MAGNETOM Aera 1.5 T; SIEMENS, Germany) without an endorectal coil and a 32-channel phased-array surface coil.

The obtained images were T2WI in turbo spin echo with fat saturation; diffusion-weighted imaging, with b values of 0, 1500, and 2000; apparent diffusion coefficient maps; and dynamic contrast-enhanced MRI. PSA density and PSA density in the transition zone were calculated by dividing PSA by TPV and TZV, respectively. Hematuria as complications was defined when transurethral coagulation or blood transfusion was performed after HoLEP. Pathologists pathologically evaluated the resected specimens.

Outcomes

The main end point of this study was the differences in the perioperative outcomes between Lumenis Pulse 120H and VersaPulse Select 80W, including operative time, resected specimen weight, rate of incidental prostate cancer, transfusion rate, and complication rates.

Statistical analysis

Three main analyses were performed. First, we performed descriptive statistics regarding clinical variables of the total population and examined patients' characteristics between the VersaPulse Select 80W and Lumenis Pulse 120H groups. Continuous variables are presented as mean and standard deviation (SD) for normally distributed variables, and as median and interquartile range for non-normally distributed variables. Categorical variables are described as percentages. Continuous variables were analyzed using *t*-test and the Wilcoxon rank-sum test for normally and non-normally distributed data, respectively. Pearson's chi-square test was used for categorical variables.

Second, we performed univariable and multivariable logistic regression analyses to seek variables associated with using Lumenis Pulse 120H in 612 patients. All variables were regarded as covariables in the univariate analysis and the variables in the multivariate analysis were chosen by the backward selection method ($p < 0.05$).

Finally, we analyzed whether there were differences in perioperative variables between the VersaPulse Select 80W and Lumenis Pulse 120H, with cohorts matched by propensity score. The propensity score was calculated through logistic regression modeling based on all preoperative factors, including presence of previous biopsy rate, age, PSA, TPV, TZV, PSA density, PSA density of the transition zone, and findings on preoperative MRI.[9] VersaPulse Select 80W and Lumenis Pulse 120H patients were then paired 1:1 on the propensity score with nearest neighbor matching.

A standard caliper size of $0.2 \times \log$ (SD of the propensity score) was used, and a standardized difference was estimated before and after matching to evaluate the balance of covariates, with a value <0.1, indicating a balance between the two groups.[10] Following 1:1 propensity score matching, perioperative outcomes, including operative time, resected specimen weight, the rate of incidental prostate cancer, transfusion rate, and complication rates, were examined using the Wilcoxon rank-sum test and Pearson's chi-square test. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using Stata version 15.1 (Stata Corp. LP, College Station, TX, USA).

Table 1. Patients' Characteristics of Holmium Laser Enucleation of the Prostate in Total Population

	Total	*Lumenis Pulse 120H*	*VersaPulse Select 80W*	p
N (%)	612 (100)	188 (30.7)	424 (69.3)	
Previous biopsy, *n* (%)	283 of 612 (46.2)	96 of 188 (51.2)	233 of 424 (55.0)	0.37
Age (years), mean (SD)	72.5 (7.1)	73.6 (7.0)	72.0 (7.1)	0.01
Preoperative PSA (ng/mL), median (IQR)	5.9 (3.2–10.4)	5.7 (2.9–11.4)	5.9 (3.4–9.9)	0.81
Total prostate volume on MRI (mL), mean (SD)	65.1 (30.1)	60.8 (27.9)	67.2 (30.9)	0.02
Transitional zone volume on MRI (mL), mean (SD)	52.3 (29.6)	49.4 (28.4)	53.8 (30.3)	0.10
PSA density [ng/(mL·mL)], median (IQR)	0.10 (0.06–0.17)	0.10 (0.06–0.19)	0.10 (0.06–0.16)	0.50
PSA density of the transition zone [ng/(mL·mL)], median (IQR)	0.13 (0.08–0.22)	0.14 (0.08–0.23)	0.13 (0.08–0.21)	0.50
Findings of the prostate cancer on MRI, *n* (%)				
None	345 of 555 (62.2)	102 of 183 (55.7)	243 of 372 (65.3)	0.03
Peripheral zone	34 of 555 (6.1)	13 of 183 (7.1)	21 of 372 (5.7)	
Transition zone	162 of 555 (29.2)	66 of 183 (36.1)	96 of 372 (25.8)	
Peripheral and transition zones	14 of 555 (2.5)	2 of 183 (1.1)	12 of 372 (3.2)	
Operative time (minutes), mean (SD)	91.4 (47.9)	76.2 (35.6)	98.1 (51.1)	<0.001
Specimen weight (grams), mean (SD)	44.4 (28.0)	43.7 (29.6)	44.7 (27.3)	0.70
Incidental prostate cancer, *n* (%)	49 (8.0)	14 (7.5)	35 (8.3)	0.73
Transfusion after HoLEP, *n* (%)	8 (1.3)	1 (0.5)	7 (1.7)	0.26
Complications, *n* (%)				
Urinary tract infection	32 of 612 (5.2)	9 of 188 (4.8)	23 of 424 (5.4)	0.27
Hematuria	22 of 612 (3.6)	8 of 188 (4.3)	14 of 424 (3.3)	
Urinary retention	15 of 612 (2.5)	1 of 188 (0.5)	14 of 424 (3.3)	
Capsular perforation	6 of 612 (1.0)	1 of 188 (0.5)	5 of 424 (1.2)	
Nadir PSA after HoLEP (ng/mL), median (IQR)	0.69 (0.42–1.13)	0.64 (0.42–1.17)	0.69 (0.42–1.17)	0.94
PSA decline (%), mean (SD)	83.4 (14.4)	86.4 (9.4)	83.3 (14.6)	0.54

HoLEP = holmium laser enucleation of the prostate; IQR = interquartile range; PSA = prostate-specific antigen; SD = standard deviation.

This study was approved of the research protocol by an institutional reviewer board and the approval number is JHTF-IRB2021.019.

Results

Table 1 gives patient characteristics before propensity score matching. Among 612 patients, preoperative prostate needle biopsy was performed in 283 patients (46.2%) and there was no prostatic carcinoma before HoLEP. The mean patient age was 72.5 ± 7.1 years with 5.9 ng/mL of median preoperative PSA. The mean TPV and TZV were 65.1 ± 30.1 mL and 52.3 ± 29.6 mL, respectively. The median PSA density and PSA density of the transition zone were 0.10 and 0.13 ng/(mL·mL), respectively. The mean operative time was 91.4 ± 47.9 minutes, mean resected specimen was 44.4 ± 28.0 g, and the rate of incidental prostate cancer was 7.7%.

Complications included hematuria in 32 (5.2%), urinary tract infection in 22 (3.6%), urinary retention in 15 (2.5%), capsular perforation in 6 (1.0%) patients, respectively. Eight patients (1.3%) received transfusion after HoLEP. Median nadir PSA after HoLEP was 0.69 ng/mL, and the mean percentage of PSA decline was 83.4%. Between Lumenis Pulse 120H and VersaPulse Select 80W, the patients with Lumenis Pulse 120H were older ($p = 0.01$), had smaller TPV ($p = 0.02$), more findings of prostate cancer on MRI ($p = 0.03$), and shorter operative time ($p < 0.001$).

Table 2 gives univariable and multivariable logistic regression analysis to examine variables associated with using Lumenis Pulse 120H. Age (odds ratio [OR]: 1.04, 95% confidence interval [CI]: 1.01–1.06, $p = 0.01$), TPV (OR: 0.99, 95% CI: 0.98–0.99, $p = 0.02$), findings of the prostate cancer in the transition zone on MRI (OR: 1.84, 95% CI: 1.22–2.77, $p = 0.004$), and operative time (OR: 0.98, 95% CI: 0.98–0.99, $p < 0.0001$) were independently associated with using Lumenis Pulse 120H.

Table 3 shows that propensity score-matched cohort comprised 364 patients: 182 in the Lumenis Pulse 120H group (50.0%) and 182 in the VersaPulse Select 80W group (50.0%). Operative time was significantly shorter with Lumenis Pulse 120H (55.2 ± 34.4 *vs* 101.4 ± 54.3 minutes, $p < 0.001$), which is a similar result to multivariable logistic regression analysis as already shown.

In contrast, no significant differences were seen in resected specimen weight (43.8 ± 29.8 *vs* 39.6 ± 22.6 g, $p = 0.36$), rate of incidental prostate cancer (7.7% *vs* 10.4%, $p = 0.36$), transfusion rate (0.6% *vs* 1.1%, $p = 0.56$), and perioperative complication rates, including urinary tract infection, hematuria, urinary retention, and capsular perforation (5.0% *vs*

Table 2. Logistic Regression Analysis of Perioperative Variables Associated with Using Lumenis Pulse 120H in 612 Patients Undergoing Holmium Laser Enucleation of the Prostate

	Univariate				Multivariate			
	OR	*95% CI*		p	*OR*	*95% CI*		p
Age	1.03	1.01	1.06	0.01	1.04	1.01	1.06	0.01
Previous biopsy								
No	Reference							
Yes	1.17	0.83	1.65	0.37				
Preoperative PSA	1.01	0.99	1.02	0.18				
Total prostate volume on MRI	0.99	0.98	0.99	0.02	0.99	0.98	0.99	0.02
Transitional zone volume on MRI	0.99	0.98	1.00	0.10				
PSA density	1.39	0.54	3.60	0.49				
PSA density of the transition zone	0.97	0.54	1.75	0.92				
Findings of the prostate cancer on MRI								
None	Reference				Reference			
Peripheral zone	1.47	0.71	3.06	0.30	1.72	0.80	3.70	0.17
Transition zone	1.63	1.10	2.41	0.01	1.84	1.22	2.77	0.004
Peripheral and transition zones	0.40	0.09	1.81	0.23	0.44	0.09	2.06	0.30
Operative time	0.98	0.98	0.99	<0.001	0.99	0.98	0.99	<0.001
Specimen weight	1.00	0.99	1.01	0.70				
Incidental prostate cancer	0.89	0.47	1.70	0.73				
Transfusion after HoLEP	0.32	0.04	2.61	0.29				
Complications								
None	Reference							
Urinary tract infection	1.24	0.51	3.02	0.63				
Hematuria	0.85	0.39	1.88	0.69				
Urinary retention	0.15	0.02	1.19	0.07				
Capsular perforation	0.44	0.05	3.76	0.45				

CI = confidence interval; OR = odds risk.

5.0%, 4.4% *vs* 2.7%, 0.5% *vs* 4.4%, 0.5% *vs* 0%, respectively, $p = 0.13$).

Moreover, Supplementary Figures S1 and S2 show learning curves of VersaPulse Select 80W and Lumenis Pulse 120H, respectively. According to these figures, increase of number of patients was not associated with operative time in both groups. This result demonstrated that operative time is probably not associated with surgeon experience but with the laser platform.

Discussion

Both multivariable logistic regression analysis and propensity score-matched cohort showed that HoLEP with Lumenis Pulse 120H significantly reduced the operative time compared with VersaPulse Select 80W. In contrast, the resected specimen weight, incidental cancer detection rate, transfusion rate, and postoperative complication rate were similar between the two groups.

Although HoLEP is considered superior to transurethral resection of the prostate in terms of blood loss, transfusion rate, postoperative catheterization, length of hospital stay, and long-term outcomes, the relatively long operative time is a crucial disadvantage of HoLEP.[11–14] VersaPulse Select 80W has a single-foot pedal, and the power of energy has to be manually changed when switching between dissection and hemostasis of the tissue. In contrast, Lumenis Pulse 120H has a dual-foot pedal that allows for switching between higher energy for dissection and lower energy for hemostasis, thus resulting in an efficient surgical procedure.[15]

Table 3. Perioperative Outcomes between VersaPulse Select 80W and Lumenis Pulse 120H After Propensity Score Matching

	Lumenis Pulse 120H	*VersaPulse Select 80W*	p
N (%)	182 (50)	182 (50)	
Operative time (minutes), mean (SD)	75.2 (34.4)	101.4 (54.3)	<0.001
Specimen weight (grams), mean (SD)	43.8 (29.8)	39.6 (22.6)	0.13
Incidental prostate cancer, *n* (%)	14 (7.7)	19 (10.4)	0.36
Transfusion after HoLEP, *n* (%)	1 (0.6)	2 (1.1)	0.56
Complications, *n* (%)			
None	163 of 182 (89.6)	160 of 182 (87.9)	0.13
Urinary tract infection	9 of 182 (5.0)	9 of 182 (5.0)	
Hematuria	8 of 182 (4.4)	5 of 182 (2.7)	
Urinary retention	1 of 182 (0.5)	8 of 182 (4.4)	
Capsular perforation	1 of 182 (0.5)	0 of 182 (0)	

In endoscopic surgery, a hemostatic procedure is important to maintain a clear field of operation for a smooth progression of the surgery. It is considered that an easier hemostatic procedure with the Lumenis Pulse 120H significantly shortened the operative time.

The mean resected specimen weight in total was 44.4 (SD: 28.0) g, which was similar to previous study (40.4 [SD: 5.7] g).[16] There was no significant difference in the resected specimen weights between VersaPulse Select 80W and Lumenis Pulse 120H. HoLEP is a surgical procedure that is expected to be effective regardless of the prostate volume, so it is thought that resected specimen weights were similar regardless of the platform.[17–19] In addition, the rate of incidental prostate cancer in total was 8.0%, which is almost similar to previous reports (5.9%–11.7%).[20–26] There was also no significant difference between the two groups.

Regarding perioperative complications, both groups experienced similar rates of complications and postoperative blood transfusion. The severity of complications was generally mild, as indicated by a systematic review. The review reported incidences of capsular perforations (2.2%), urinary retention (0.2%), bladder injury (2.4%), ureteral orifice injury (0.4%), hematuria, and clot retention (0.2%) associated with HoLEP. However, all these cases were classified as grades 1 to 2 according to the Clavien–Dindo classification, signifying relatively minor complications.[27]

Another study found that patients with a history of anticoagulation therapy had a higher incidence of severe complications and blood transfusions when undergoing HoLEP with a 100 W holmium laser generator (VersaPulse).[28] Although the blood transfusion rate was similar between VersaPulse Select 80W and Lumenis Pulse 120H in this study, the latter, which offers efficient hemostasis with a dual-foot pedal, may contribute to a decrease in severe complications and blood transfusion rates.

In addition, MOSES technology can be used in the Lumenis Pulse 120H. This technology divides the laser wave into two phases: the first phase separates the water by creating a bubble cavity, and the second phase transfers the laser energy to the target. The incorporation of MOSES technology increases the amount of laser energy transferred to the target. In contrast, conventional holmium lasers cannot control energy consumption because of the formation of vapor bubbles. A review of HoLEP with MOSES technology demonstrated shorter enucleation time, reduced hemostasis time, and decreased laser time.[29] The increased energy modulation with pulse optimization for BPH may also contribute to shortening the learning curve of the HoLEP procedure.[30]

This study had some limitations. First, it was a retrospective cohort study conducted at a single institution. Second, all HoLEPs were performed by one surgeon, with VersaPulse Select 80W in the first stage and Lumenis Pulse 120H in the second stage. Although Supplementary Figures S1 and S2 showed that increase of number of patients may not be associated with operative time in both groups, respectively, it is not completely denied that the improved skill reduced the operative time in the latter period, when Lumenis Pulse 120H was used. Furthermore, in other important clinical assessments, we were unable to demonstrate differences in postoperative pain and urinary continence at both lower and higher energies.

A randomized controlled trial in which multiple surgeons and institutions with different skills perform HoLEP is needed to further validate the clinical differences in both platforms. This was the first study to report that Lumenis Pulse 120H without MOSES technology significantly reduced the operative time. Furthermore, this cohort study had the most cases compared with previous reports, and the study design matched by propensity score from preoperative patient data excluded confounding factors as much as possible. The results obtained using these data were considered reliable.

Conclusions

In conclusion, Lumenis Pulse 120H significantly shortened the operative time, because of higher energy and easy switching between the two laser energy settings for enucleation and hemostasis. This platform may resolve longer operative time than other surgical procedures for BPH, which is considered a disadvantage of HoLEP.

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Authors' Contributions

T.B. contributed to conceptualization, methodology, investigation, data curation, and writing–original draft. K.N. was involved in investigation and data curation. A.O. carried out writing–review and editing. Y.K. carried out conceptualization and methodology. T.O. took charge of resources. H.S. oversaw supervision.

Author Disclosure Statement

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Supplementary Material

Supplementary Figure S1
Supplementary Figure S2

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Abbreviations Used

BPH = benign prostatic hyperplasia
CI = confidence interval
HoLEP = holmium laser enucleation of the prostate
IQR = interquartile range
MRI = magnetic resonance imaging
OR = odds ratio
PSA = prostate-specific antigen
SD = standard deviation
T2WI = T2-weighed imaging
TPV = total prostate volume
TPZ = transitional zone volume

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Evaluation of Renal Function and Stent Durability Following Resonance Stent Placement for Benign Disease

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Abstract

Introduction: The metal-based Resonance stent (RS) has traditionally been placed in patients with malignant ureteral obstruction; as such, the long-term utility of RS among patients with benign ureteral obstruction (BUO) remains underinvestigated.

Methods: We retrospectively reviewed our database for patients with BUO who underwent RS placement between 2010 and 2020. The impact of chronic RS placement on renal function was evaluated by estimated serum creatinine-based glomerular filtration rate (eGFR), furosemide renal scan, and CT-based renal parenchymal volume measurement. The number of and reason for RS stent exchanges during the follow-up period, incidence of encrustation, and the average indwell time were recorded. A cost analysis of placing the RS *vs* a polymeric stent was performed.

Results: Among 43 RS patients with BUO, at a mean follow-up of 26 months, there was no change in eGFR ($p = 0.99$), parenchymal volume ($p = 0.44$), or split renal function of the stent-bearing side on renal scan ($p = 0.48$). The mean RS indwell time was 9.7 months. Eleven patients (26%) underwent premature stent replacement (6 cases) or removal (5 cases). Stents in 9 patients (32%) were encrusted, of which 4 (44%) required laser lithotripsy. Overall, 25 patients (58%) and 12 patients (28%) had a mean stent indwell time of ≥6 months and ≥12 months, respectively. Placing an RS resulted in a 52%, 37%, and 5.6% cost reduction compared with a regular polymeric stent placement, where it was exchanged every 6, 4, or 3 months, respectively.

Conclusions: RS deployment in the patient with a BUO results in cost-effective maintenance of renal function and of renal parenchymal volume at a mean follow-up of 2 years; however, only 28% of patients fulfilled the 1-year criterion for RS indwell time.

Keywords: stent, ureter, ureteral obstruction/therapy

Introduction

Chronic ureteral obstruction is a challenging issue that may have detrimental genitourinary and systemic ramifications.[1]

Although indwelling polymeric ureteral stents were initially intended for temporary relief of ureteral obstruction, they are now being utilized more frequently for patients who have either declined or undergone unsuccessful operative repair of benign ureteral obstruction (BUO) (i.e., endoureterotomy, end-to-end anastomosis, pyeloplasty, Boari flap with psoas hitch, or ileal replacement).[2] While percutaneous nephrostomy drainage is also a viable alternative, multiple studies have demonstrated no significant benefit for survival or quality of life (QOL).[3] For this reason, indwelling ureteral stents are more often used. These stents are constructed of soft plastic materials, which are prone to failure due to extrinsic compression or encrustation, thereby necessitating

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stent exchanges, every 3 to 6 months.[4–8] Moreover, the discomfort associated with an indwelling stent has negative implications on the patient's QOL.[9,10]

Primarily utilized in patients with inoperable malignant ureteral obstruction (MUO), the Resonance stent (RS) (Cook Medical, Bloomington, IN) is a cobalt–chromium–nickel–molybdenum alloy-based stent. The stent is noncompressible and is promoted as being relatively resistant to encrustation and epithelial tissue ingrowth, allowing for a recommended indwell time of 12 months.[11–13] In contrast, nonmetallic stents are at increased risk of developing obstructive bacterial biofilms or extrinsic compression during longer indwell times.[14] Although several studies have evaluated the RS among patients with MUO, its effectiveness in preserving renal function and long-term durability among patients with BUO has yet to be investigated.[15–20]

Materials and Methods

Permission for this retrospective review was obtained from our institutional internal review board. Patients were included if:

1. They have undergone RS placement for BUO between January 2010 and October 2020.
2. A preoperative serum creatinine (Cr) value was available within 9 months before RS placement (39 patients with labs 4 months prior).
3. A preoperative CT scan was available within 10 months before RS placement.
4. A preoperative nuclear renal furosemide scan was available within 2 months before surgery.
5. A postoperative serum Cr value was available ≥3 months after surgery.
6. A postoperative CT scan was available ≥3 months after RS placement.
7. A postoperative nuclear renal furosemide scan was available at ≥22 days after surgery.

Baseline demographic and clinical data, as well as intraoperative and postoperative variables were recorded. Due to the retrospective design of this study, no prior follow-up interval was determined, and as such, renal function outcomes were recorded at the time of longest follow-up after surgery.

RS durability was defined as the time interval between two RS placements or between an RS placement and removal. Premature failure of the RS was noted if replacement or removal was required within 6 months after RS placement.

Renal function

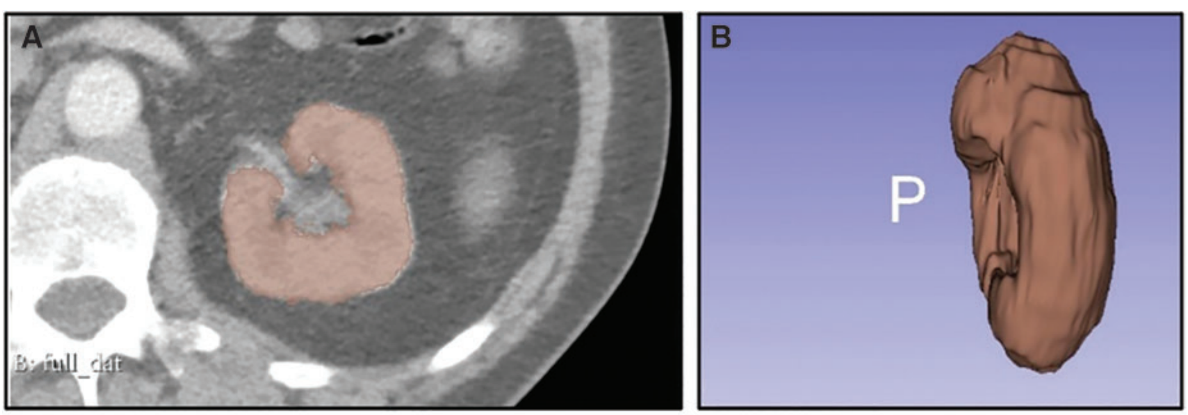
Four parameters were used to characterize the pre- and post-placement RS renal function: (1) serum Cr levels; (2) estimated glomerular filtration rate (eGFR); (3) split renal function; and (4) renal parenchymal volume. Patients were classified into chronic kidney disease stages according to the Kidney Disease Improving Global Outcomes classification.

Renal parenchymal volumes

CT images were uploaded to 3D Slicer® software version 4.0.[21] Both contrast-enhanced and non-enhanced images were used. Utilizing the software's threshold-based tools, automated segmentations were performed on axial images and further manually refined to ensure that only renal parenchyma was included in the segmentations. The renal parenchymal volume was determined (R.B.) (Fig. 1).

Cost analysis

RS and polymeric stent costs, as well as the mean charges for ureteral stent placement were provided by our hospital. The cost of ureteral stent placement does not vary with the material of the stent. Costs included overall operating room costs as well as laboratory, pharmacy, radiology costs. Surgeon and anesthesiologist fees were not included in this



C

1	Segment	Number of voxels [voxels]	Volume [mm3] (1)	Volume [cm3] (1)
2	renal parenchyma	151174	142172	142.172

FIG. 1. Parenchymal volume determination. (**A**) Kidney parenchyma label map creation on 3D Slicer®. (**B**) 3D rendering of the label map. (**C**) Renal parenchyma segmentations' number of voxels conversion into actual parenchymal volume.

analysis as at our institution all types of ureteral stents incur the same service costs. To avoid confounding factors related to hospitalization, we excluded any patient who had the stent placed/exchanged in an inpatient setting. Patients with ureteroscopy, laser lithotripsy, or bilateral ureteral stent insertion at the time of stent exchange were also excluded from the cost analysis.

Statistical analyses

Categorical demographic variables are classified as counts and percentages, while continuous variables are expressed as means with standard deviations. Baseline clinical data before and after RS placement were compared using paired-sample two-tailed *t*-tests for continuous variables, with *p*-values <0.05 labeled statistically significant. All statistical analyses were performed using SYSTAT® version 13.2 (SYSTAT, Palo Alto, CA).

Results

The patient population ($N=43$) was stratified into subgroup A consisting of 32 patients (74%) who did not require any removal or replacement of the stent within 6 months of initial RS placement and subgroup B consisting of 11 patients (26%) with premature failure of the RS requiring either replacement (6 patients) or removal (5 patients) of the RS within 6 months of the initial placement (Fig. 2). Table 1 further describes the demographic characteristics of the studied population.

The reasons for premature RS removal/replacement were as follows: (1) unrelieved ureteral obstruction with hydronephrosis, (2) unmanageable stent symptoms, (3) inflammation and/or infection (i.e., recurring urinary tract infections [UTIs], multidrug-resistant UTIs, sepsis), and (4) definitive surgical intervention (Table 2). Among the six cases in subgroup B requiring premature replacement of the stent, five cases had their stent replaced due to ureteral obstruction with persistent hydronephrosis and confirmed UTI while one was due to unmanageable stent symptoms (flank pain).

Of the five cases of subgroup B requiring premature removal of the RS stent, two had ureteral obstruction with/without hydronephrosis, one had a confirmed infection, one had ongoing hydronephrosis and UTI, and one underwent definitive surgical management. Multiple independent factors (age, sex, preoperative Cr, hypertension, diabetes, hyperlipidemia, preoperative hydronephrosis, BUO location, and etiology) were also assessed for univariate associations with premature RS failure; however, none of these factors displayed a statistically significant association.

The mean indwell time for RS was 9.7 months (range 3–33 months): patients underwent a stent exchange on an average of 1.1 times per year. A stratified analysis of subgroups A and B showed an average indwell time of 10.9 months (range 3–33 months) and 6.0 months (range 3–12 months), respectively ($p=0.014$). In sum, 25 patients (58%) and 12 patients (28%) had a mean stent indwell time of ≥6 and ≥12 months, respectively. At a mean follow-up of 26 months, there was no statistically significant difference between preoperative and postoperative serum Cr ($p=0.68$), eGFR ($p=0.99$), renal volume ($p=0.44$), and split renal function on the stent-bearing side ($p=0.48$) (Table 3). Although preoperative renal function has been previously shown to be a determinant of RS failure in patients with MUO, we found no statistically significant difference ($p=0.36$) in RS indwell time for patients with eGFR of >60 mL/min/1.73 m^2 (mean indwell 10.5 months) *vs* those with eGFRs <60 mL/min/1.73 m^2 (mean indwell 8.7 months).[22] Moreover, we found no statistically significant association between preoperative Cr and RS durability ($p=0.28$).

At the time of stent replacement/removal, 9 patients (21%) had encrustation. The surgeon of record noted no encrustation at the time of stent replacement/removal in 19 patients (44%) and failed to comment on encrustation in 15 patients (35%). Among the nine encrusted stents, four required laser lithotripsy for their removal. The mean indwell time of RS with encrustation was 12.5 months (range 5–23 months) *vs* 9.75 months (range 3–24 months) for patients with no noted encrustations (Table 4). In patients with encrusted stents, two of the nine patients had been taking potassium citrate.

The etiology of BUO was analyzed between the two subgroups. In subgroup A, iatrogenic ureteral stricture was the most common etiology. This developed mostly after endoscopic surgery (34.4%), followed by abdominopelvic surgery (9.4%) and radiation therapy (6.3%). The rest of the ureteral strictures in subgroup A was associated with extrinsic compression (9.37%), congenital obstruction (3.12%), and trauma (3.12%). In one third of the patients (34.3%) in subgroup A, no specific cause for the stricture was provided or identifiable. In subgroup B, radiation-induced ureteral stricture (36.4%) was the most common etiology, followed by

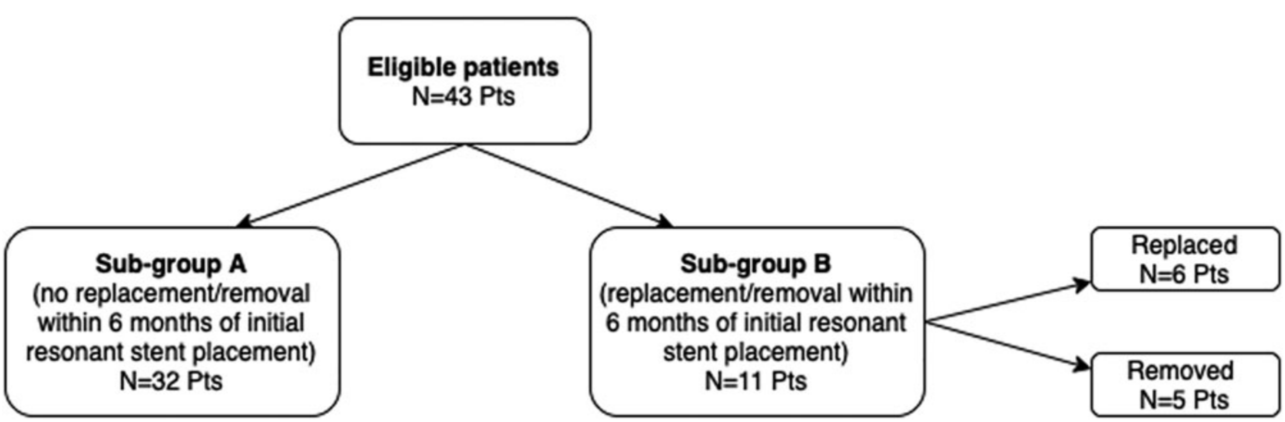


FIG. 2. Studied population stratification.

Table 1. Baseline Demographics and Patient Characteristics

	n (%)
Demographics ($n = 43$)	
Age (years), mean ± SD	62.7 ± 14.2
Gender	
Females	23 (53)
Males	20 (47)
Race	
White	29 (67)
African American	0
Asian	8 (19)
Other	6 (14)
BMI (kg/m^2), mean ± SD	28.0 ± 6.8
Comorbidities ($n = 43$)	
CCI	
0	4 (9)
1	4 (9)
2	4 (9)
3	10 (23)
4	7 (16)
5	4 (9)
6	3 (7)
7	3 (7)
8	2 (5)
11	1 (3)
12	1 (3)
Preoperative CKD	
1	5 (12)
2	17 (40)
3a	7 (16)
3b	9 (21)
4	5 (12)
5	0 (0)
Hypertension	28 (65)
Diabetes	12 (28)
Hyperlipidemia	13 (30)
Prior indwelling tubes (i.e., stent, nephrostomy tube) ($n = 43$)	
Unspecified	1 (2)
Right sided indwelling tube	8 (19)
Left sided indwelling tube	15 (35)
Bilateral indwelling tubes	3 (7)
No history of prior indwelling tubes	16 (37)
Preoperative hydronephrosis ($n = 43$)	
No	8 (19)
Yes	35 (81)
Unspecified	5 (30)
Mild	5 (12)
Moderate	7 (16)
Severe	18 (42)
Prior urolithiasis ($n = 43$)	
No	29 (67)
Yes	14 (33)
Obstruction location ($n = 43$)	
UPJ	11 (26)
Proximal ureter	3 (7)
Midureter	5 (12)
Distal ureter	19 (44)
Mixed	5 (12)

BMI = body mass index; CCI = Charlson comorbidity index; CKD = chronic kidney disease; SD = standard deviation; UPJ = ureteropelvic junction.

idiopathic ureteral stricture (27.3%), congenital ureteral stricture (18.2%), and extrinsic compression (18.2%).

With a cost of $49.50 for a polymeric stent, $890.40 for an RS, and a mean charge per ureteral stent placement of $8,692 (range $7,423–$9,961), placing a single RS is 8.8% more expensive than placing a polymeric stent. In our study of 43 patients, the total annual cost of using the RS would be $709,481; this considers the actual recorded stent durability of each of the 43 cases, including prematurely removed or replaced ureteral stents as well as those few cases in which the stent lasted for more than a year. In comparison, if polymeric stents would have been used for the same cohort of 43 patients and required replacement every 3, 4, or 6 months, the costs would be 52%, 37%, and 5.6% higher.

Discussion

The management of BUO is a challenge in which the urologist must seek a balance between renal function preservation and the patient's QOL.

The protective effect on renal function seen with RS drainage is hypothesized to be attributed to the coiled wire construction, which remains patent regardless of external pressures up to 32 lbs *vs* 10 lbs for standard polymeric stents.[13] In contrast, a study on 103 patients with benign ureteral strictures managed by copolymeric Double-J stents noted that 51% of patients had a renal functional decline of >20% over a 3- to 6-month period; the presence of a UTI was the most common risk factor.[23]

The RS mean indwell time in our study was 9.7 months, similar to the 8.2 months noted by Corrales et al.[24] This systematic review, however, did not distinguish between BUO and MUO; it is our hypothesis that it is a bit easier to overcome a BUO given its usually more finite distribution, less likely progressive, and presumably less compressive force. Our findings with BUO are in keeping with the work of Chow et al. with MUO; RS increased the stent indwell time by 4 months *vs* a polymeric stent.[25]

We recommend follow-up within the initial 3 to 6 months of stent placement in all patients with a BUO. Early failure can thus be remedied before serious sequelae develop. In our study, 11 patients (26%) had a stent failure within 6 months; only 12 patients (28%) were able to maintain their RS for a full year.

The RS alloy is designed to reduce encrustation and prevent tissue ingrowth, *theoretically* bolstering its ability to remain patent and minimize any risk of UTI by reducing microbial growth and biofilm formation. However, further objective data evaluating the RS anti-encrustation properties have yet to be forthcoming.[26] In our subgroup of patients who experienced premature RS failure, 27% had encrustation while 64% developed an UTI.

The risk of stent encrustation increases with the dwell time. Previous studies have shown that in patients with a polyurethane-based stent, the risk of encrustations is 9.2% for stents removed before 6 weeks, 47.5% for stents removed between 6 and 12 weeks, with an increased risk of 76.3% for stents removed after 12 weeks.[27] Similarly, Kawahara et al. found that the rate of silicone ureteral stent encrustation was 26.8%, 56.9%, and 75.9% for indwelling times of less than 6 weeks, 6 to 12 weeks, and more than 12 weeks, respectively.[14] Although described as encrustation-resistant, several

Table 2. Causes and Outcomes of Patients with Premature Replacement or Removal of Resonance Stent

Case no.	*Interval between initial RS placement and first exchange and/or interval between initial RS placement and final removal (months)*	*Reason*	*Management after RS removal*
Case 1	Exchanged (4.2)	Ureteral obstruction due to mid/distal ureteral stricture + infection and/or inflammation (confirmed UTI)	Required placement of nephrostomy tube
	Removed (7)	Infection and/or inflammation (confirmed UTI)	
Case 2	Removed (4.4)	Infection and/or inflammation (confirmed UTI)	Required placement of nephrostomy tube
Case 3	Exchanged (5.9)	Ureteral obstruction with hydronephrosis of unknown etiology + infection and/or inflammation (confirmed UTI)	Immediately underwent long-term surgical intervention (ureteroneocystostomy with psoas hitch + Boari flap)
	Removed (20)	Long-term surgical intervention	
Case 4	Removed (4.7)	Ureteral obstruction with hydronephrosis	Salvage with placement of Double J-stents
Case 5	Removed (4.1)	Ureteral obstruction	Deceased before exchange/removal (septic shock likely due to intra-abdominal source)
Case 6	Removed (3.3)	Long-term surgical intervention	Immediately underwent long-term surgical intervention (nephrectomy)
Case 7	Exchanged (4.9)	Ureteral obstruction with hydronephrosis + infection and/or inflammation (confirmed UTI)	Required placement of nephrostomy tube
	Removal (17.8)	Infection and/or inflammation (confirmed UTI)	
Case 8	Removal (3.5)	Ureteral obstruction with hydronephrosis + infection and/or inflammation (confirmed UTI)	Eventually underwent long-term surgical intervention (nephrectomy)
Case 9	Exchanged (4.4)	Ureteral obstruction with hydronephrosis + infection and/or inflammation (confirmed UTI)	N/A[a]
Case 10	Exchanged (5.8)	Unmanageable stent symptoms (flank pain)	Required placement of nephrostomy tube
	Removed (48.4)	Ureteral obstruction with hydronephrosis + unmanageable stent symptoms (flank pain)	
Case 11	Exchanged (5.5)	Ureteral obstruction with hydronephrosis + infection and/or inflammation (confirmed UTI)	Required long-term surgical intervention (ileal conduit diversion)
	Removal (10.3)	Infection and/or inflammation (confirmed UTI) + long-term surgical intervention	

[a]Resonance stent still in place.
N/A, not applicable; RS = Resonance stent; UTI = urinary tract infections.

studies have reported a risk of encrustations associated with RS placement ranging between 0.7% and 11%.[24]

In our study, if one relies only on operative notes in which the surgeon commented on the presence/absence of encrustation, the rate of encrustation (i.e., 9/28 cases) was three times higher than in the literature: 32%. Of note, in 15 cases, there was no comment regarding stent encrustation; if one considered this to indicate an absence of encrustation, then the encrustation rate would fall to 21%. We are confident in stating that significant encrustations requiring

Table 3. Renal Function Outcomes in Resonance Stent Placement

Parameter	*Preoperative, mean ± SD*	*Postoperative, mean ± SD*	p
Serum Cr (mg/dL)	1.3 ± 0.7	1.3 ± 0.7	0.68
eGFR (mL/min/1.73 m^2)	60.4 ± 25.8	60.3 ± 25.0	0.99
Split function (%) stent-bearing kidney	42.9 ± 21.9	46.6 ± 27.6	0.48
Renal volume (cm^3)	134.1 ± 61.0	127.4 ± 71.4	0.44

Cr = creatinine; eGFR = estimated glomerular filtration rates.

Table 4. Perioperative Outcomes

	n (%)
Intraoperative outcomes ($n=43$)	
Operative time (minutes), mean ± SD	54.1 ± 65.3
Postoperative outcomes ($n=43$)	
Follow-up (months), mean ± SD	25.8 ± 24.9
Postoperative CKD	
1	5 (12)
2	13 (30)
3a	13 (30)
3b	9 (21)
4	2 (5)
5	1 (2)
Number of resonant stent replacements during follow-up, mean ± SD	1.1 ± 1.4
Duration of indwelling stent (months), mean ± SD	9.7 ± 6.2
Stents encrusted	
Unspecified	15 (35)
No	19 (44)
Yes	9 (21)
Removal method for encrusted stents ($n=9$)	
Unspecified	1 (11)
Graspers only	4 (44)
Graspers + laser use	4 (44)
Use of Urocit-K during follow-up period in patients with encrustation ($n=9$)	
Yes	2 (22)
No	7 (78)
Initial stent removed with no future exchanges	
Before 6 months	4 (57)
After 6 months	3 (43)
Group B only ($n=11$)	
Stent replaced/removed within 6 months of placement due to stent failure	
Removed	5 (45)
Replaced	6 (55)
Long-term follow-up outcomes in patients with stent replacement/removal within 6 months of placement due to stent failure	
Required ongoing resonant stent exchanges	1 (9)
Required long-term surgical intervention (i.e., nephrectomy, reconstruction, diversion)	4 (36)
Required placement of nephrostomy tube	4 (36)
Salvage with placement of Double J-stents	1 (9)
Deceased before exchange/removal	1 (9)

laser lithotripsy to remove the stent occurred in only 9.3%, as even in those cases in which there was no comment regarding encrustations, there was also no report of laser lithotripsy.

There is a paucity of information regarding the costs of placing an RS for BUO. Taylor et al. reported a cost reduction of 48%, 61%, and 74% when placing an RS in patients with chronic ureteral obstruction and previous polymeric stent failure after three, four, or six stent exchanges.[28] One flaw in this analysis is that it overestimated the RS positive cost savings as the study compared polymeric stent exchanges with an anticipated RS indwell time of 1 year. In contrast, when accounting for the actual indwell time of the RS, López-Huertas et al. found a 43% annual reduction for each patient when utilizing RS.[29] In our study, taking into account the indwell time of the RS among all patients, the total annual cost of using an RS to treat BUO would be $709,480.896; this amount is 52%, 37%, and 5.6% less than changing a polymeric stent every 3, 4, or 6 months. Thus, although the initial cost of placing a single metallic stent exceeds the cost of a polymeric stent by 8.8%, the advantage of a longer indwell time with fewer necessary stent exchanges favors the use of RS for managing chronic BUO.

Although the RS has proven to be a cost-effective tool in the decompression of BUO with favorable patency success rates of 56% to 100%, its use has been limited clinically perhaps due to the relatively small subset of patients suffering from BUO and the lack of high-quality data regarding its use. In addition, hospital product purchasing practices may further discourage the availability of the RS given that buying multipurpose polymeric stents in bulk would be more economic in the short-term than buying 10-fold more expensive RS in smaller quantities. Moreover, with the limited availability of these stents in hospital systems comes the inherent limited familiarity with the appropriate technique required to place an RS given its occluded end design, making placement and exchange slightly more challenging than traditional stents.

To the best of our knowledge, there has been no published literature to date describing renal function in terms of changes in renal parenchymal volumes or split renal function after RS placement in a study group larger than 40 patients.[15–20] In addition, defining RS premature failure and understanding its determinants are critical as it will set the stage for improvement of patient counseling and allow for the development of standardized management guidelines while also helping guide future researchers in constructing stronger study designs focused on improving patients outcomes.

The limitations of our study are related to its retrospective design. In addition, we were unable to address QOL with RS as our patients did not routinely complete a standardized questionnaire.[30] Furthermore, the presence of stent encrustation could not be accurately addressed as in over one third of cases, the surgeon of record failed to specifically comment on the presence or absence of encrustations that were too slight to mandate laser fragmentation.

Conclusions

RS deployment in patients with a BUO proved to be a cost-effective means for preservation of renal function and maintenance of parenchymal volume during a mean follow-up of 2 years; however, durable stent indwelling time of a year occurred in only 28% of patients.

Authors' Contributions

The authors confirm contribution to the article as follows: Study conception and design: R.V.C., J.L., R.M.P., S.N.A., Z.E.T., and P.J. Data collection: R.B., K.V., A.D.C., A.R., A.B., K.L.M., and A.P. Analysis and interpretation of results:

R.B., A.D.C., and K.V. Draft article preparation: R.V.C., J.L., Z.E.T., A.D.C., R.B., and K.V. All authors reviewed the results and approved the final version of the article.

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Abbreviations Used

BMI = body mass index
CCI = Charlson comorbidity index
CKD = chronic kidney disease
Cr = creatinine
CT = computed tomography
eGFR = estimated glomerular filtration rates
BUO = benign ureteral obstruction
MUO = malignant ureteral obstruction
QOL = quality of life
RS = Resonance stent
SD = standard deviation
UPJ = ureteropelvic junction
UTI = urinary tract infections

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Initial Postoperative Prostate Specific Antigen and PSA Velocity Are Important Indicators of Underlying Malignancy After Simple Prostatectomy

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Abstract

Background: There is a paucity of guidelines for prostate-specific antigen (PSA) monitoring after simple prostatectomy (SP) despite these patients remaining at risk for prostate cancer (PCa). Our objective was to determine if PSA kinetics can be a potential indicator of PCa after SP.
Methods: A retrospective review was performed of all simple prostatectomies at our institution from 2014 to 2022. All patients who met criteria were included in the study. Relevant clinical variables were collected preoperatively, including PSA value, prostate size, and voiding symptoms. Surgical and urinary function outcomes were analyzed.
Results: A total of 92 patients were divided into two groups based on malignancy status. Sixty-eight patients did not have PCa, while 24 patients had known PCa before surgery (14) or were diagnosed as having incidental PCa from the pathological specimen (10). Patients with benign prostates had an initial postoperative PSA value of 0.76 ng/mL compared with 1.68 ng/mL for those with cancer ($p < 0.01$). PSA velocity for the first 24 months after surgery was 0.042 ± 1.61 ng/(mL·year) for the benign cohort compared with 1.29 ± 1.02 ng/(mL·year) for the malignant cohort ($p = 0.01$). Voiding improvements were noted by objective (postvoid residual and flow rate) and subjective (American Urological Association symptom score and quality of life score) measures in both groups.
Conclusions: PSA interpretation and monitoring after SP have not been well established. Our study indicates that initial postoperative PSA value and PSA velocity are important indicators of underlying malignancy in patients after SP. Further efforts are needed to establish threshold values and formal guidelines.

Keywords: lower urinary tract symptoms, simple prostatectomy, prostate specific antigen, prostate cancer

Introduction

Men suffering from lower urinary tract symptoms (LUTS) with associated benign prostatic hyperplasia (BPH) have several treatment options, including medical therapy, catheterization, or surgical intervention. According to American Urological Association (AUA) guidelines, simple prostatectomy (SP) may be recommended for men with prostates larger than 80 g.[1] These men with enlarged prostates often have an elevated prostate-specific antigen (PSA) level, which is nonspecific and also a marker of prostate cancer (PCa).[2,3] PSA interpretation in these men is challenging.[4–10]

The surgical pathology from the removed adenoma in SP is insufficient for diagnosing PCa compared with radical prostatectomy, and SP is not an oncological therapy. These patients remain at future risk of cancer, so the ability to risk stratify patients remains a necessity. Currently, the PSA value after SP deemed concerning for malignancy, recommended PSA surveillance, and worrisome PSA trends are yet to be established.

Prior literature on BPH surgery indicates that the initial postoperative PSA level can guide urologists on which patients need to be monitored more closely for malignancy.[11–13] However, research in pure SP cohorts is limited. Patients who

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undergo SP have larger prostates than those undergoing transurethral resection of the prostate (TURP) and often (although not always) holmium laser enucleation of the prostate (HoLEP).

The remaining peripheral zone (PZ) from a 100-g prostate is larger than the PZ from a 40-g prostate. Therefore, postoperative PSA findings from other BPH procedures cannot be generalized to this patient population. Particularly for men aged 55 to 69 years who undergo SP, a better understanding of PSA monitoring is of utmost importance.

In this study, we hypothesized that there will be a difference in the PSA trends after SP for patients who have BPH only compared with patients with known or incidentally found PCa.

Methods

A retrospective review was performed of patients who underwent SP at a single institution from 2014 to 2022. The study design was approved by the Institutional Review Board. Both open simple prostatectomy (OSP) and robotic simple prostatectomy (RASP) were included. All men included in the study had documented pre- and postoperative PSA values. Men with biopsy-proven, but untreated, PCa were included in the study, although they were excluded from PSA evaluation if/when they began cancer treatment.

All patients were seen before surgery to capture subjective and objective voiding parameters. History of prostate biopsy, prior PSA tests, known PCa, and other relevant clinical variables were recorded. Patient prostate volume was calculated by MRI, transrectal ultrasound, or CT. Medical treatment of BPH was documented pre- and postoperatively. Patients taking a 5-alpha reductase inhibitor had their PSA value corrected in data analysis according to established standards.[14]

Indications for surgery included a markedly enlarged prostate gland (>80 g) and catheter dependence, acute urinary retention, refractory gross hematuria, or intractable LUTS. Prostatic tissues from all procedures were sent for pathological analysis.

Postoperatively, PSA velocity was calculated for patients with at least 2 PSA values within the 24 months after surgery. PSA doubling time was also calculated.[15] Subjective and objective voiding parameters were collected. For patients undergoing further PCa treatment, the treatment course was recorded.

The primary outcome of the study was to compare postoperative PSA levels in patients with BPH *vs* PCa after SP.

The statistical analysis compared pre- and postsurgical measures within groups as well as differences between benign and malignant groups. Categorical variables were assessed using the chi-square test, and continuous variables were compared using paired and independent *t* tests or Wilcoxon signed rank test after assessment of data normality using the Shapiro–Wilk test.

Data analysis was performed using Prism—GraphPad, version 9.5.0 (GraphPad Software, Boston, MA).

Results

A total of 141 patients underwent SP during the study period. Of these, 92 patients met inclusion criteria and 49 were excluded due to the absence of both pre- and postoperative PSA data in our records (being a referral center, most of these patients chose long-term follow-up closer to home). Thirty-one patients underwent OSP (34%) and 61 underwent RASP (66%).

Patients were stratified into groups based on malignancy status. Sixty-eight patients did not have PCa, while 24

Table 1. Baseline Patient Characteristics

	Benign	*Malignant,* n *(%)*	p
No. of patients	68	24	
Known malignancy		14	
Grade Group 1		7 (50)	
Grade Group 2		3 (21.4)	
Grade Group 3		1 (7.1)	
Grade Group 4		2 (14.3)	
Grade Group 5		1 (7.1)	
Incidental malignancy		10	
Grade Group 1		6 (60)	
Grade Group 2		3 (30)	
Grade Group 3		0 (0)	
Grade Group 4		1 (10)	
Grade Group 5		0 (0)	
Age (years)	70.3 ± 7.1	69.9 ± 4.9	0.78
Median follow-up (days)	360 (IQR: 153–857)	305 (IQR: 139–630)	0.73
Preoperative prostate size (g)	151.6 ± 66.2	126.4 ± 33.1	0.076
Tissue removed (g)	98.8 ± 73.0	87.9 ± 53.4	0.51
Estimated % reduction	66.5 ± 57.2	70.1 ± 41.9	0.77
Preoperative PSA level (ng/mL)	11.4 ± 9.2	13.8 ± 9.7 (n = 19)	0.32
		Known: 14.7 ± 13.0	
		Incidental: 12.8 ± 4.4	0.67
Preoperative PSA density (ng/mL^2)	0.08 ± 0.06	0.1 ± 0.07	0.04
Preoperative 5-ARI use	41 (60.3%)	12 (50%)	0.38

5-ARI = 5-alpha reductase inhibitor; IQR = interquartile range; PSA = prostate-specific antigen.

patients either had known PCa preoperatively (14) or were diagnosed as having PCa as a result of the pathological analysis of tissue from surgery (10). Within the benign group, 51/68 had preoperative PSA levels >4 ng/mL.

Twenty-three patients underwent MRI, 37 underwent biopsy, and 14 underwent both without a diagnosis of PCa. Of the 10 patients with incidentally found PCa, 7 had a PSA level >4 ng/mL. Eight men underwent biopsy (including all 7 with elevated PSA) and 3 underwent MRI. All patients in the known PCa group had biopsy-proven disease before SP.

Patients without PCa had an average age of 70 years and median follow-up of 360 days. These patients had an average prostate size of 151.6 g, preoperative PSA level of 11.4 ng/mL, and PSA density of 0.08 ng/mL^2. Patients with prostate malignancy had an average age of 70 years with a median follow-up of 305 days. These patients had an average prostate size of 126.4 g ($p = 0.08$), preoperative PSA level of 13.8 ng/mL ($p = 0.32$), and PSA density of 0.1 ng/mL^2 ($p = 0.04$).

Of the 14 patients with known PCa, 5 started androgen deprivation therapy before surgery and were excluded from PSA analysis. There was no difference in PSA values before surgery between patients with known and incidentally discovered malignancy ($p = 0.67$) (Table 1).

Urinary outcomes are shown in Figure 1. A total of 17 patients (25%) required an indwelling catheter and 6 (8.8%) required intermittent catheterization in the benign group. Postoperatively, no patients required either of these adjuncts. The flow rate improved significantly for the first 90 days and was durable over the 1st year. Postvoid residual (PVR) was also significantly improved at both 0 to 3 and 3 to 12 months postoperatively.

The average AUA symptom score (AUA-SS) before surgery was 19.1 with a quality of life (QoL) index of 3.9. These were both improved after SP. In the malignancy group, 5 patients (20.8%) required a catheter before surgery and 3 (12.5%) required clean intermittent catheterization. After SP, no patients required a catheter. The flow rate improved, although this was not significant.

PVR was significantly improved at 0 to 3 months, although not at 3 to 12 months, after surgery. AUA-SS and QoL score were improved at both time points. Four of 62 patients (6.4%) continued finasteride after surgery in the benign group compared with 1/24 (4.2%) in the malignant group.

Table 2 shows PSA kinetics. The initial postoperative PSA level was significantly lower in the benign group (0.8 *vs* 1.7 ng/mL, $p < 0.01$). PSA was reduced by 89.3% in the benign group and 76.6% in the malignant group ($p = 0.10$). PSA doubling time was 38.4 months for patients with BPH compared with 8.3 months for those with cancer ($p = 0.47$).

PSA velocity for the first 24 months after surgery showed a 0.04 ng/(mL·year) average increase for the benign cohort, compared with 1.4 ng/(mL·year) in the malignant group (on active surveillance) ($p = 0.01$). The mean postoperative PSA values were calculated at various time points and compared between the BPH-only and active surveillance groups (Fig. 2).

Significant differences were noted from 0 to 6 months (0.6 ± 0.7 *vs* 1.2 ± 1.1 ng/mL, $p = 0.02$), 6 to 12 months (0.6 ± 0.7 *vs* 1.8 ± 1.3 ng/mL, $p = 0.01$), and 12 to 24 months (1.0 ± 1.3 *vs* 3.0 ± 2.3 ng/mL, $p = 0.01$).

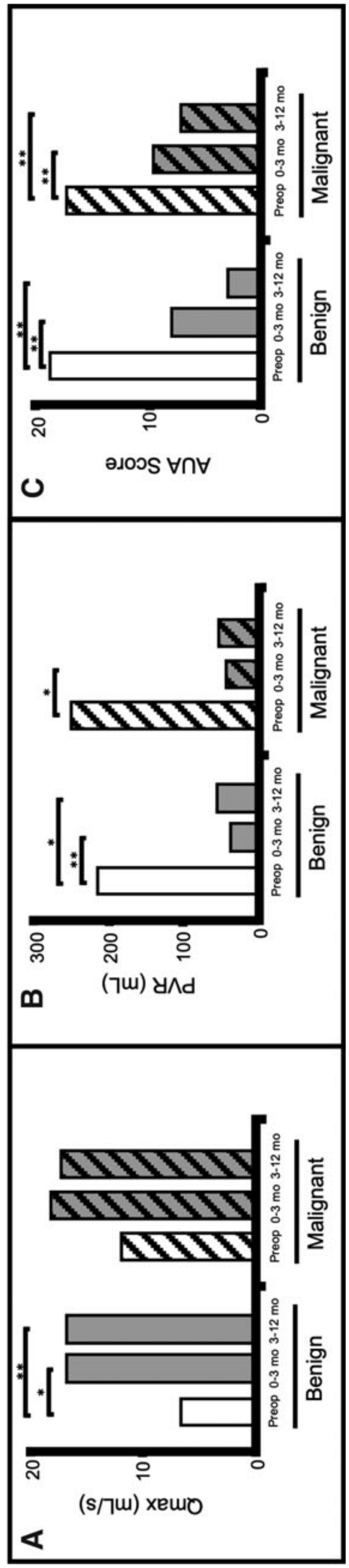

FIG. 1. Urinary outcomes. Comparison of **(A)** Qmax, **(B)** PVR, and **(C)** AUA-SS in benign and malignant groups at preoperative, 0 to 3 months postoperative, and 3 to 12 months postoperative time points. $*p < 0.05$ and $**p < 0.01$. AUA-SS = American Urological Association symptom score; PVR = postvoid residual; Qmax = maximum urine flow rate.

Table 2. Prostate-Specific Antigen Outcomes and Kinetics

	Benign	*Malignant*	*p-value*
Preoperative PSA level (ng/mL)	11.4 ± 9.2	13.8 ± 9.7	0.32
First postoperative PSA level (ng/mL)	0.8 ± 0.7	1.7 ± 1.7	<0.01
% PSA reduction	89.3 ± 17.6	76.6 ± 53.9	0.10
PSA doubling time (months)	38.4 ± 121.2 ($n = 17$)	8.3 ± 5.3 ($n = 9$)	0.47
PSA velocity at 24 months [ng/(mL·year)]	0.04 ± 1.6 ($n = 25$)	1.4 ± 1.0 ($n = 10$)	0.02

An exploratory analysis was performed that excluded patients with known PCa before SP. In the incidental PCa group, the preoperative PSA level was 14.7 ng/mL with a PSA density of 0.1 ng/mL^2, neither of which was significantly different from the benign group ($p = 0.32$ and $p = 0.13$, respectively). The initial postsurgical PSA level was 1.6 ng/mL, which was higher than in the benign group ($p < 0.01$).

These patients had a PSA doubling time of 7.75 months ($p = 0.55$) and PSA velocity of 1.4 ng/(mL·year) ($p = 0.04$) over the 24 months after surgery.

Discussion

PCa screening after SP can be challenging given the paucity of data on expected PSA characteristics as well as lack of guidelines. These patients remain at risk for future malignancy and a better understanding of this clinical scenario is warranted.

In this study, we compared PSA values after SP between men with BPH only and those with PCa. Our results indicate that the initial postoperative PSA value after SP is elevated for patients with underlying PCa. Furthermore, postoperative PSA velocity is increased in patients with malignancy. Unlike prior studies, the reduction in PSA levels was not significantly different between groups.

Prior literature disagrees on the correlation between preoperative PSA and incidentally discovered PCa. In our study, preoperative PSA alone was not useful to differentiate patients with underlying carcinoma, unlike some prior studies.[16] After surgery, there was a substantial reduction in PSA whether or not a patient had histologic BPH or underlying malignancy (89.3% *vs* 76.6%, $p = 0.10$), although this difference was not significant.

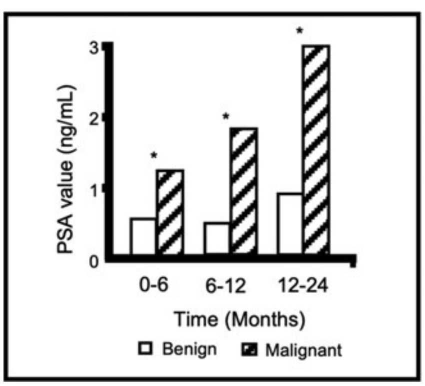

FIG. 2. Comparison of average prostate-specific antigen levels after simple prostatectomy between benign and malignant groups at 0 to 6 months ($n = 16$ malignant and $n = 43$ benign), 6 to 12 months ($n = 8$ malignant and $n = 16$ benign), and 12 to 24 months ($n = 7$ malignant and $n = 17$ benign) postoperatively. *$p < 0.05$. PSA = prostate-specific antigen.

As a result, our data also did not support percent reduction in PSA as a means of cancer risk stratification. This contrasts the findings of Elmansy et al. in a post-HoLEP population, who proposed that PSA reduction of less than 50% was indicative of patients who should be followed closely for early detection of PCa.[13] Notably, the preoperative PSA values of our patients were higher than those included in existing analyses,[4,11,13,17–20] which may have influenced these findings.

Objectively, men with BPH with or without PCa had an improvement in urine flow rate and PVR after surgery. Subjectively, AUA-SS and QoL indices were significantly improved compared with preoperative values in benign and malignant groups. In fact, both AUA-SS and QoL score were improved at 0 to 3 months and continued to improve at 3 to 12 months after surgery.

Improvement in LUTS after SP is consistent with existing literature.[19,21–23] Our study indicates that this procedure can be a therapeutic option for urinary symptoms in men independent of malignancy status. While SP has been a well-established therapy for BPH, in some instances, it may be a valuable component of therapy for men with PCa to improve urination and QoL scores.

At our institution, SP may be offered to a rare subset of men with PCa; for example, men with marked prostatomegaly with PCa desiring active surveillance or focal therapy with concomitant debilitating LUTS or those patients who refuse radical prostatectomy. In any of these scenarios, shared decision-making is imperative, and these patients meet with urology, medical oncology, and radiation oncology to help navigate their disease.

Perhaps most importantly, our findings suggest that after SP, men with histologic BPH alone have a lower initial postoperative PSA level than patients with PCa (0.8 *vs* 1.7 ng/mL, $p < 0.01$). Existing literature has not clearly established an expected or concerning postoperative PSA level after SP. The first data on PSA after SP showed an average PSA value of 1.08 ng/mL in 6 patients with BPH,[3] which has been mirrored by more recent studies.[18,19]

Less is known about men with incidentally discovered PCa or who are at higher risk for future PCa. When considering postoperative PSA values, more robust data exist regarding transurethral prostate reduction surgery. In 2000, Wolff and colleagues proposed a PSA value of 2 ng/mL after TURP as a marker for patients at high risk of malignancy.[12] However, when compared with TURP, SP is performed in patients with a larger prostate, presumably leaving a larger residual PZ.

We do not think that findings from TURP literature can be applied to patients after SP. More recently, conflicting data have emerged regarding PSA after prostate enucleation. One study found no difference in PSA levels after HoLEP in 90 patients with or without prostate malignancy.[17] On the other hand, Abedali reports a higher PSA level at first postoperative measurement after HoLEP for patients with incidental PCa (1.6 *vs* 0.6 ng/mL for the benign group) and recommends prostate biopsy for patients with PSA value >1.[20]

Similarly, Lambert and colleagues noted a concerning PSA cutoff value of 1.73 for patients with future PCa risk after HoLEP.[4] While HoLEP and SP use an enucleation plane to debulk the prostate, there are critical differences in surgical approaches and often in preoperative gland sizes. We posit that PSA monitoring after HoLEP may be similar to SP in some patients, but this is not generalizable to all patients undergoing SP. Our study indicates a difference in the initial postoperative PSA values in the malignant and benign groups after SP, although it does not have the power to provide a recommended cutoff value.

Over the 2-year follow-up period, PSA velocity after SP differed between patients with BPH and those with PCa on active surveillance [0.04 *vs*. 1.4 ng/(mL·year), $p = 0.02$]. Existing literature on this is conflicted. Marks et al. reported no difference in PSA velocity for patients with stage T1a–T1b disease and BPH after TURP,[24] while more recent data, including SP patients, have suggested that there is indeed a difference and that patients with PSA velocity >0.38 ng/(mL·year) had high specificity for PCa.[11] Our data support PSA velocity as an important indicator and that both initial postoperative PSA value and postoperative PSA velocity after SP can be used to identify higher-risk patients.

Our study is the largest to our knowledge that comprised a cohort of pure simple prostatectomies and compared post-surgical PSA values in patients with benign and malignant pathologies. We feel it is compelling in the quest to provide more formal recommendations on PSA follow-up and management after SP, especially for men aged 55 to 69 years with >10- to 15-year life expectancy and ongoing malignancy risk.

Our study is limited by its retrospective nature, and a larger study is needed to provide definitive PSA cutoff values. Given the wide range of prostate gland sizes in patients who undergo SP (>80 g), a postoperative PSA threshold may ultimately prove difficult to establish. Based on our length of PSA follow-up, we could not extrapolate our findings beyond 24 months.

Future research is warranted to strengthen our findings and further elucidate specific postoperative PSA parameters to guide urologists.

Conclusions

PSA interpretation and monitoring after SP have not been well established. Our study indicates that initial postoperative PSA value and PSA velocity are important indicators of underlying malignancy in patients after SP. Further efforts are needed to establish threshold values and formal guidelines.

Authors' Contributions

All authors listed in this article meet the ICMJE authorship criteria. A.J.L. was involved in conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, and writing—original draft. T.D. was involved in conceptualization, investigation, and writing—review and editing. T.N.M. was involved in conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing—original draft, and supervision.

Author Disclosure Statement

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Abbreviations Used

5-ARI = 5-alpha reductase inhibitor
AUA = American Urological Association
AUA-SS = American Urological Association symptom score
BPH = benign prostatic hyperplasia
CT = computed tomography
HoLEP = holmium laser enucleation of the prostate
IQR = interquartile range
LUTS = lower urinary tract symptoms
MRI = magnetic resonance imaging
OSP = open simple prostatectomy
PCa = prostate cancer
PSA = prostate-specific antigen
PVR = postvoid residual
PZ = peripheral zone
Qmax = maximum urine flow rate
QoL = quality of life
RASP = robotic simple prostatectomy
SP = simple prostatectomy
TURP = transurethral resection of the prostate

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An Autonomous Continuous Bladder Irrigation System

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and Monica Farcas, BEng, MEng, MD, FRCSC[1–3]

Abstract

Introduction and Objective: Continuous bladder irrigation (CBI) is used in a variety of clinical settings, including post-transurethral surgery and the emergency department. Currently, CBI administration relies on nurses to diligently monitor and switch irrigation bags, as well as titrate the inflow rate based on effluent color. Inappropriate administration can result in discomfort to patients, clot urinary retention, repeat injury to the pathologic or surgical site, extended hospital stays, and even operative management. Our objective was to create an autonomous CBI system that decreases the incidence of disrupted irrigation flow and monitors the outflow to alert clinicians of critical events.
Methods: 3D printing and off-the-shelf microcontrollers were used to design a device to fit the needs identified by stakeholders at our institution. An *in vitro* model of the bladder was created to test our design. The mechanical, electrical, and software subsystems were adjusted accordingly to meet our design requirements.
Results: Our *in vitro* CBI model was able to simulate routine CBI administration with sudden bleeding. Bovine blood was used to simulate the bleeding events. A device was created that met identified stakeholder needs. Accurate detection of critical bleeding events, catheter blockage, and empty irrigation bags were achieved. The device responds to bleeding appropriately by increasing the irrigation rate. When the catheter is blocked, it stops the irrigation and alerts the nurse. Our system accurately titrated the irrigation rate to match a set outflow blood level parameter, conserving irrigation and minimizing nursing workload. Continuous monitoring of CBI effluent was recorded.
Conclusions: We anticipate our device will decrease the cognitive load on nurses in busy clinical settings and improve workflow. Moreover, the detection of critical events will likely decrease patient morbidity. Continuous monitoring of the CBI outflow may prove to be a new clinical decision-making tool for ongoing hematuria. Clinical trial is pending.

Keywords: continuous bladder irrigation, clot retention, transurethral surgery, gross hematuria, automation, patient safety

Introduction

Continuous bladder irrigation (CBI) is used extensively in a variety of clinical settings, including post-transurethral surgery and gross hematuria presentations to the emergency department.[1] CBI is a key component of postoperative inpatient care as it prevents clot urinary retention and allows the surgical site to heal. In the emergency department, patients with clot retention are manually irrigated free of clot and started on CBI. CBI may be the only intervention needed for the pathologic site to heal in this situation. CBI outflow color is evaluated during patient assessments and is

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used as a clinical sign of ongoing bleeding in the urinary tract. Currently, CBI administration is a subjective process whereby nurses visually assess the effluent color and subjectively titrate the inflow rate to ultimately prevent clot formation.

This process requires diligent monitoring of irrigation bags, continuous reassessment of outflow color, and replacement of irrigation bags when they are empty. Nurses may have to check the administration as frequently as every 15 to 30 minutes to ensure smooth operation.[1] If the irrigation bags are depleted or the outflow is blocked, either by a clot or a kink in the associated tubing, CBI can be interrupted whereas the clinician is unaware. This interruption can result in significant pain, clot retention, repeat injury to the pathologic or surgical site, extended hospital stays, and even emergency operative management.[2]

CBI administration is labor intensive and subjective, and incorrect administration can lead to significant patient morbidity. To our knowledge, there have only been two attempts to tackle this problem. In 2016, Ding et al. randomized 146 patients who underwent a transurethral resection of prostate to receive postoperative CBI with either an automated regulatory device or conventional administration.[3] They found that the group that used the device had significantly decreased incidence of clot retention and cystospasm compared with the control group. However, little detail is provided on the device or its performance characteristics and since 2016, no such devices have been available for commercial purchase and research in this area appears stagnated.

Furthermore, 20/70 patients experienced clot retention postoperatively in the control group compared with 8/76 in the experimental group. The high incidence of clot retention postoperatively in the control group calls into question the generalizability of the findings. In 2022, an abstract was presented at the American Urological Association conference that describes an open source, noninvasive, and inexpensive assembly for automatic hematuria monitoring during CBI.[4] The design details are available online and the results appear to show good correlation for hematuria estimation against known serial dilutions of bovine blood. However, this device does not titrate the inflow of irrigation based on those hematuria estimations and thus does not administer CBI autonomously. Moreover, although the device can determine if the outflow is slowing, it is unable to differentiate whether it is caused by empty irrigation bags or, more critically, a catheter blockage, which is paramount to prevent patient injury.

Our objective was to develop an autonomous CBI system to mitigate some of the pitfalls of manual CBI administration. Our goal is to decrease the incidence of disrupted irrigation flow and thus patient morbidity associated with CBI, decrease the burden on nurses performing the task, and standardize CBI administration.

Methods

IRB approval was obtained (REB 23-044). Stakeholder needs were determined through interviews with nurses, residents, fellows, and staff at our institution. Computer-aided design (CAD) software, 3D printing, and off-the-shelf hardware and microcontrollers were used to design a patent-pending device to fit these needs. Software controllers were designed in-house using Python programming language deliberately so that it may be ported relatively easily to different microcontrollers.

A device with the following features was created:

(1) Ability to control inflow rate of irrigation based on CBI effluent blood concentration.
(2) Ability to automatically switch between irrigation bags (up to four 3-L bags) once a bag is empty.
(3) Ability to notify clinicians through audible alarm in advance of when all bags have depleted.
(4) Ability to notify clinicians through audible alarm when effluent has been bloody for an extended duration of time even though the system is running at the maximum inflow rate.
(5) Ability to notify clinicians through audible alarm when outflow is blocked, whereas at the same time automatically stopping inflow to prevent patient discomfort and possible bladder rupture.
(6) Ability to record data on instillation volume of inflow and outflow, catheter blockage, unexpected irrigation cessation, and effluent blood concentration for the entire duration of CBI administration.

The device consists of three components: (1) irrigation flow controller, (2) outflow monitor, and (3) integration controller. A schematic is shown in Figure 1. All components of the device will fit on a standard hospital irrigation pole so that the patient will be able to ambulate with one pole just like how patients ambulate with CBI currently without the device.

Irrigation flow controller

The irrigation flow controller subsystem was designed to have the ability to control the inflow rate of irrigation and to automatically switch between irrigation bags (up to four) after each bag is depleted. A stepper motor is connected to a 3D printed pinching mechanism (Fig. 2A), which can control the irrigation inflow from completely open to completely closed. The inflow rate and need to switch irrigation bags are determined by weight sensors attached to a standard intravenous pole on which the irrigation bags hang (Fig. 2B). The motor is controlled by an Arduino Nano®, which in turn receives commands to increase or decrease irrigation based on the current situation as determined by the integration controller described as follows.

Outflow monitor

The outflow monitor consists of two parts: (1) effluent blood detector and (2) an outflow rate detector (Fig. 2C, D).

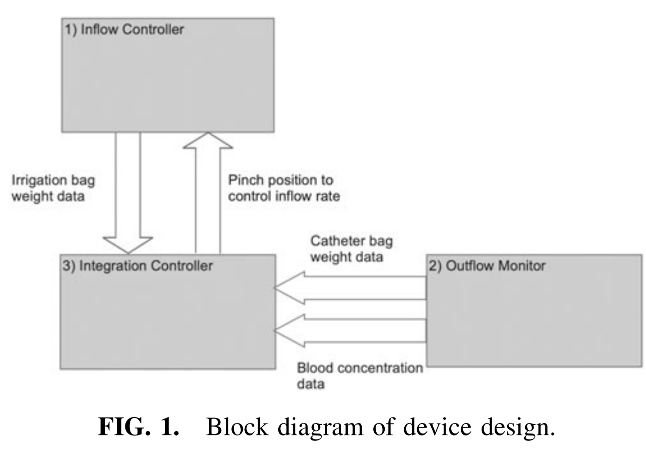

FIG. 1. Block diagram of device design.

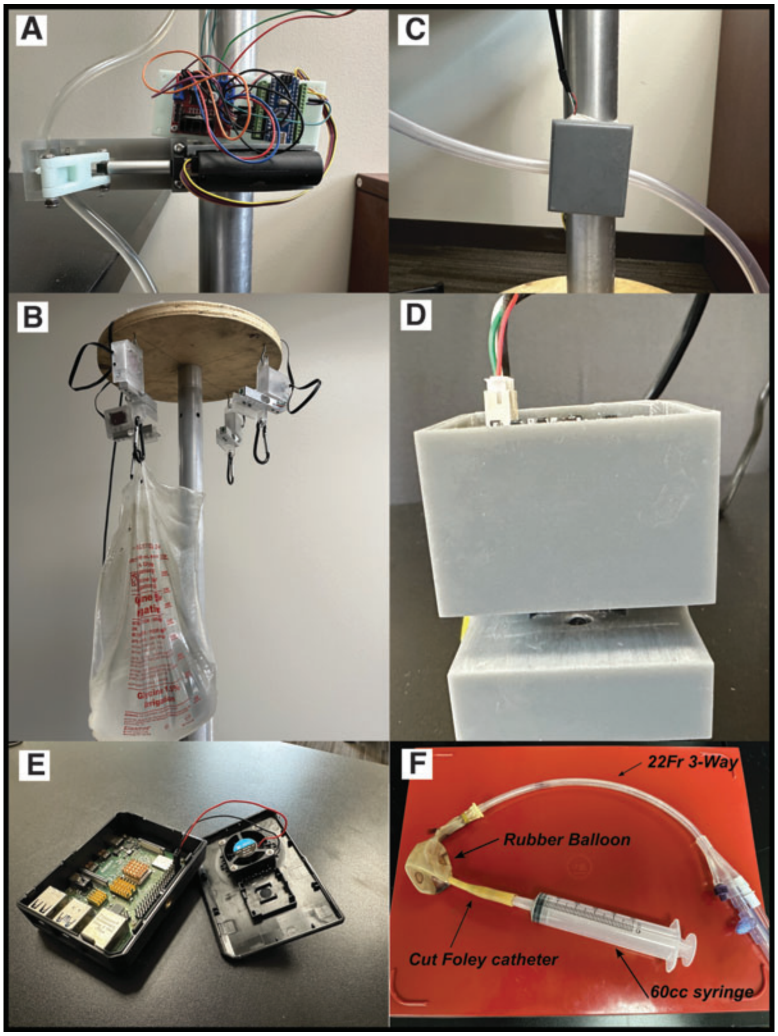

FIG. 2. Irrigation flow controller. **(A)** Photo of the pinching mechanism and Arduino. **(B)** Photo of weight sensor and irrigation bags. **(C)** Outflow blood detector mounted on irrigation pole. **(D)** Inside outflow blood detector showing camera and opposing light-emitting diode. Weight sensor not pictured. **(E)** Integration controller. Photo of Raspberry Pi 4® Model B. **(F)** *In vitro* bladder model.

The Foley catheter bag tubing is attached to the outflow effluent detector. This detector is housed in a 3D printed encasing that surrounds the tubing to block out ambient light. It can theoretically be placed anywhere along the outflow tubing. We placed it in a dependent part of the tubing so that the detector could have more effluent to sample and to avoid air bubbles, which may make the effluent falsely appear clear.

When placed in this location, bubbles are not persistent in the tubing, particularly at higher flow rates. Within the housing, a light-emitting diode emits white light through the tubing and is received by a light sensor on the other side (an off-the-shelf USB web camera; ELP OV5640), which computes the intensity of light that passes through the tubing. We refer to the signal produced by the blood detector as a light intensity score. The outflow rate detector consists of a weight sensor where a regular catheter bag can be hung. It continuously measures the outflow rate using rate-of-change calculations. The monitoring system operates at 10 Hz; a high enough frequency to obtain accurate effluent assessments and detect critical events.

Integration controller

Signals from the outflow monitor are filtered by an integration controller and processed to titrate the CBI inflow rate based on the outflow light intensity score and rate. This controller algorithm was written and implemented on the low-cost computer; the Raspberry Pi® (Fig. 2E). The titration algorithm was determined by expert consensus (Appendix A1). The controller prioritizes safety of CBI administration and increases the flow rapidly when outflow becomes bloody and slowly decreases the flow rate when the outflow is clear.

In addition, the controller integrates all information from the system and delivers the alarms to the critical events described earlier. Of note, the integration controller compares the volume of outflow to the volume of inflow. If the volume of inflow is less than the volume of outflow by a set percentage for a set duration of time, an alarm is triggered. The most likely scenario of an inflow–outflow mismatch is a catheter blockage but can also represent a situation where the inflow is lost from the system (e.g., disconnected CBI components or bladder perforation). If an inflow–outflow mismatch is detected, the inflow is stopped automatically in addition to alerting the clinician.

In vitro *bladder model*

An *in vitro* model of the bladder and CBI was created to test our design (Fig. 2F). A 22F three-way Foley catheter was attached to a rubber balloon. A hole was cut into the balloon where a cut two-way catheter was fashioned to allow administration of bovine blood (through a 60 cc syringe) into the balloon to simulate bleeding.

Results

Outflow sensor characteristics

The outflow sensor was able to accurately detect the blood concentration of the effluent flowing through the Foley bag tubing. Tubes of bovine blood at 0%, 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 75%, and 100% concentrations were prepared by serial dilution (Fig. 3). The outflow effluent intensity was taken for 5 seconds at each concentration, sampling at 10 Hz for a total of 50 samples. Figure 4 shows the scatter of the log intensities at each concentration. The log intensity has a very small variance at each concentration and scales linearly with concentration providing excellent sensor characteristics to accurately detect blood concentration in the outflow effluent. The experiment was performed in an office building setting with ambient overhead lights on and off without significant difference in intensity score at each concentration.

Experiment 1: CBI inflow titration

For this experiment, CBI was initially running clear when a bolus of bovine blood was injected into the *in vitro* bladder model [Fig. 5 at point (a)]. The device accurately detected outflow blood concentration and titrated the inflow rate accordingly by increasing flow rate for high blood concentration and decreasing it for low concentration. Of note, although not depicted, the device will set off an alarm if it is running at maximum flow rate for a prolonged period without resolution of hematuria. In our experiment, this period was set to 10 seconds to ensure the alarm works but can be set to a more realistic duration during clinical implementation.

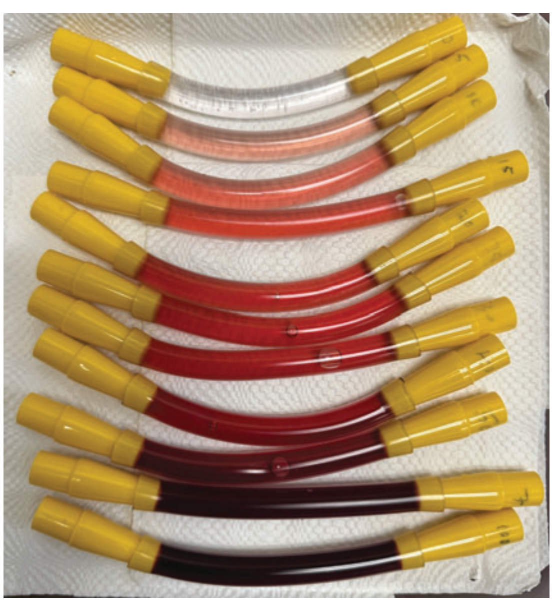

FIG. 3. Bovine blood at 0%, 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 75%, and 100% concentrations from *top* to *bottom*.

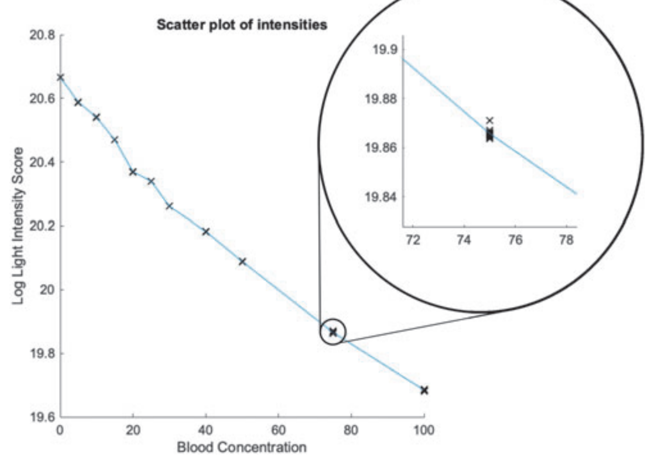

FIG. 4. Scatterplot of log outflow intensity *vs* blood concentration. A closer look reveals tight spread of log light intensity score at each concentration.

Experiment 2: CBI outflow blockage detection

For this set of experiments, CBI was initially running clear. A bolus of blood was injected into the *in vitro* model (Fig. 6i) at point (a). Thereafter, at point (b), the outflow was clamped. The device detected the blockage of the outflow and set off an

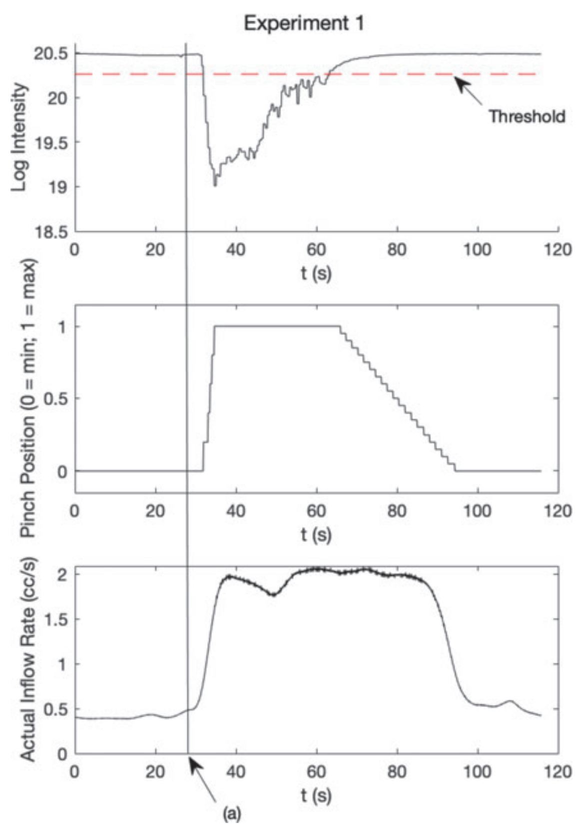

FIG. 5. Experiment 1 graphs of log intensity score, pinch position of inflow controller, and actual flow rate measured by the system. At point (a), a bolus of bovine blood is introduced into the *in vitro* bladder model.

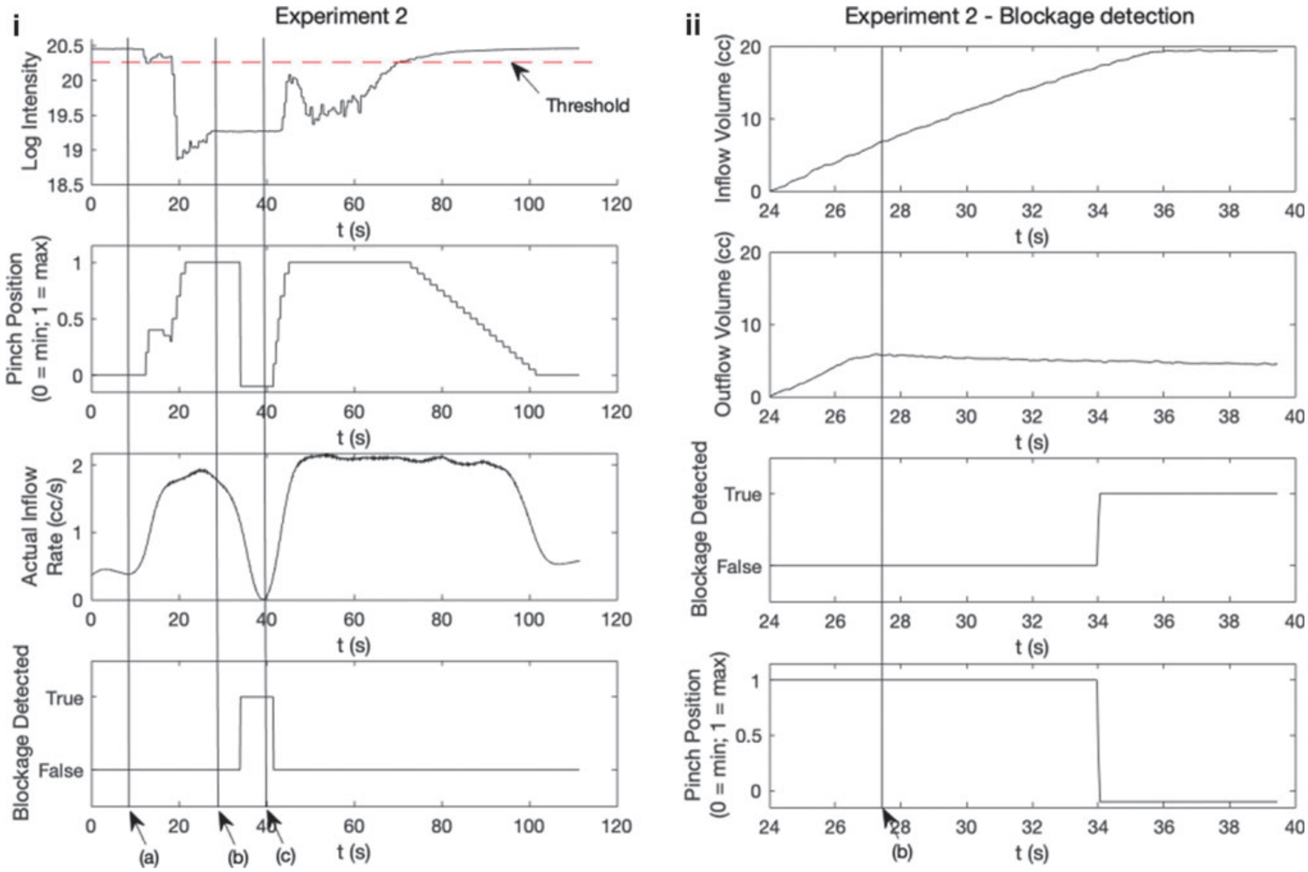

FIG. 6. (i) Experiment 2 graphs of log intensity score, pinch position of inflow controller, actual inflow rate, and blockage detection determination. At point (a), a bolus of bovine blood is introduced into the *in vitro* bladder model. At point (b), the outflow is clamped to simulate outflow obstruction. At point (c), the clamp is removed to simulate release of outflow obstruction. (ii) Examination of the determination of blockage in Experiment 2. Graphs of inflow volume, outflow volume, determination of blockage, and pinch position of inflow controller are shown for the period when the outflow is clamped [point (b)]. Negative pinch position denotes complete cessation of irrigation inflow.

audible alarm. Detection of catheter blockage is achieved by comparison of inflow volume and outflow volume (Fig. 6ii). The inflow was stopped (depicted as a negative pinch position to denote complete cessation of inflow below the minimum running rate). At point (c), the blockage was relieved, and instillation of irrigation resumed. The blood was cleared, and the irrigation flow was titrated back down to the minimum flow.

Discussion

We have created and described an autonomous CBI system that accurately measures effluent blood concentration, titrates the inflow rate, and automatically switches between irrigation bags. Such a completely automated system has not been previously described in literature to our knowledge. Although Ding et al. had conducted a randomized trial with an automated CBI device, details about the devices, including its hematuria measurement accuracy were not described. In this study, we have been able to show a high confidence in estimating effluent hematuria concentration through our light intensity score. The system responds quickly and appropriately to bleeding in the urinary tract in our *in vitro* model. When outflow is blocked, the system's safety features stop instillation of irrigation to prevent high intravesical pressures and bladder rupture.

Our outflow detector operates at 10 Hz and our integration controller operates at an even higher frequency to integrate the signals from the other sensors. Thus, this system can respond to changes 10 times per second. We used a simplistic titration algorithm built on expert consensus that prioritizes patient safety (as opposed to conservation of irrigation fluid). The variables of how quickly to titrate instillation and the length of duration to wait before notifying a clinician are all adjustable and subject to further investigation. Currently, these variables are set to allow efficient demonstration that our system works in our *in vitro* experiments. Before clinical implementation, these can be further optimized by expert consensus to improve patient safety whereas decreasing the nursing intensive task of switching bags too frequently.

The integration controller is built on a Raspberry Pi, which can record and transmit information over Wi-Fi. Alerts need not be only auditory but can be programmed to send to remote devices such as mobile phones through text message, Electronic Medical Records (EMRs), or other mobile applications. In fact, decreasing the number of audible alarms from numerous medical devices in patient rooms is necessary to prevent alarm fatigue and even delirium in patients.[5] Beyond improving safety and workflow, we believe our device has the potential to inform clinical decision-making as it records effluent blood concentration during the entire duration of CBI administration. This newly available clinical information can estimate blood loss and guide management decisions such as whether to pursue operative management or if further investigations are necessary.

The device has a small physical footprint and is easy to install and use. We do not foresee significant barriers to clinical application, although packaging and human factors design need to be optimized to ensure seamless clinical integration. The total cost of our design is ∼$250 CAD. Our design has been optimized for speed and ease of development and not for cost, reliability, or durability. In the future iterations, these additional factors will be considered as they become relevant to our product. We estimate the cost of the device can be reduced by at least 50% by using lower power components that can meet our specifications. These readily available lower power components were not selected for our prototype as they would add design time and effort without contributing to our current design goals.

Next steps to bring our device to the clinical setting include optimization of our titration algorithm, cleaning up human factors design to allow easy acceptance by nursing staff on inpatient wards and the emergency department, and performing a clinical trial to validate improved quality of CBI delivery. Clinical endpoints in the trial include patient comfort, occurrence of clot retention, length of stay in hospital, and early detection of need for reoperation.

Conclusion

We have developed an autonomous CBI system. We believe that this system will ultimately decrease nursing workload and improve clinical outcomes for patients by preventing inappropriate CBI administration and providing more detailed clinical information about ongoing hematuria. A clinical trial to validate the device's clinical utility is underway.

Authors' Contributions

Methodology, software, investigation, formal analysis, and writing—original draft by K.-H.F. Methodology and writing—review and editing by S.S. Investigation and methodology by R.J. and J.L. Investigation by S.M. Conceptualization, methodology, software, engineering design, investigation, writing—review and editing by B.C. Conceptualization, supervision, writing—review and editing, project administration, and funding acquisition by M.F.

Author Disclosure Statement

No competing financial interests exist.

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Abbreviations Used
CBI = continuous bladder irrigation
CAD = computer-aided design

(*Appendix follows* →)

Appendix

Appendix A1. Pseudocode for Titration Algorithm

Loop while CBI device running
Get intensity score (measure of clarity of effluent from detector)
If intensity score above threshold, (effluent is clear and not hematuric)
  If time since last increase > ***minimum_increase_time_before_decrease*** AND
  Time since last decrease > ***minimum_decrease_time_before_decrease*** AND
  Time since start of running CBI > ***minimum must_run_at_start_time***
    Decrease flow rate by a set ***decrease_rate_step*** (if minimum rate not reached)
  Else
    Keep current flow rate
Else (intensity score below threshold, effluent is more hematuric than acceptable)
  if time since last increase > ***minimum_increase_time_before_increase***,
    Increase flow rate by a set ***increase_rate_step*** (if maximum rate not reached)
  Else
    Keep current flow rate

Note: Bolded and italicized text represent variables that can be adjusted. These variables have been set conservatively in our initial design to increase flow rate quickly in response to hematuria and decrease flowrate slowly when clear.

Definitions:

minimum_increase_time_before_decrease: minimum time the CBI will run at the current flow rate after increasing flow rate in response to hematuria before allowing a decrease in flow rate

minimum_decrease_time_before_decrease: minimum time the CBI will run at the current flow rate after decreasing flow rate in response to clear effluent before allowing another decrease

minimum must_run_at_start_time: minimum time to run the CBI at a faster rate at the initiation of CBI. CBI is usually initiated immediately postoperatively or after an acute bleed and presentation to the emergency department. This feature forces the CBI to run at a faster rate to allow a period of healing before attempting to slow down the rate in response to clear effluent.

minimum_increase_time_before_increase: minimum time the CBI will run at the current rate after an increase in flow rate in response to hematuria. This period of time allows the change in flow rate to be reflected in the effluent before another decision is made to increase the flow rate again.

decrease_rate_step: step size of decreasing flow rate

increase_rate_step: step size of increasing flow rate

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