TECHNOLOGY ADVANCEMENTS, SOCIAL MEDIA AND INNOVATIONS IN URO-ONCOLOGY AND ENDOUROLOGY

EDITED BY: Bhaskar K. Somani, Bhavan Prasad Rai, B. M. Zeeshan Hameed and Nithesh Naik

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TECHNOLOGY ADVANCEMENTS, SOCIAL MEDIA AND INNOVATIONS IN URO-ONCOLOGY AND ENDOUROLOGY

Topic Editors:
Bhaskar K. Somani, University of Southampton, United Kingdom
Bhavan Prasad Rai, Freeman Hospital, United Kingdom
B. M. Zeeshan Hameed, Father Muller Medical College, India
Nithesh Naik, Manipal Academy of Higher Education, India

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Felix KH Chun,
University Hospital Frankfurt, Germany

*CORRESPONDENCE
Nithesh Naik
nithesh.naik@manipal.edu

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Editorial: Technology advancements, social media and innovations in uro-oncology and endourology

B M Zeeshan Hameed[1,2,3], Nithesh Naik[2,3,4]*, Bhavan Prasad Rai[2,5] and Bhaskar K. Somani[2,6]

[1]Department of Urology, Father Muller Medical College, Mangalore, Karnataka, India, [2]iTRUE (International Training and Research in Uro-Oncology and Endourology) Group, Manipal, India, [3]Curiouz TechLab Private Limited, BIRAC-BioNEST, Manipal Government of Karnataka Bioincubator, Manipal, India, [4]Department of Mechanical and Industrial Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [5]Department of Urology, Freeman Hospital, Newcastle Upon Tyne, United Kingdom, [6]Department of Urology, University Hospital Southampton NHS Trust, Southampton, United Kingdom

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Editorial on the Research Topic
Technology advancements, social media and innovations in uro-oncology and endourology

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Urology is making rapid technological advances with innovations in the field of uro-oncology and endourology. This is amply supported by social media in creating awareness of these new advancements. As the landscape of minimally invasive urology changes, to highlight and address this area of research, this Research Topic in "Frontiers in Surgery" was dedicated to collecting high-quality scientific contributions focusing mainly on technology advancements, social media, and innovations in Uro-oncology and Endourology.

The research topic includes articles (Gan et al. 2022, Cao et al. 2022, Wu et al. 2022, Chaudhary et al. 2022, Naik et al. 2022, Naik et al. 2022, Hameed et al. 2022, Hameed et al. 2022, Durutovic et al. 2022, Sparwasser et al. 2022, Zhou et al. 2021, Hu et al. 2022, Mao et al. 2022, Deng et al. 2022) that highlight three papers on endoscopic management, two of which are related to benign prostate hyperplasia (BPH) (Gan et al. 2022, Cao et al. 2022, Wu et al. 2022). A single-center experience on the role of "Immediate Transurethral Plasma Kinetic Enucleation of the Prostate Gland (i-TUPKEP) for Treatment of Benign Prostatic Hyperplasia-Associated Massive Hemorrhage (BHM)" Gan et al. (2022) carried a retrospective analysis of 49 patients. The preliminary data suggest that i-TUPKEP is a feasible technique for BHM and relieving BPH symptoms. Cao et al. (2022) in their study identified the role of

"Transurethral Incision of the Bladder Neck (TUIBN) at Three Points with a Needle-Type Electrode for Bladder Neck Contracture (BNC)" Cao et al. (2022). 53 patients showed successful treatment using TUIBN, and the study concludes that it is a safe and reliable option in patients with BNC. Wu et al. (2022) in their endoscopic study focused on the "Removal of large fibrotic bladder blood clots using prostatic tissue morcellator under real-time ultrasound guidance". Real-time ultrasound guidance combined with prostate tissue morcellator shows it to be the safe and effective procedure for the removal of large fibrotic bladder clots in all nine patients.

The research topic includes six articles that highlight the role of innovative technologies in urological patient care (Chaudhary et al. 2022, Naik et al. 2022, Naik et al. 2022, Hameed et al. 2022, Hameed et al. 2022, Durutovic et al. 2022, Sparwasser et al. 2022). Chaudhary et al. 2022 look at YouTube videos as a source of patient information for ureteric stent placement Chaudhary et al. (2022). The observations of their study concluded that the majority of videos are of poor overall quality and lack pertinent information suggesting the need for creating comprehensive unbiased videos. Naik et al. (2022) in the review raise an important concern by considering the various aspect of artificial intelligence (AI) on the ownership of responsibility and legal and ethical considerations in healthcare Naik et al. (2022). Naik et al. (2022) highlighted the patient's perception and feedback on the role of telemedicine and telehealth Naik et al. (2022). They examined recent research on video consulting in urology clinics for hematuria referrals and follow-up appointments for benign prostatic hyperplasia (BPH), kidney stone disease (KSD), and urinary tract infections (UTIs) and found that they are extremely acceptable and satisfactory. Telemedicine, a competent, cost-effective patient-care technology, has been effectively applied in numerous healthcare settings and specialties for such patients Naik et al. (2022).

Role of 3D printing in endourology is discussed as being helpful to visualize patient anatomy and aiding in pre-operative planning and training Hameed et al. (2022). The application of virtual reality augmented reality and mixed reality in endourology and urolithiasis is also discussed Hameed et al. (2022). Simulation-based training with these new immersive technologies allows improved training and should be a part of the curriculum. Otas et al. (2022) discussed 3D imaging segmentation and 3D rendering process for precise PCNL puncture, which may have widespread use and adoption for complex stone treatment Durutovic et al. (2022). The assessment of a novel smart-glass-based point-of-care fusion approach for mixed reality-assisted targeted prostate biopsy, suggests that this has the potential to improve accuracy for the detection of prostate cancer Sparwasser et al. (2022).

The research by Zhou et al. (2021) evaluates and predicts cancer-specific survival among patients with radical prostatectomy for prostate cancer. Nearly 96,000 patients were considered in the study and were divided into training and validation cohorts, to develop a competing risk nomogram to predict cancer-specific death for these patients Zhou et al. (2021). Hu et al. (2022) performed a retrospective analysis of 213 patients who underwent balloon dilatation for ureteral stricture and show that the long-term effect of three stents was better than that of single or double stents Hu et al. (2022). A successful robotic-assisted modified Y-shaped ileal orthotopic neobladder reconstruction is presented in 21 patients by Mao and colleagues Mao et al. (2022) A case report of renal pseudoaneurysm after flexible ureteroscopy and lasertripsy is mentioned by Deng et al. They suggest reducing operative time and intrarenal pressure to prevent these complications Deng et al. (2022).

Through a string of articles focussing on technology, innovation, and social media this special issue addresses a series of topics in uro-oncology and endourology. These outcomes will be useful for urology trainees and consultants alike and are likely to help and enhance their clinical practice. It will help them gain insight into newer and cutting-edge advances in the field of minimally invasive urology.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication. All authors contributed to the article and approved the submitted version.

Conflict of interest

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Predicting Cancer-Specific Survival Among Patients With Prostate Cancer After Radical Prostatectomy Based on the Competing Risk Model: Population-Based Study

*Xianghong Zhou†, Shi Qiu†, Kun Jin†, Qiming Yuan, Di Jin, Zilong Zhang, Xiaonan Zheng, Jiakun Li, Qiang Wei and Lu Yang**

Department of Urology, National Clinical Research Center for Geriatrics and Center of Biomedical Big Data, Institute of Urology, West China Hospital of Sichuan University, Chengdu, China

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Bhaskar K. Somani, University of Southampton, United Kingdom

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Pietro Pepe, Cannizzaro Hospital, Italy
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***Correspondence:**
Lu Yang
wycleflue@163.com

†These authors have contributed equally to this work

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Introduction: We aimed to develop an easy-to-use individual survival prognostication tool based on competing risk analyses to predict the risk of 5-year cancer-specific death after radical prostatectomy for patients with prostate cancer (PCa).

Methods: We obtained the data from the Surveillance, Epidemiology, and End Results (SEER) database (2004–2016). The main variables obtained included age at diagnosis, marital status, race, pathological extension, regional lymphonode status, prostate specific antigen level, pathological Gleason Score. In order to reveal the independent prognostic factors. The cumulative incidence function was used as the univariable competing risk analyses and The Fine and Gray's proportional subdistribution hazard approach was used as the multivariable competing risk analyses. With these factors, a nomogram and risk stratification based on the nomogram was established. Concordance index (C-index) and calibration curves were used for validation.

Results: A total of 95,812 patients were included and divided into training cohort (n = 67,072) and validation cohort (n = 28,740). Seven independent prognostic factors including age, race, marital status, pathological extension, regional lymphonode status, PSA level, and pathological GS were used to construct the nomogram. In the training cohort, the C-index was 0.828 (%95CI, 0.812–0.844), and the C-index was 0.838 (%95CI, 0.813–0.863) in the validation cohort. The results of the cumulative incidence function showed that the discrimination of risk stratification based on nomogram is better than that of the risk stratification system based on D'Amico risk stratification.

Conclusions: We successfully developed the first competing risk nomogram to predict the risk of cancer-specific death after surgery for patients with PCa. It has the potential to help clinicians improve post-operative management of patients.

Keywords: competing risk analyses, prostate cancer, radical prostatectomy, post-surgery, predicting model

INTRODUCTION

Prostate cancer (PCa) is one of the most common genitourinary tumors. In 2020, it is estimated to cause 33,330 deaths in the United States (1). Radical prostatectomy (RP) has been confirmed as an effective primary treatment for patients with localized PCa (2). However, although with the advancement of surgical techniques, a large number of patients undergoing RP have obtained survival benefits, there are still about 25% of patients who will develop biochemical recurrence, distant metastasis, or even death caused by PCa (3–6). At present, it is still controversial as to which kind of patients need to receive active post-operative adjuvant treatment or receive conservative watchful waiting (7). It is important to identify the patients with a higher risk of recurrence or death, and they may benefit more from post-operative adjuvant treatments.

Some research teams have developed tools to stratify the risk of recurrence or death for PCa patients. For example, D'Amico risk stratification, CAPRA Scoring System, and Stephenson nomogram are commonly used in clinical (8–10). These tools mainly used several clinicopathological parameters such as prostate specific antigen (PSA) level, clinical stage, Gleason Score (GS), and pathologic extent to predict the prognosis. However, these tools are still flawed. They are mainly developed based on a small number of patients, the weight between the various prognostic factors is not clear enough and some studies have pointed out that their prediction accuracy is often <70% (11, 12). In addition, many patients with PCa are elderly people with many comorbidities, and they are more likely to die from cardiovascular disease, infection, or other non-tumor factors. Therefore, it is more difficult for researchers to accurately determine the prognosis of patients (13, 14).

To circumvent these defects, with the approach of competing risk analyses, we evaluated the factors affecting prostate cancer-specific survival (CSS) at a large cohort. Furtherly we developed a prognosis nomogram and construct a risk stratification that may have potential clinical implications to help clinicians identify the patients with a high risk of cancer-specific death after RP.

We present the following article in accordance with the TRIPOD Checklist.

METHODS

Patient Selection

All patients' information was obtained from The Surveillance, Epidemiology, and End Results (SEER) database (2004–2016). SEER database is a public cancer dataset made up of 18 population-based cancer registries. It has covered about 25% population of the United States (14). From the SEER database, patients with a diagnosis of adenocarcinoma of the prostate (International Classification of diseases-O-3 code: C61.9) between 2004 and 2016 were selected. Inclusion and exclusion criteria were shown in the flowchart in detail (**Figure 1**). With a ratio of 7:3, all the patients were randomly divided into the training cohort and validation cohort.

Variables and Endpoint

For each patient, the information extracted from the SEER database included age at diagnosis, marital status, race, pathological extension, regional lymphonode status, PSA level, pathological GS, and follow-up information. For continuous variables including age at diagnosis and PSA level, X-tile software (Yale University, USA) was used to assess the optimal cut-off values by the minimal *p*-value approach (15) (**Figure 2**). The optimal cut-off values for age at diagnosis were ≤5.9, 6.0–14.9, >14.9. The optimal cut-off values for PSA level were ≤5.9, 6.0–14.9, >14.9.

Cancer-specific death (CSD) was used as the primary endpoint. CSD was measured by all deaths caused by prostate cancer, complications of treatments, or unknown processes in patients with active tumors. Other cause-specific death (OCSD) was measured by all deaths caused by non-cancer events and seen as the competing event of the CSD. Follow-up time was defined as the time between the first treatment and the patient's death or last follow-up.

Statistical Analysis

For categorical variables, a χ^2-test was used to evaluate the difference between the training cohort and validation cohort, and the results were presented as the frequency with its proportion. In the training cohort, we estimated the cumulative incidence function (CIF) for CSD and tested the survival differences by Gray's test to discover potential prognostic variables with a p-value < 0.05. Subsequently, we performed competing risk multivariable analyses based on the Fine and Gray's proportional subdistribution hazard approach to identify these independent prognostic variables with a p-value < 0.05. All the independent prognostic factors were selected to construct a nomogram to predict 5-year CSD probabilities for PCa patients after RP.

To validate the performance of the nomogram, in both two cohorts, the discrimination of the nomogram was assessed by Harrell's concordance index (C-index). The value of C-index ranged from 0.5 to 1, and a higher C-index means better discrimination for the prediction model (16). Besides, the calibration curve with 1,000 resamples of bootstrapping was used to compare the predicted survival outcome with the actual survival outcome. The closer the calibration curve was to the standard curve, the closer the survival outcome predicted by the nomogram was to the actual survival outcome (17).

In addition, we developed a risk stratification based on the nomogram risk score. The cut-off values of risk scores were determined using X-tile software. Then we compare the discrimination abilities of the risk stratification with the European Association of Urology (EAU) risk stratification based on D'Amico stratification (2).

The statistical software R (version 3.4.3, The R Foundation) was used in the above statistical analyses. A p-value < 0.05 was considered statistically significant.

Abbreviations: PCa, Prostate cancer; CI, confidence interval; RP, radical prostatectomy; SRT, salvage radiotherapy; GS, Gleason Score; CSS, cancer-specific survival; CSM, cancer-specific mortality; CIF, cumulative incidence function; PSA, prostate specific antigen; SEER, the Surveillance, Epidemiology, and End Results; CSD, Cancer-specific death; OCSD, Other cause-specific death; EAU, European Association of Urology; ISUP, International Society of Urological Pathology; AUA, American Urological Association.

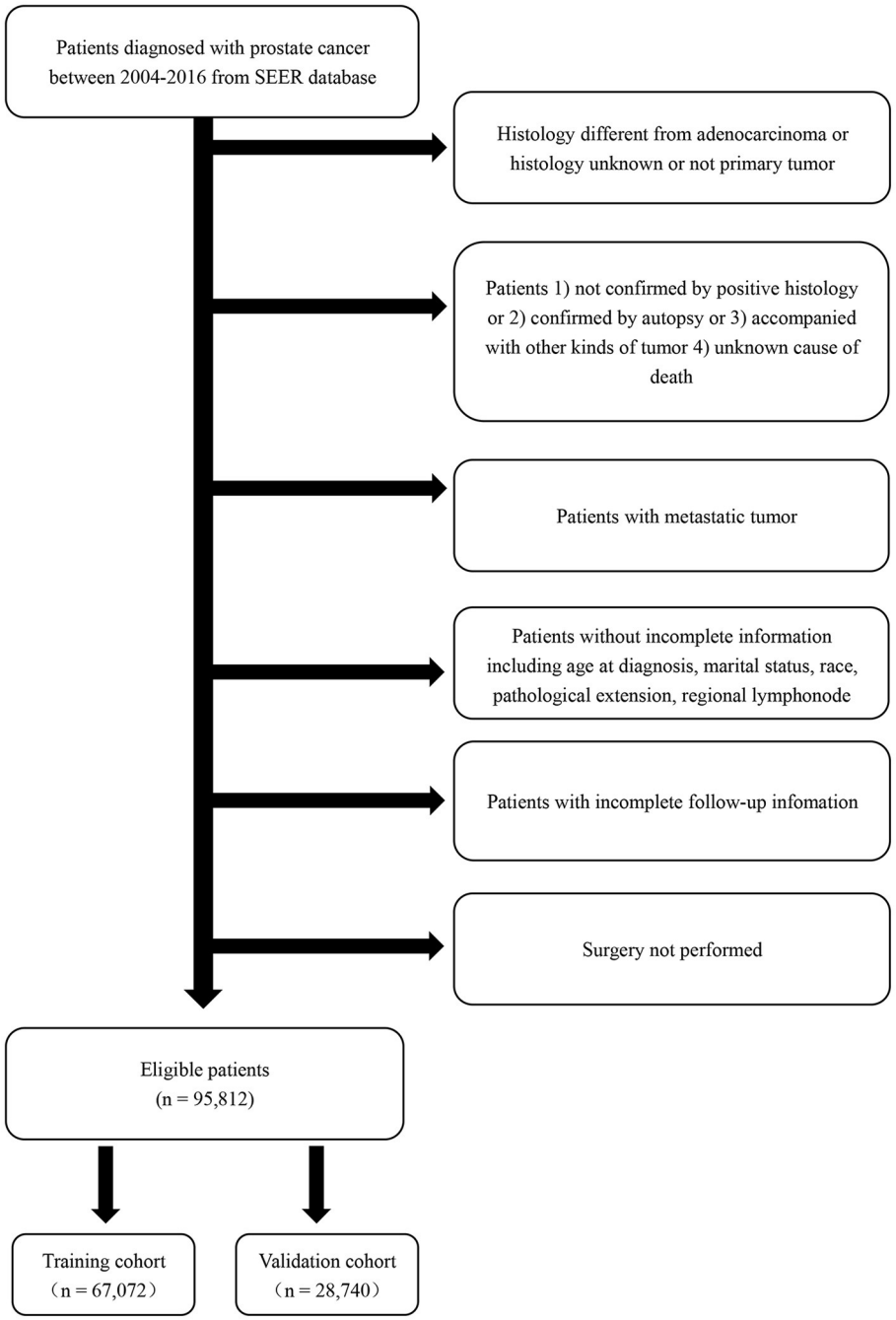

FIGURE 1 | Flowchart describing the inclusion and exclusion criteria of patients in the Surveillance, Epidemiology, and End Results (SEER) database, 2004–2016.

RESULTS

Patient Characteristics

Finally, a total of 95,812 eligible patients were included in this study. Among them, 67,072 patients were assigned to the training cohort, while 28,740 patients were assigned to the validation cohort. **Table 1** showed the characteristics of patients in detail. Between the training cohort and validation cohorts, there were no statistically significant differences except for the age at diagnosis.

Identification of Independent Prognostic Factors

We performed the analyses of CIF and Gray's test as the univariable analyses. The results showed that age, race, marital status, pathological extension, regional lymphonode status, PSA level, and pathological GSwere the factors with a significant impact on CSD. The Fine and Gray's proportional subdistribution hazard approach was performed as the

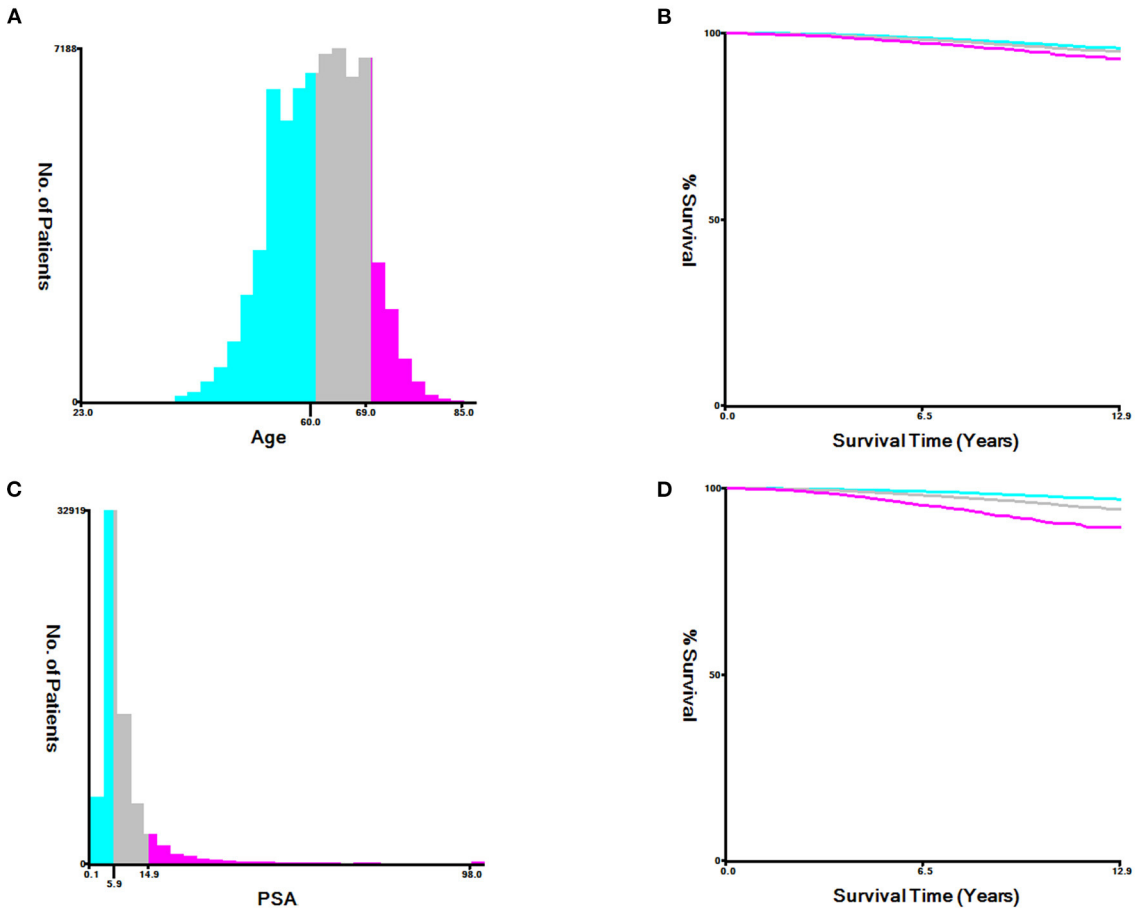

FIGURE 2 | Determination of the optimal cut-off values of age at diagnose **(A,B)**, and prostate specific antigen (PSA) level **(C,D)**. The Optimal cut-off values were identified by the X-tile software according the difference of cancer-specific survival outcomes.

multivariable analyses. And the results were consistent, in which age, race, marital status, pathological extension, regional lymphonode status, PSA level, and pathological GS were the significant prognostic factors of CSD. These variables could be thought of as the independent prognostic factor for predicting the CSS of PCa patients after RP. The detailed results of univariable and multivariable analyses were showed in **Table 2**.

Development and Validation of the Competing Risk Nomogram

Based on the results of univariable and multivariable competing risk analyses, age, race, marital status, pathological extension, regional lymphonode status, PSA level, and pathological GS were used to construct the nomogram for predicting the probability of 5-year CSD for PCa patients after RP (**Figure 3**). The detailed score of each nomogram variable was listed in **Table 3**.

We performed the analyses of C-index and calibration curve to validate the reliability of the nomogram. For the training cohort, the C-index was 0.828 (%95CI, 0.812–0.844). For the validation cohort, the C-index was 0.838 (%95CI, 0.813–0.863). The relatively high C-index (>0.8) showed the good predictive ability of this nomogram. Meanwhile, in both training cohort and validation cohort, the calibration curves showed a good agreement between the 5-year CSD predicted by nomogram and actual 5-year CSD (**Figure 4**).

Establishment of Risk Stratification for Cancer-Specific Death After RP

According to the score corresponding to each nomogram variable, we calculated the total risk score for each patient in both the training cohort and the validation cohort. By the X-tile approach, patients were divided into three risk groups based on the total risk score from the nomogram. The low-risk group included patients with 0–66 points, the middle-risk group included patients with 67–105 points, and the high-risk group included patients with no <106 points.

In order to verify the predictive value of this risk stratification, we compared it with the EAU risk stratification based on D'Amico stratification. EAU risk stratification is one of the most popular risk stratification tools for PCa patients, which can divide patients into three groups including low-risk, medium-risk, and high-risk. In both training cohort and validation cohort, we

TABLE 1 | Descriptive characteristics of 95,812 prostate cancer patients undergoing radical prostatectomy between 2004 and 2016 from the Surveillance Epidemiology and End Results database.

Variable	Primary cohort (n = 95,812)		Training cohort (n = 67,072)		Validation cohort (n = 28,740)		
	Number	%	Number	%	Number	%	p-value
Age							<0.001
≤60	39,159	40.9	26,320	39.2	12,839	44.7	
61–69	45,207	47.2	32,783	48.9	12,424	43.2	
≥70	11,446	11.9	7,969	11.9	3,477	12.1	
Race[a]							0.247
White	78,440	81.9	54,968	82.0	23,472	81.7	
Black	12,182	12.7	8,524	12.7	3,658	12.7	
Other	5,190	5.4	3,580	5.3	1,610	5.6	
Marital status							0.110
Married	77,053	80.4	54,030	73.4	23,023	73.8	
Single[b]	18,759	19.6	13,042	21.1	5,717	21.2	
Pathological extension							0.080
Organ-confined	67,469	70.4	47,120	70.3	20,349	70.8	
Extracapsule-invasion	18,041	18.8	12,655	18.9	5,386	18.7	
Seminal vesicle invasion	9,371	9.8	6,658	9.9	2,713	9.4	
Adjacent structures invasion	931	1.0	639	1.0	292	1.0	
Regional lymphonode status							0.346
Negative	91,526	95.5	64,044	86.4	27,482	95.6	
Positive	4,286	4.5	3,028	13.6	1,258	4.4	
PSA level (ng/ml)							0.777
≤5.9	45,664	47.7	31,971	47.7	13,693	47.6	
6.0–14.9	39,882	41.6	27,886	41.6	11,996	41.7	
>14.9	10,266	10.7	7,215	10.8	3,051	10.6	
GS							0.131
≤6	23,522	24.6	16,444	24.5	7,078	24.6	
7 (3 + 4)	40,563	42.3	28,334	42.2	12,229	42.6	
7 (4 + 3)	16,887	17.6	11,809	17.6	5,078	17.7	
7(N/A)	108	0.1	73	0.1	35	0.1	
8	6,908	7.2	4,878	7.3	2,030	7.1	
9	7,581	7.9	5,379	8.0	2,202	7.7	
10	243	0.3	155	0.2	88	0.3	
EAU risk classification							0.455
Low risk	3,316	3.5	2,306	3.4	1,010	3.5	
Intermediate risk	5,250	5.5	3,654	5.4	1,596	5.6	
High risk	76,649	80.0	53,630	80.0	23,019	80.1	
Unknown	10,597	11.1	7,482	11.2	3,115	10.8	

[a]*Black: African American, White: Caucasian, Other: American Indian/AK Native, Asian/Pacific Islander.*
[b]*Single: Divorced, Separated, Single (never married), Widowed, unmarried.*

plotted the CIF curves for different risk groups based on the risk stratification of the nomogram or EAU risk stratification (**Figure 5**). Compared with our risk groups, the degree of separation of CIF curves of CSD between groups was more obvious than EAU risk stratification. Meanwhile, in both two cohorts, The high-risk group identified by our risk stratification had a significantly higher CSD risk than OCSD, while the high-risk group in the EAU risk stratification did not. The results showed that the novel risk stratification based on the nomogram had better prognostic discrimination than EAU risk stratification.

DISCUSSION

In this study, based on a large cohort of 95,812 patients from SEER database, we identified seven risk factors and construct a competing risk nomogram based on these prognostic factors to predict the probability of the occurrence of CSD within 5 years after RP for each patient with PCa. Furthermore, based on the difference in nomogram scores, we developed a novel risk stratification for post-operative CSD in patients with PCa. Our risk stratification has potential clinical value and may

TABLE 2 | Univariate analyses and multivariate competing risk analyses of prognostic factors influencing cancer-specific survival outcomes in the training cohort.

Variable	Univariate analyses (CIF) *p*-value	Multivariate competing risk analyses sdHR (95%CI)	*p*-value
Age	<0.001		
≤60		Ref.	
61–69		1.098 (0.972–1.240)	0.132
≥70		1.308 (1.103–1.551)	0.002
Race[a]	0.024		
White		Ref.	
Black		1.225 (1.043–1.440)	0.014
Other		0.698 (0.529–0.920)	0.010
Marital status	<0.001		
Married			
Single[b]		1.253 (1.099–1.429)	<0.001
Pathological extension			
Organ-confined		Ref.	
Extracapsule-invasion		2.273 (1.956–2.641)	<0.001
Seminal vesicle invasion		3.576 (3.039–4.207)	<0.001
Adjacent structures		4.245 (3.261–5.525)	<0.001
Invasion			<0.001
Regional lymphonode status	<0.001		
Negative		Ref.	
Positive		1.917 (1.647–2.231)	<0.001
PSA level (ng/ml)	<0.001		
≤5.9		Ref.	
6.0–14.9		1.252 (1.043–1.440)	<0.001
>14.9		1.430 (1.214–1.686)	<0.001
GS	<0.001		
≤6		Ref.	
7 (3 + 4)		1.647 (1.291–2.101)	<0.001
7 (4 + 3)		3.150 (2.441–4.065)	<0.001
7 (N/A)		3.980 (1.253–12.641)	0.019
8		5.065 (3.900–6.583)	<0.001
9		10.827 (8.448–13.874)	<0.001
10		20.528 (13.803–30.978)	<0.001

[a]*Black: African American, White: Caucasian, Other: American Indian/AK Native, Asian/Pacific Islander.*

[b]*Single: Divorced, Separated, Single (never married), Widowed, unmarried.*

CIF, cumulative incidence function; sdHR, subdistribution hazard ratio; Ref., reference.

help clinicians better identify patients who still need active intervention after RP. The results showed that the discrimination of our stratification system was not weaker than the commonly used EAU risk stratification based on D'Amico stratification.

Competing risk nomogram is a kind of widely used risk predicting model in many fields in oncology such as lung cancer, breast cancer, and colorectal cancer (18–20). The nomogram can incorporate many key factors of the disease into the prognosis prediction model and can consider the weight of each variable to make the prediction model more accurate. In addition, the graphical representation helps to more intuitively evaluate the individual situation of each patient, which is more practical (21). At the same time, competing risk nomogram has its unique advantages compared to traditional nomogram or other prognosis predicting models. The competitive risk nomogram is based on competing risk analysis methods such as CIF and Fine and Gray's proportional subdistribution hazard approach, rather than the Kaplan-meier method and Cox proportional risk regression commonly used in other types of models. Competitive risk analyses not only consider the survival and death of patients but also consider the impact of death caused by other factors on the endpoints of interest such as CSD. This is especially important in the research of PCa, because a large part of PCa patients may die due to other factors before developing CSD (13). To our knowledge, there is still no research reported on the competitive risk prognosis prediction model for the prognosis of PCa patients after RP.

In the field of PCa, the currently commonly used nomogram is Stephenson nomogram. It is developed by Stephenson et al. to predict disease progression after salvage radiotherapy (SRT), with data from a multi-institutional retrospective cohort of 1,540 patients. Seven variables were used to construct the nomogram including PSA before SRT, surgical margins, GS, PSA double time before SRT, lymph node metastasis, and androgen deprivation therapy administration before or during SRT (22). However, there are still some defects with Stephenson nomogram. Due to the limitation of inclusion and exclusion criteria, it is not widely applicable to PCa patients who have received RP. At the same time, it paid little attention to hard endpoints such as CSD. In the cohort of the original study, its c-index was 0.69 (compared to 0.83 of our nomogram), and the c-index obtained after the test in another study was even lower (23). Another post-operative nomogram proposed by Cleveland Clinic in recent years has become more and more widely used in clinical practice (24). This nomogram mainly consisted of PSA level at the time of biochemical recurrence (BCR), pathological GS, seminal vesicle invasion, extraprostatic extension, preoperative PSA, and time to BCR. This study is based on the population of PCa patients with BCR after surgery and can predict the probability of patients eventually developing CSD. In the internal validation of 2,254 patients in the study, the c-index of the nomogram was 0.74, which was lower than the C-index of 0.83 obtained by our proposed nomogram in a cohort of 67,072 patients. At the same time, the clinicopathological parameters required by our nomogram can be obtained within a short period after surgery. Therefore, our nomogram has advantages in guiding patients' initial post-operative management compared with this nomogram that incorporates PSA dynamic parameters.

In our study, the competing risk analyses identified 7 prognostic factors including age, race, marital status, pathological extension, regional lymphonode status, PSA level, and pathological GS. Among them, GS had the greatest influence on survival outcomes. Many studies have reported the relationship between GS and the prognosis of PCa (25–27). International Society of Urological Pathology (ISUP) reported that GS can be divided into five groups [2–6, 7 (3 + 4), 7 (4 + 3), 8, ≥9] according to prognosis, and this was consistent with our research results (27). With the increase of GS, the patient's nomogram score was also increasing, that is to say, the possibility

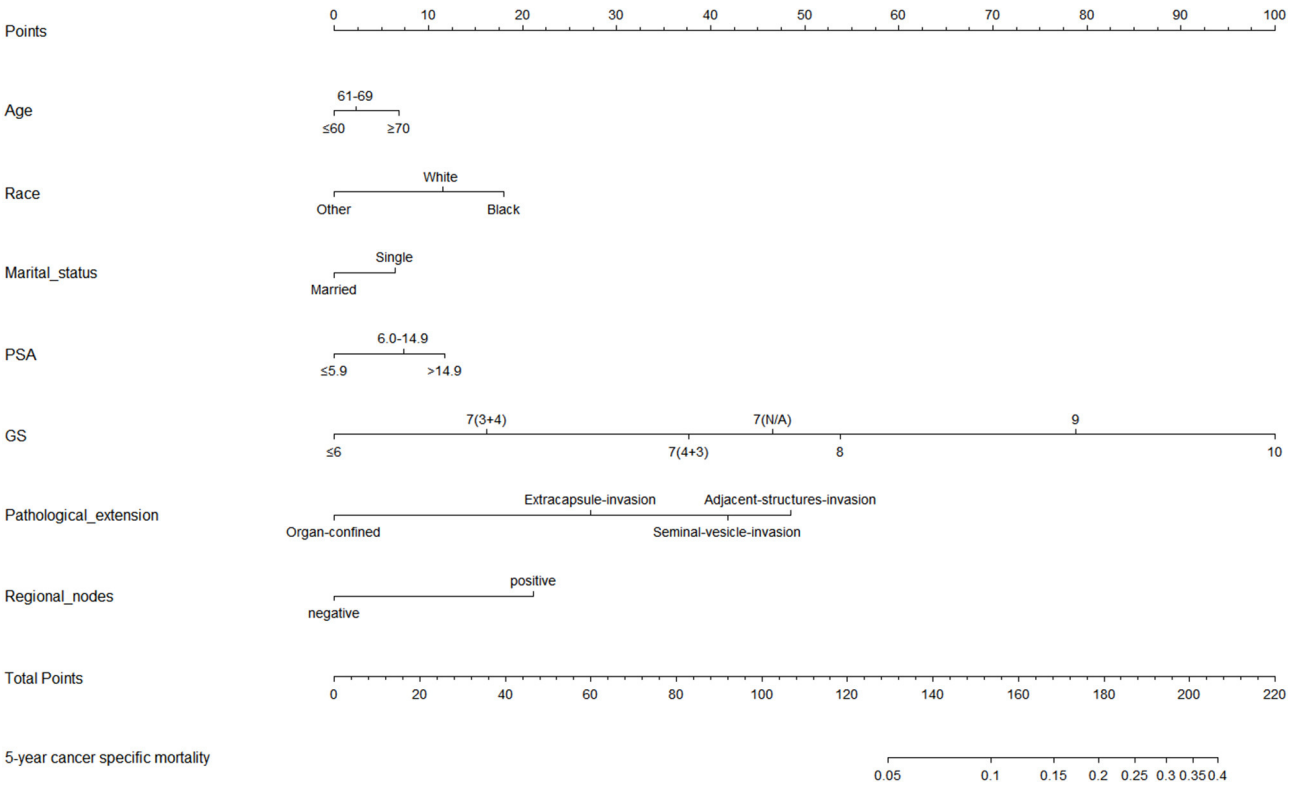

FIGURE 3 | Nomogram for predicting the cancer specific mortality (CSM) at 5 years in prostate cancer patients undergoing radical prostatectomy. (1) Black: African American, White: Caucasian, Other: American Indian/AK Native, Asian/Pacific Islander. (2) Single: Divorced, Separated, Single (never married), Widowed, unmarried.

of the patient developing CSD within 5 years was increasing. In the nomogram, we could find that GS $4 + 3 = 7$ group was with an obviously higher score than GS $3 + 4 = 7$ group. This was also consistent with the latest American Urological Association (AUA) clinical guideline, which indicated that many pieces of research had demonstrated that the prognosis of GS 4+3 was significantly worse than GS $3 + 4$ (28, 29). The pathological extension was another important prognostic factor whose weight was second only to GS. It has been widely accepted that poor pathological findings such as extracapsular invasion and seminal vesicle invasion are related to disease recurrence and poor prognosis (30–32).

In addition to the above-mentioned well-known prognostic factors, our study also found the impact of race and marital status on the prognosis of PCa patients. Our nomogram showed that African Americans had the highest risk of CSD after RP, followed by Caucasian and other races. This finding was consistent with some studies published in recent years. According to statistics from researchers, the average annual incidence of PCa among African Americans was 60% higher than that of Caucasian men. Besides, compared with other races, African Americans have the highest mortality rate (33, 34). The causes of the result were very complicated. For example, In the United States, PCa tended to be larger in African Americans and was more likely to metastasize than white men (35). From a genetic perspective, some gene mutations related to disease progression are more common in African Americans, such as TP53 mutations and MYC amplification (36). Several risk-associated single nucleotide polymorphisms were found to be overexpressed in African Americans (37). At the same time, African Americans may face some social barriers such as health insurance, which may affect the treatment and management of the disease (38). Our competing risk analyses also identified marital status as an independent prognostic factor. More and more researchers have paid attention to the impact of this sociological factor on the disease. Outcomes of numerous studies showed that married marital status was a protective factor for the occurrence and development of a variety of tumors, including PCa. Marriage may be a multifaceted representation of many protective factors including social support (39, 40).

EAU risk stratification based on D'Amico stratification is currently a common risk stratification system for PCa patients, which divided patients into Low-risk group, Intermediate-risk group, and High-risk group for predicting the risk of disease recurrence (2, 41). In our study, we compared the novel risk stratification based on the nomogram with EAU risk stratification. The results showed that our risk stratification system had better discrimination with a C-index over 0.8 and could better detect patients at higher risk of the occurrence of post-operative CSD after adjustment of competing risk analyses. The high-risk group obtained through our risk stratification had a significantly higher risk of CSD than OCSD, which could better

TABLE 3 | Detailed risk scores of all independent prognostic factors in the nomogram.

VariablesAge	Nomogram risk score	Variables Regional lymphonode status	Nomogram risk score
≤60	0	Negative	0
61–69	2	Positive	21
≥70	7	**PSA level (ng/ml)**	
Race		≤5.9	0
White	11	6.0–14.9	7
Black	18	>14.9	12
Other[a]	0	**GS**	
Marital status		≤6	0
Married	0	7 (3 + 4)	16
Single[b]	6	7 (4 + 3)	38
Pathological extension		7 (N/A)	47
Organ-confined	0	8	54
Extracapsule-invasion	27	9	79
Seminal vesicle invasion	42 at 5 years	10	100
Adjacent structures invasion	49		
Total points	**Predicted probability of 5-year CSM**		
154	0.10		
179	0.20		
195	0.30		
207	0.40		

CSM, cancer specific mortality.

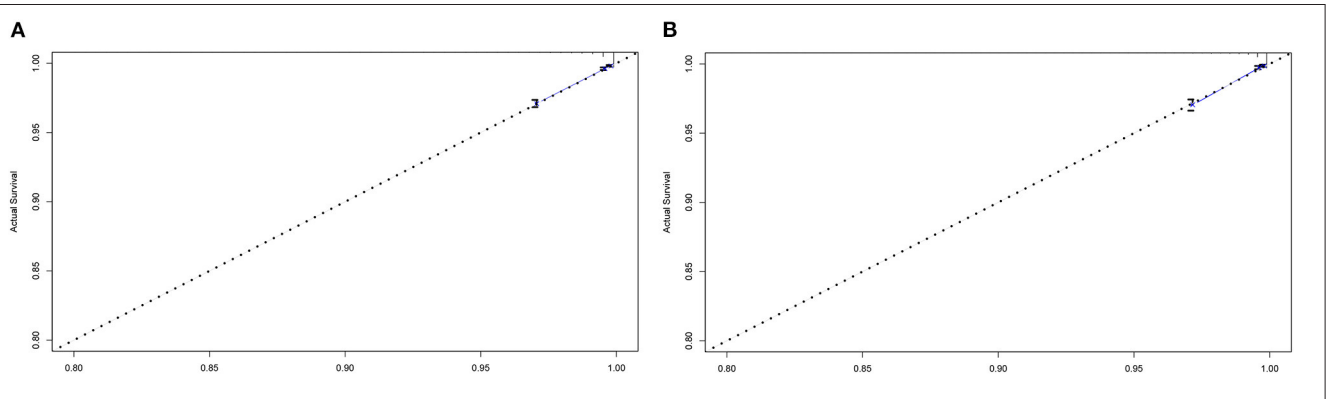

FIGURE 4 | Calibration curves for comparing the degree of agreement between the actual survival outcome and the survival outcome predicted by the nomogram in the training cohort **(A)** and the validation cohort **(B)**. The horizontal axis is the survival rate predicted by the nomogram, and the vertical axis is the actual survival rate. The dashed line indicates the predicting survival rate completely fits the actual survival rate.

exclude the interference of death caused by non-tumor factors on the model. Our advantages may come from many aspects, such as a large cohort, more prognostic factors, and independent analyses of competing risks. At the same time, our research provides quantitative and graphical prognostic tools, which help to make more accurate assessments of each patient.

Our study revealed 7 main independent prognostic factors that affect the occurrence of CSD in patients after RP and explored the application of these factors in identifying high-risk patients through the nomogram and risk stratification. At present, the guidelines pointed out that there were multiple managements for patients undergoing RP, including adjuvant treatment, salvage treatment, watchful waiting, etc. However, due to the lack of high-quality prospective data, the inclusion and exclusion criteria of patients are still controversial (2). Although radical surgery has been implemented, many men may still need adjuvant or salvage treatment to prevent or delay clinical metastasis, thereby reducing the likelihood of patients dying from tumors (42). However, because the frequency of clinic5al metastasis or death in PCa patients is generally low, the choice of adjuvant therapy in all men may mean a large amount of overtreatment. Moreover, adjuvant therapy has obvious side

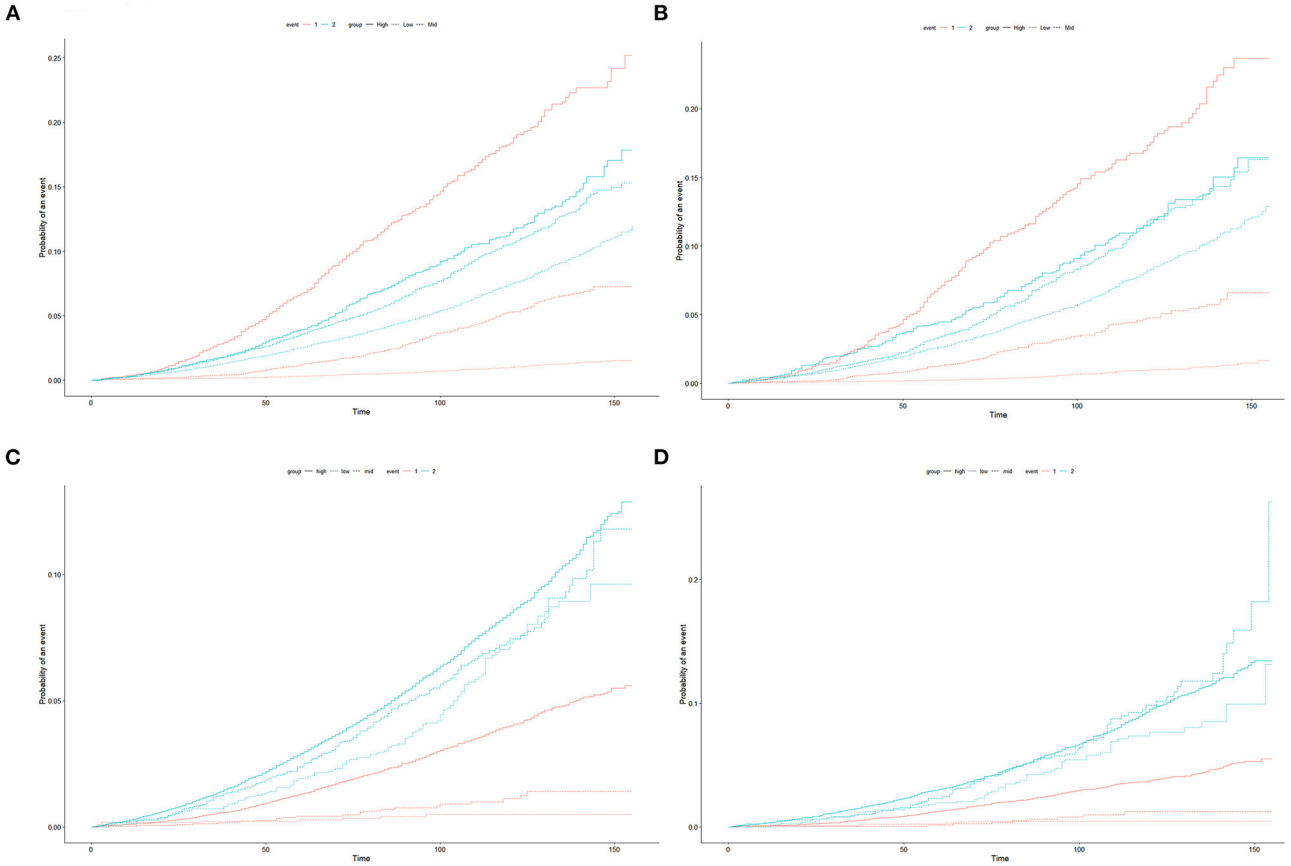

FIGURE 5 | Cumulative incidence function (CIF) curves of different risk stratification systems for cancer specific mortality (CSM) in prostate cancer patients undergoing surgery. Nomogram risk stratification and EAU risk stratification based on D'Amico risk stratification were tested in the training cohort **(A,C)** and validation cohort **(B,D)**. As event 1, cancer-specific death was represented by red lines, and other cause-specific death was represented by event 2, and blue lines.

effects. Adjuvant radiotherapy is an independent predictor of urinary incontinence and intestinal dysfunction, and androgen deprivation therapy may further aggravate post-operative erectile dysfunction (42, 43). Therefore, good prognostic stratification tools after RP to wisely guide the use of adjuvant therapy is urgently needed. In 2019, the EAU prostate cancer guidelines update proposed that the risk of subsequent metastasis after prostate cancer surgery, as well as PCa CSD and overall mortality, can be determined by initial clinical and pathological factors (Tstage, ISUP grade) and PSA dynamics (PSA double time and PSA failure interval) to predict (44). This update is consistent with our findings that ISUP grade is significantly associated with important clinical endpoints after prostate cancer surgery. However, because data of PSA kinetics was obtained from long-term follow-up after surgery, the application of PSA kinetics in formulating short-term patient management strategies after surgery is limited. Our research mainly includes data that can be easily obtained in a short period after surgery to help clinicians consider the patient's post-operative management plan promptly. For example, in our risk stratification system, patients in different risk groups have significantly different clinical endpoints. For high-risk patients, more aggressive post-operative management strategies, such as the use of adjuvant therapy after surgery, may be required. For patients in the low-risk group, the present study provides insights into which men can adopt more conservative post-operative management strategies, such as watchful waiting.

The prognostic model proposed in our study incorporates the most basic and most accessible clinicopathological information, making it applicable to almost all urological tumor centers. In addition, the application of some new technologies can bring more accurate clinical information to improve our clinical management. In recent years, the role of multiparametric magnetic resonance imaging (mpMRI) in the diagnosis and prediction of prognosis for PCa patients has received extensive attention from researchers. It is reported that mpMRI can significantly reduce the number of unnecessary repeat prostate biopsies (45). Some researchers have tried to use mpMRI to determine risk stratification for PCa patients (46). The results showed that the fusion of mpMRI data and clinicopathological data can significantly improve the predictive model's ability to predict the recurrence of PCa disease, compared to traditional predictive models that only have clinical data. Prostate-specific membrane antigen positron emission tomography (PSMA-PET)

is another novel PCa visualization technology, which is characterized by high-precision visualization of primary PCa masses and provides superior accuracy at initial staging. At the same time, in a small-scale cohort, researchers reported the high accuracy of PSMA-PET-derived radiomics features for the diagnosis of visually unknown PCa (47). A newly reported study proposed a nomogram combining clinical information and PSMA-PET information. In the high-risk prostate cancer population cohort, the results showed that the fusion prognostic prediction model had an important prognostic effect on important clinical endpoints, and its performance was better than currently used prognostic tools (48). Some studies on the prognosis of PCa have made progress at the genetic level. For example, PCa susceptibility variants are found to be closely related to the prognosis of PCa, called single nucleotide polymorphisms, which are mainly involved in tumor cell invasion (49). The presence or absence of DNA repair-related changes in BRCA1 or BRCA2 has been reported to have a significant impact on the clinical endpoint after radical treatment of PCa (50). Evaluation of the TMPRSS2:ERG fusion gene, PTEN, the Prolaris test, the Decipher test, and the Oncotype DX Genomic Prostate Score can also provide important information helping improve the individual management for PCa patients (51). Some studies have established prognostic models based on the expression of immune-related genes and autophagy-related genes, which had considerable accuracy in predicting BCR (52, 53). However, at present, due to the lack of equipment, funds, and technical personnel, the implementation of mpMRI, PSMA-PET, and genetic evaluation are still limited (54). Our prediction model still has relatively high accuracy even when only common clinicopathological parameters are included, so our research results may be more practical. In the future, an improved prognostic prediction model that integrated these novel technologies will be able to better guide accurate clinical decision-making, and it will also be the goal of our team's future exploration.

There are still several limitations to our study. First, our research is based on a large retrospective cohort. We still need more prospective clinical trials to contribute more precise data. Second, in the data included in our study, there is a lack of data on the use of adjuvant therapy. This is due to the data limitation of the database. Our study included nearly 100,000 patients, and a large number of study populations made it difficult to follow up patients with post-operative adjuvant therapy. Many studies on the risk factors of prostate cancer recurrence after surgery have not included information about the adjuvant treatment of patients (24, 55). In current randomized trials and observational studies, there are conflicting data on the effects of early post-operative radiotherapy and early androgen deprivation therapy on CSD (24). Our risk stratification system performed well in validation, and the lack of adjuvant treatment data had little impact on our research results. Although based on the SEER database, many research teams have developed a series of well-known clinical prognosis prediction models, but the SEER database still has some inherent limitations (56–58). The lack of adjuvant treatment records, changes in data reports, patient migration, and selection bias are some of the problems in large-scale real-world studies based on the SEER database. In the future, we look forward to construct a relatively small prospective cohort and try to use these parameters to further optimize the nomogram and risk stratification system. Finally, we also lack additional independent external validation sets, and this is our important work goal in the future.

CONCLUSIONS

In conclusion, we performed a competing risk analysis based on a larger cohort of 95,812 patients with non-metastatic PCa from the SEER database. We also identified 7 independent prognostic factors of the occurrence of CSD after RP and constructed a competing risk nomogram utilizing the 7 factors for detecting the risk of CSD for each patient. A risk stratification system was established based on the nomogram to help clinicians better identify patients at high risk of CSD after surgery.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

XZho, KJ, SQ, QY, QW, and LY are responsible for designing the study, writing, collecting data, analysis, and final approval of the article. DJ and KJ are responsible for a part of analysis and revision. ZZ, XZhe, and JL are responsible for a part of writing and revision. All authors have read and approved the final manuscript.

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Immediate Transurethral Plasma Kinetic Enucleation of the Prostate Gland for Treatment of Benign Prostatic Hyperplasia-Associated Massive Hemorrhage: A Single-Center Experience

Yu Gan[1], *Liang Deng*[2], *Qiangrong He*[2], *Chao Li*[2], *Leye He*[2] *and Zhi Long*[2]*

[1] *Department of Urology, Xiangya Hospital, Central South University, Changsha, China,* [2] *Andrology Center, Department of Urology, The Third Xiangya Hospital, Central South University, Changsha, China*

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Edited by:
Bhaskar K. Somani, University of Southampton, United Kingdom

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***Correspondence:**
Zhi Long
longzhi522@163.com

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Purpose: Benign prostatic hyperplasia-associated massive hemorrhage is a urological emergency. We evaluated the outcome from immediate transurethral plasma kinetic enucleation of the prostate gland (i-TUPKEP) for BHM treatment.

Methods: We retrospectively analyzed the records of 49 patients with acute BMH who underwent i-TUPKEP between January 2014 and November 2018 at our institution. The hemostatic effect, International Prostate Symptom Score (IPSS), and quality of life (QoL) score were evaluated preoperatively as well as 3, 6, and 12 months postoperatively. Postoperative follow-up also included measurement of the peak flow rate (Q_{max}) and post-void residual urine volume (PVR). Clinical characteristics, weight of resected tissue, duration of bladder irrigation, duration of hospital stay, complications, as well as the time required for enucleation and resection, were recorded.

Results: BMH causes were attributed to transurethral surgery (17/49, 34.7%), violent catheterization (13/49, 26.5%), cystoscopy (10/49, 20.4%), and urethral dilatation (9/49, 18.4%). Bleeding was from different sites of prostate-gland tissues during i-TURKEP. i-TUPKEP-controlled BMH effectively induced immediate, notable, and lasting improvements in the IPSS and QoL score. Q_{max} was close to normal, and the PVR was within the physiological range, postoperatively. Long-term complications were not observed.

Conclusion: Our preliminary data suggest that i-TUPKEP is a feasible method for controlling BHM and relieving BPH symptoms.

Keywords: benign prostatic hyperplasia, transurethral plasma kinetic enucleation of the prostate gland, hemorrhage, lower urinary tract symptoms, minimally invasive

INTRODUCTION

Hematuria is a common complication of benign prostatic hyperplasia (BPH), which is often caused by injury to the prostatic urethra and gland (1). Although mild bleeding can be controlled through conservative treatment methods (2, 3), massive hemorrhage due to transurethral examination and/or surgery can develop into a urological emergency (4, 5). Rapid and extensive deposition of blood clots in the bladder can lead to catheter blockage, induction of bladder contractions, and aggravation of pain. Moreover, persistent blood loss without effective control can induce cardiovascular and cerebrovascular complications or lead to hemorrhagic shock and, sometimes, death (6, 7). Therefore, eliminating blood clots from the bladder and controlling BPH-associated massive hemorrhage (BMH) at the earliest opportunity is crucial.

In general, BMH indicates a need for surgical intervention. However, most patients with BPH patients are elderly and likely to have one or more diseases, so the risks of surgery and anesthesia increase exponentially (5, 8). Transurethral resection of the prostate gland (TURP) is a minimally invasive method to treat BMH. During TURP, blood clots can be cleared and the bleeding points can be found and treated by electrocoagulation. Nevertheless, good control of bleeding is a major challenge for the urologists (9). Some of the bleeding sites may be hidden in prostate-gland tissue, which will be shrunken and edematous. Moreover, residual prostatic tissue after TURP in this setting is likely to become a new bleeding site. In some cases, patients have to undergo another surgical procedure to stop the bleeding, which leads to an overall increased risk of complications (5, 6).

Transurethral plasma kinetic enucleation of the prostate gland combines the traits of a bipolar plasma kinetic device and enucleation of the prostate gland. TUPKEP has notably improved the efficacy and safety of transurethral surgical procedures for patients with BPH, especially with respect to bleeding control (10, 11).

Reports on TUPKEP application for BMH are rare. In consideration of the advantages of TUPKEP, we postulated that this method may be an alternative method for controlling BMH. After accumulating sufficient experience in using TUPKEP for BPH, we explored the efficacy and safety of TUPKEP for controlling BMH.

Our institution employs TUPKEP to eliminate blood clots and enucleate and resect the hyperplastic prostate gland in a one-stage emergency procedure for treating BMH, which is defined as "immediate TUPKEP" (i-TUPKEP). Here, we focused on evaluating the outcomes of i-TUPKEP for treating BMH.

MATERIALS AND METHODS

Ethical Approval of the Study Protocol

The patients provided written informed consent before i-TURKEP. The study protocol was approved by the Ethics Review Board of Third Xiangya Hospital at Central South University (Changsha, China).

Study Design

We retrospectively analyzed the records of 837 consecutive patients who underwent TUPKEP between January 2014 and November 2018 at Third Xiangya Hospital.

Inclusion Criteria

The criteria for study inclusion were patients receiving TUPKEP for the following reasons: (i) BPH with active hemorrhage and extensive blood clots deposited in the bladder; (ii) continuous bladder irrigation was obstructed frequently and failed to alleviate pain and bladder contractions; (iii) BMH occurred immediately after inappropriate transurethral surgery or actions (e.g., repeat violent catheterizations, urethral dilatation, and cystoscopy).

Exclusion Criteria

The exclusion criteria were a history of: (i) carcinoma in the prostate gland; (ii) taking anticoagulants or coagulation disorders in the perioperative period; (iii) myocardial infarction, cerebral infarction, or cerebral hemorrhage within 3 months before TUPKEP; (iv) neurogenic bladder, urethral stricture, or surgery of the lower urinary tract.

Assessment Parameters

The patients underwent tests for the prostate-specific antigen (PSA) level; the hemoglobin level; serum levels of electrolytes, glucose, lipids, myocardial enzymes, brain natriuretic peptide, D-dimer; coagulation function; and liver and kidney functions. After hospital admission, blood-pressure measurement, electrocardiography, chest radiography, abdominal ultrasonography, and computed tomography were also conducted. Lower urinary tract symptoms (LUTS) were evaluated by the International Prostate Symptom Score (IPSS) and the Quality of Life (QoL) score based on status over the previous month before hospital admission. The prostate volume was assessed using transrectal ultrasonography (12). Owing to indwelling catheters, the patients did not undergo testing of the urinary flow rate or post-void residual urine volume (PVR) before surgery.

Preoperative Treatments

Intravenous access was established rapidly. Central venous catheterization was undertaken if the patient had complications related to anemia and reduced blood pressure. Fluid rehydration and blood transfusion were carried out, and vasoactive drugs were administered (if necessary) based on the patient's condition. The preoperative blood pressure was maintained above 100/60 mmHg. All the patients were given antibiotics 30 min before the surgical procedure and received general anesthesia. All surgical procedures were undertaken by the same senior surgeon, who had >10 years of extensive experience in carrying out minimally invasive surgical procedures for BPH.

Instruments and i-TUPKEP Procedure

An isoionic bipolar electrical cutting system (Gyrus Medical, Cardiff, Wales) used 200 W and 100 W for cutting and coagulation, respectively. Physiologic (0.9%) saline served as the irrigation fluid. A 27-Fr resectoscope with a loop was placed in

the bladder through video-assisted endoscopic guidance system. Initially, blood clots were removed from the bladder using an Ellik evacuator. If removal of blood clots by the Ellik evacuator was difficult, the loop could be used for cutting them into small pieces. Overall observation of the urethra, verumontanum, prostatic urethra, bladder, and bilateral ureter orifices was done to determine the bleeding site. The main method of TUPKEP was based on the experience described by Xu and colleagues (13). The improvement we made was that the hyperplastic gland in the 12 o'clock position was resected in a retrograde fashion from the apex toward the bladder neck by the loop electrode instead of enucleation. A small and thin "pad" of the gland located between the 12 o'clock position of the urethral glands and apex was retained to improve urinary continence.

Definition of "Surgical Success" and Postoperative Treatments

The success of the surgical procedure was defined as no-active bleeding after the surgical procedure. An indwelling, standard 20-F three-way catheter was used after the procedure, which was connected with a pump containing.9% saline for continuous irrigation of the bladder. Drainage was halted until hematuria had resolved sufficiently. As a routine procedure, the catheter was extracted 5 days after completion of the surgical procedure.

Follow-Up

The patients were evaluated using the IPSS, QoL score, PSA level, hemoglobin level, blood pressure, the weight of all the prostatic fragments (in g), as well as the time needed for enucleation and resection and postoperative bladder irrigation during the perioperative period. Follow-up was conducted at 3, 6, and 12 months after surgery, which included assessment of the IPSS, QoL score, maximum urine flow rate (Q_{max}) and the PVR. Postoperative complications were classified using the Clavien–Dindo system (14).

Statistical Analyses

Data are the median, with minima and maxima. Mann–Whitney U test was used to analyze the differences between two independent samples, while Wilcoxon signed-rank test was used to analyze the differences between two related samples. Statistical

TABLE 1 | Perioperative characteristics of the patients with BMH (median, minima to maxima).

	Urethral dilatation	Catheterization	Cystoscopy	TURP
Patients number ($n = 49$)	9	13	10	17
Age (year)	72 (66–78)	72 (65–82)	71 (65–79)	74 (67–80)
PV (ml)	84 (62–87)	79 (66–107)	82 (61–97)	60 (49–73)
IPSS	33 (28–35)	30 (29–35)	29 (27–36)	30 (28–33)
QoL	4 (3–5)	4 (3–5)	4 (3–5)	4 (4–5)
PSA (ng ml^{-1})	2.6 (1.1–3.5)	2.5 (1.7–3.5)	2.4 (1.5–3.1)	2.7 (2.2–3.6)
Bleeding site				
Apex lobe	0	0	0	7
Lateral lobe	2	4	3	2
Top lobe#	0	0	0	8
Mid lobe	7	9	7	0
Operative time (min)	51 (41–75)	56 (41–64)	52 (43–59)	31 (25–42)
Enucleation time	25 (17–33)	25 (18–32)	23 (18–27)	17 (14–20)
Resection time	26 (21–42)	27 (20–39)	28 (25–34)	14 (9–24)
SBP (mmHg)				
Pre-operation	109 (100–121)*	106 (97–123)*	110.5 (108–123)*	95 (86–108)
Post-operation	123 (117–134)	130 (114–141)	121 (111–135)	130 (116–139)
Preoperative hemoglobin (g l^{-1})	99 (91–107)	97 (87–110)	101.5 (96–108)	88 (84–95)*
Decrease in hemoglobin (g dl^{-1})	1.5 (0.6–2.2)	1.3 (0.6–2.8)	1.6 (1–2.5)	1.6 (1.1–2.5)
Decrease in sodium (mmol l^{-1})	0.3 (0.2–0.5)	0.4 (0.2–0.8)	0.4 (0.2–1.5)	0.4 (0.2–0.8)
Resected tissue weight (g)	34 (26–39)	34 (24–45)	35.5 (26–45)	27 (19–34)
Blood transfusion	0	0	0	1
Pre-operation	1	0	2	10
During operation	0	0	0	1
Post-operation	0	0	0	0
Irrigation time (hour)	3 (2–7)	4 (2–7)	3.5 (2–6)	4 (2–5)
Hospitalization (day)	6 (6–7)	6 (6–7)	6 (6–7)	6 (5–6)

*BMH, benign prostatic hyperplasia-associated massive hemorrhage; IPSS, international prostate symptom score; PSA, prostate-specific antigen; QoL, quality of life; SBP, systolic blood pressure; TRUS, transrectal ultrasonography; UTI, urinary tract infection; VUR, vesicoureteral reflux; PV, prostate volume; Mann–Whitney U test was used to analyze the differences between the TURP group and urethral dilatation, catheterization or the cystoscopy group with *denoting $p < 0.05$; #Top lobe is located in the 12 o'clock position.*

analyses were conducted using SPSS 20.0 (IBM, Armonk, NY, USA). $p < 0.05$ was considered significant.

RESULTS

Bleeding Causes

Of the 837 participants, 49 patients satisfied the inclusion criteria mentioned above. **Table 1** outlines the baseline demographic data (including vital signs, anemia severity, and LUTS). The major cause of massive hemorrhage was TURP: 17 patients (17/49, 34.7%) had received TURP before hospital admission. Of the 17 patients who had a history of TURP, eight patients (8/17, 47.1%) had received an emergency transurethral procedure one to two times to control bleeding and to clear blood clots before being transferred to Third Xiangya Hospital. Six patients (6/17, 35.3%) had suffered from hemorrhagic shock before the surgical procedure, with one of them being assisted by mechanical ventilation for pulmonary dysfunction before hospital admission. Other causes included inappropriate transurethral actions (e.g., repeatedly violent catheterization; 13/49, 26.5%), cystoscopy (10/49, 20.4%), and urethral dilatation (9/49, 18.4%).

The systolic blood pressure upon hospital admission was significantly lower in the patients who had ever received TURP (median 95 mmHg, $p < 0.05$) than that for other patients. Anemia was much more severe in the patients who had a TURP history (hemoglobin: median 88 g/L, $p < 0.05$), and 10 (10/17, 58.8%) of these patients required an infusion of homotypic concentrated erythrocyte suspension before the surgical procedure, whereas only three (3/32, 9.4%) patients without a TURP history needed a transfusion.

Bleeding Locations

The bleeding site was demonstrated to be from the prostatic urethra intraoperatively. The patients without a TURP history commonly had edema, hyperemia, and ulceration in the prostatic urethral mucosa, along with dilated submucosal veins. Parts of the urethral mucosa or urethral glands were injured, which were mainly located in the mid lobe (23/32, 71.9%) and lateral lobes (9/32, 28.1%). Edema was present in the prostatic urethral mucosa of all the patients with a TURP history. The wound surface of these patients was uneven and, in general, had active bleeding, located mainly at the 12 o'clock position (8/17, 47.1%) and apex of the prostate gland (7/17, 41.1%), followed by the lateral urethral glands (2/17, 11.8%) (**Table 1**).

Intraoperative Situation

i-TUPKEP was achieved for all the patients. In the patients with a TURP history, several residual hyperplastic glands were retained, and the surgical capsule could be identified readily from the verumontanum position for enucleation.

The surgical procedure was completed with stable vital signs and without transurethral resection syndrome for all the patients. Only one (1/49, 2%) patient needed a blood transfusion intraoperatively, and no patient (0/49) needed a blood transfusion postoperatively. Also, bleeding was controlled effectively in all the patients (**Table 1**).

TABLE 2 | Follow-up data stratified by the causes of BMH (median, minima to maxima).

Parameter	Urethral dilatation	Catheterization	Cystoscopy	TURP
Patients number ($n = 49$)	9	13	10	17
IPSS				
Baseline	31 (29–35)	31 (29–35)	33 (29–35)	30 (28–33)
3 months	14 (13–19)*	14 (10–19)*	17 (13–19)*	14 (11–17)*
6 months	12 (8–16)*	12 (8–16)*	15 (8–17)*	13 (10–16)*
12 months	14 (10–16)*	15 (11–15)*	13 (9–16)*	12 (10–15)*
QoL				
Baseline	4 (3–5)	4 (3–5)	4 (4–5)	4 (4–5)
3 months	3 (2–3)*	2 (2–3)*	3 (2–3)*	2 (2–3)*
6 months	2 (2–3)*	2 (2–3)*	2 (2–3)*	2 (2–2)*
12 months	2 (2–2)*	2 (2–3)*	2 (2–2)*	2 (2–3)*
Qmax (ml s^{-1})				
3 months	12 (10–16)	13 (11–16)	14 (10–15)	15 (12–16)
6 months	12 (11–14)	12 (10–16)	13 (11–14)	14 (12–16)
12 months	13 (12–15)	14 (12–15)	13 (12–15)	14 (12–15)
PVR (ml)				
3 months	28 (27–34)	27 (24–31)	29 (27–34)	27 (23–34)
6 months	29 (27–30)	25 (25–30)	29 (27–30)	27 (25–30)
12 months	28 (25–29)	25 (21–28)	27 (25–29)	25 (23–30)

*Qmax, maximum flow rate; PVR, post-void residual urine volume; Wilcoxon signed-rank test was used to analyze the differences between the baseline and 3 months, 6 months, or 12 months with *denoting $p < 0.05$.*

Follow-Up

All the patients completed the first follow-up 3 months after the surgical procedure. Also, 91.8% (45/49) of the patients returned to Third Xiangya Hospital for review 6 and 12 months after the surgical procedure, whereas four (4/49, 8.2%) patients were lost to follow-up. The IPSS and QoL score improved significantly compared with that before surgery ($p < 0.05$). During 12-month follow-up, the IPSS and QoL score remained relatively stable. The mean value of Q_{max} was close to normal, and the PVR was within the physiological range (**Table 2**).

Treatment-Related Adverse Events

Dysuria was identified in two patients (2/49, 4.1%) after the first time the catheter was extracted. The catheter was inserted again, and antibiotic therapy was used for 1 week. Two patients could urinate by themselves after extubation again. Seven cases (7/49, 14.3%) were complicated with a urinary-tract infection within 2 weeks of completion of the surgical procedure, and nine cases (9/49, 18.4%) had irritation or pain within the urinary tract, but relief was obtained after receiving symptomatic treatments. Only one patient (1/49, 2%) with a TURP history suffered from transient urinary incontinence, but his symptoms resolved within 2 weeks with daily training of the levator ani muscle. Anterior urethral strictures occurred 3 months after the surgery for three patients (3/49, 6.1%). The optimal treatment method

TABLE 3 | Treatment-related adverse events.

AEs	Urethral dilatation	Catheterization	Cystoscopy	TURP
Patients number ($n = 49$)	9	13	10	17
Dysuria (Clavien-Dindo Grade I for all)	1	0	1	0
Urinary tract irritation/pain	2	1	2	4
Clavien-Dindo Grade I	2	0	1	1
Clavien-Dindo Grade II	0	1	1	3
UTI	1	2	1	3
Clavien-Dindo Grade I	0	1	0	2
Clavien-Dindo Grade II	1	1	1	1
TUI (Clavien-Dindo Grade I for all)	0	0	0	1
US (Clavien-Dindo Grade III for all)	0	0	1	2

AEs, adverse events; UTI, urinary tract infection; TUI, temporary urinary incontinence; US, urethral stricture.

was regular urethral dilation after anesthesia of the urethral mucosal surface using 2% lidocaine. Recurrent active hematuria, secondary operation, or death was not recorded (**Table 3**).

DISCUSSION

Several aggressive transurethral actions [e.g., catheterization (15), urethra dilation (16), and cystoscopy (17)] can injure the mucosa, submucosal vessels, and, in particular, the hyperplastic mid lobe of the prostate gland, which may result in formation of a false passage and bleeding. We observed the mid lobe to be the most common bleeding site in the patients without a TURP history.

Massive hemorrhage is a severe complication of TURP (5, 18). In our study, the apex (7/17, 41.2%) and top lobe (12 o'clock position, 8/17, 47.1%) were the most common bleeding sites in the patients with a TURP history. For inexperienced surgeons, incomplete electrocoagulation on the uneven wound surface resulting from incomplete resection of hyperplastic glands, especially at sites of a relatively blinded area of the resectoscope (e.g., the 12 o'clock position of glands), may lead to severe bleeding. Moreover, to protect the external sphincter, some surgeons do not undertake efficient hemostasis at the apex of the prostatic urethra (which was also a common bleeding site in the patients in the present study). We observed that it was more urgent to deal with BMH secondary to TURP.

In addition to systemic support, the basic principles of BMH treatment are: (i) removing blood clots from the bladder; (ii) controlling bleeding; (iii) keeping the bladder drainage unobstructed (of which controlling bleeding is the core procedure). The means of hemostasis are compression of the bladder neck by a catheter balloon (19), transurethral surgery (5), and open surgery (20). Furthermore, if the patient suffers excessive loss of blood and cannot tolerate anesthesia or surgery, selective prostatic artery embolization (PAE) may be considered (21, 22). However, compression of the bladder neck and PAE cannot be employed to remove blood clots and relieve obstruction of the bladder outlet, and the hemostatic effect of these actions is uncertain. Open surgery is not first-line treatment if minimally invasive surgery is possible and safe. Therefore, if the condition permits, transurethral surgery is an ideal option for BMH because it meets all of these three principles stated above and elicits less trauma.

TURKEP combines the advantages of transurethral surgery, open prostatectomy, and a bipolar plasma kinetic system. TUPKEP is characterized by complete hemostasis, little bleeding, safety, and effective relief of bladder-outlet obstruction (10, 23, 24). During TUPKEP, a relatively loosened gap between the peripheral (surgical "capsule") zone and the transitional zone can be exposed readily by blunt dissection (25). The surface of the capsule is smooth and characterized by a pale color and clear supply vessels. In our i-TUPKEP procedure for the patients with a TURP history, we could obtain access to the capsule and carry out enucleation. The residual glands after the previous TURP procedure can be utilized as indicators to expose the capsule.

Our single-center experience indicated that complete enucleation of proliferative glands with active bleeding and coagulation on the capsule surface could achieve effective hemostasis from the source. The bipolar plasma kinetic system can produce localized high-frequency energy, which passes through the conductive irrigation solution (0.9% saline) to tissue. In the cutting mode, if energy is sufficient, the solution is converted into a vapor layer with energy-charged particles, which touch the tissue to be resected directly, and cause its disintegration with low thermal damage to surrounding tissue. In the coagulation mode, a locally limited energy field with high power density is produced to coagulate bleeding vessels at the tissue surface. The energy is focused without being wasted on deeper tissue layers, which is efficient and safe. Owing to these traits of the system, during i-TUPKEP, the view of the surgical field upon the capsule surface is clear without damage after coagulation. Furthermore, after enucleation, electrosurgical excision of ischemic glands becomes safer and more rapid. Postoperatively, owing to improvement of contraction of the surgical capsule, the risk of re-bleeding on the wound surface is decreased markedly (26).

None of our patients suffered from active bleeding again after i-TUPKEP. The relief of symptoms due to BPH after i-TUPKEP was also satisfactory. During 12-month follow-up, the subjective indicators (the IPSS and the QoL score) of LUTS were improved, and the objective indicators (Q_{max} and PVR) were in the physiological range. However, the patients completed the questionnaires in a state of pain, which could have caused a bias in the rating process. In the future studies, more indicative parameters (e.g., the pain score) should be used for correction and evaluation.

Transient incontinence is a common complication associated with TUPKEP (27). During the surgical procedures, we carried out a small part of glands at the 12 o'clock position of the capsule and was kept as an "isolation pad." The latter can protect the urethral sphincter from thermal damage during

electrocoagulation. In our study, only one patient suffered from temporary incontinence. Infection is another common adverse event during transurethral surgery. Postoperatively, especially for the patients with small glands, inflammatory stenosis is prevalent in the prostatic urethra, which can result in dysuria after extubation (28, 29). Two cases in this setting were observed in our study, but, after placement of an indwelling catheter for 1 week and infection control, the urination symptoms improved.

Our study had five main limitations. First, our study had a retrospective design. Second, this was a single-center study. Third, the follow-up period was short (12 months). Fourth, the study cohort was small (49 cases). Fifth, i-TUPKEP was first-line treatment for BMH in our institute during the study period. Hence, there was no other method (e.g., TURP) for comparison with i-TUPKEP.

Prospective controlled studies with long-term follow-up can provide a more detailed description of the efficacy and safety of i-TUPKEP and aid exploration of the best treatment method for BMH.

CONCLUSIONS

This was a preliminary study. Nevertheless, if preparation is satisfactory, i-TUPKEP can be employed to treat patients with BPH with BMH. Ideally, i-TURKEP should be carried out by a surgeon with experience in TUPKEP.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Review Board of Third Xiangya Hospital at Central South University (Changsha, China). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ZL, LH, and YG designed the research. LD, QH, and CL reviewed the medical records and collected the data. ZL and YG analyzed the data and wrote the manuscript. All authors contributed to the article and approved the submitted version.

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Evaluation of YouTube Videos as a Source of Patient Information for Ureteric Stent Placement: A Quality Assessment Study

Kapil Chaudhary, Abhishek Chandna, Sudheer Kumar Devana, Aditya Prakash Sharma, Shantanu Tyagi and Shrawan K. Singh*

Department of Urology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Objective: To assess the quality of YouTube videos on ureteric stent placement (USP) as a source of patient available.

Methods: YouTube was searched using search terms "DJ stenting," "Double J stenting," and "ureteric stenting." The initial 100 videos displayed with each of the above mentioned search terms were scrutinized. The selected videos reviewed by 3 independent consultant urologists against a pre-agreed scoring system based upon European Association of Urology (EAU) patient information sheet on ureteric stent placement. The videos were scored qualitatively and quantitatively based on the scores achieved in various domains of the scoring Performa. Data was also collected for the number of views, likes, dislikes, and time duration of each video.

Results: A total of 22 videos which fulfilled the inclusion criteria were reviewed. All the videos were uploaded by healthcare organizations or healthcare websites. None of the videos were classified as "Good" based on reviewer scores and only one video was classified as "acceptable." Fourteen videos were classified as "very poor" with a score of <5/20. General information about stents was described by majority of the studies whilst preoperative information, procedure description, danger signs, and follow up were scarcely described by most videos.

Conclusion: Majority of YouTube videos on USP are of poor overall quality and lack pertinent information. This calls for creation of comprehensive and unbiased videos for patient information on USP.

Keywords: YouTube, Double J stent (JJ stent), patient information, social media, quality assessment

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B. M. Zeeshan Hameed,
Father Muller Medical College, India
Lazaros Tzelves,
National and Kapodistrian University of Athens, Greece

****Correspondence:***
Aditya Prakash Sharma
aditya.p.sharma@gmail.com

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INTRODUCTION

Ever since its inception in 2005, YouTube has taken the social media platforms by storm. It attracts users all around the globe, with more than 2 billion users logged-in each month, generating billions of hours of views and videos each day (1). Its widespread availability has culminated in its utilization not only as a source of entertainment, but also a useful repository of information. YouTube has the potential to serve as a useful medium for sharing and disseminating heath related information and education (HRIE) as well. Apart from being an expansive storehouse of videos, it is also a social

networking interface where the users can interact with each other. This interaction, in turn can influence decision making as well as the thought process of the users. Over 70% of internet consumers have accessed HRIE online (2–4), with a substantial proportion relying on information acquired over the internet for decision-making (3).

Urinary diversion in the form of ureteric stent placement (USP) is one of the most commonly performed urological procedures worldwide for both elective and emergency indications. Being an invasive procedure, involving the placement of a foreign body within the urinary tract, anxiety and confusion among patients is understandable. In this regard, Video-sharing platforms (VSPs) like YouTube are frequently accessed by the patients in quest of answers for their procedural doubts and to get themselves familiar with the basic technicalities of USP.

There is a plethora of content on USP available on YouTube, but unregulated uploading of videos, irrespective of medical credentials and expertise makes them vulnerable for marketing gimmicks, publicity stunts or even scientific propagandas with no level of evidence (3, 5, 6). Consequently, the viewers seeking information on USP are likely to be influenced by the content of these videos. It thus becomes imperative to ascertain the quality of such content available for general public and medical professionals alike. Through this study, we intend to assess the quality of video content available on YouTube for USP against a standard (EAU patient information sheet) (7).

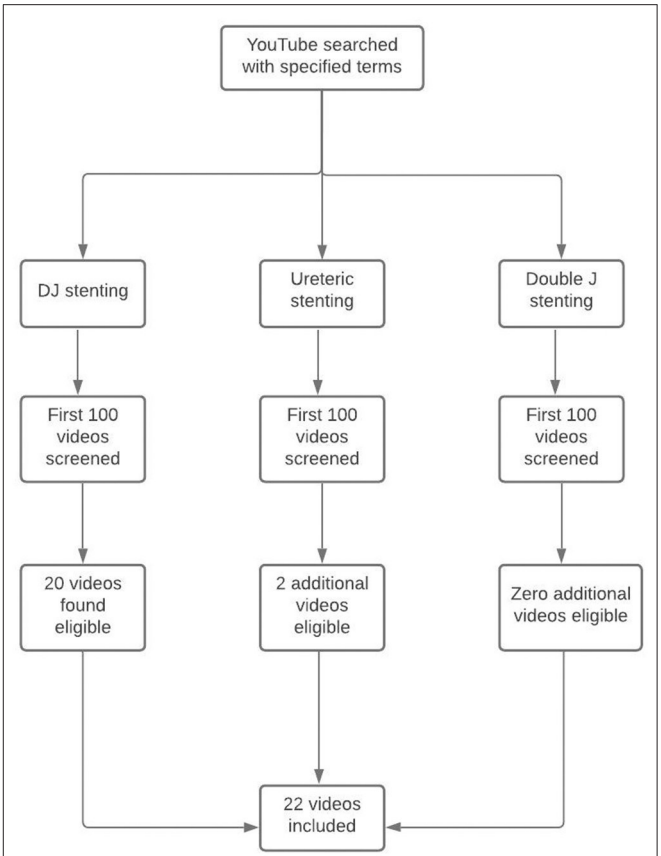

FIGURE 1 | Video selection process and content.

MATERIALS AND METHODS

On 21st August 2021, at Chandigarh, India, the search function on YouTube was queried with the search terms "DJ stenting," "Double J stenting," and "ureteric stenting." The initial 100 videos displayed on YouTube in context of the searches made with the aforementioned terms were scrutinized. This was based on the premise that it would be highly unlikely for an individual to scroll beyond the first 100 videos. The exclusion criteria were videos with patient testimonials, videos directed toward the surgeon or urologist for placement of ureteric stent, videos in languages other than English, videos not focused on DJ stenting and videos without verbal audio. All the enlisted videos were scrutinized by a consultant urologist (KC) and 22 videos were found suitable to be included in the study (**Figure 1**). No filters were applied for duration or for date of uploading. Data was collected for total number of views, video duration, number of likes, dislikes, number of comments, and source of the video.

The selected videos were thereafter reviewed independently by three urology consultants (KC, SK, and AS) using a pre-agreed scoring system as listed in **Table 1**. These criteria were based upon the European Association of Urology (EAU) patient information sheet on double-J stent placement (7). This was deemed as a good and reliable source of patient information, that an ideal video should also contain. The criteria had a total score of 20 and a qualitative rating was awarded based on the reviewer's score: "Very poor" (0–5), "Poor" (6–10), "Acceptable" (11–15), and "Good" (16–20). The reviewer's ratings were then compared.

Data was stored in SPSS program (Version 23, IBM corporation; Armonk, NY, USA). The data was expressed as numbers and percentages. To assess the reliability of inter-observer assessment, intra-class correlation coefficient was calculated and qualitative ratings were evaluated by utilizing Fleiss kappa. All statistical tests were two-sided and were performed at a significance level of $p < 0.05$.

RESULTS

A total of 22 videos were found to fulfill the inclusion criteria. The mean time duration of the videos was 158.6 ± 128.1 s (20–464 s). The total number of views was 14,47,832 with a median of 34,500 views. The number of likes received by a video ranged from zero to 971 and dislikes ranged from 0 to 93 (**Table 2**). All the videos were uploaded by healthcare organizations or healthcare websites. The median number of comments per video were 7 (0–48.25).

The kappa statistic for inter-observer correlation was 0.698, and intra-class correlation was 0.925. Of the 22 videos, none of the videos received a rating of "Good" and 14

TABLE 1 | Scoring criteria for videos, based on European Association of Urology patient information sheet (1 point for each criteria).

Serial No.	Criteria	Information	Maximum Score
1.	Information on DJS	Description of DJS Indication of DJS	2
2.	Preoperative information	Need for urine culture Withholding anti-platelets/anti-coagulants Anesthesia-local vs. general	3
3	Procedure description	Positioning Use of cystoscope Use of contrast Radiation exposure Stent placement	5
4.	Stent related symptoms	Burning micturition Blood tinged urine Lower abdominal discomfort Frequent micturition	4
5.	Danger signs	High grade fever Urine retention Gross haematuria Severe pain despite analgesics	4
6.	Follow-up	Timing of stent removal How is stent removed	2
	Total score	20	

TABLE 2 | YouTube characteristics of the analyzed videos.

Variables	Values
Number of videos	22
Length of the video (mean in seconds)	158.6 ± 128.1
Likes per video (median)*	109 (6–293.5)
Dislikes per video (median)*	10 (1.75–37.75)
Comments (median)*	7 (0–48.25)
Views (median)*	34,500 (7,900–95,100)
Video ratings based on average scores by reviewers	
Good (16–20)	0
Acceptable (11–15)	1
Poor (6–10)	7
Very poor (0–5)	14

**Median values are reported with interquartile range in brackets.*

of the videos received a rating of "Very poor" based on the reviewer's scores (**Table 3**). The mean average scores for all the reviewers was <5 (4.59, 4.45, and 4.55 for I, II, and III consultant, respectively) falling in the "very poor" category (**Table 2**). Only one video was unanimously rated as more than 10 by all reviewers, culminating to a qualitative category of "acceptable," while none of the videos was awarded a score of >15 by any of the reviewers. General information about the stent like its description and indication for placement was described by most of the studies (14/22; **Supplementary Table 1**). Information on preoperative work-up, stent related symptoms, procedural description, and follow-up was not described by majority of the videos (**Supplementary Table 1**).

TABLE 3 | Mean scores of each consultant in different scoring criteria.

Scoring criteria (maximum score)	Consultant I	Consultant II	Consultant III
Information on DJ stent (2)	1.59	1.55	1.77
Preoperative information (3)	0.23	0.14	0.18
Procedural description (5)	0.73	0.5	0.55
Stent related symptoms (4)	1	1	1.05
Danger signs (4)	0.32	0.5	0.32
Follow-up (2)	0.73	0.77	0.68
Total score (20)	4.59	4.45	4.55

DISCUSSION

The present study analyzed the quality of health related information on ureteric stent placement available to patients via YouTube videos. Majority of the videos failed to provide good quality information about USP to the patients, ranking as "very poor" when rated by 3 independent consultant urologists. Though a good number of videos provided basic information about ureteric stents, most of them failed at explaining about the procedure, preoperative requirements, complications, danger signs as well as the follow-up for such stents. None of the videos confirmed to all the attributes outlined by the EAU patient information sheet for ureteric stenting.

Only one video received a total score of more than 10 by all the reviewers, lasting for 7 min 44 s, yet it failed to describe the procedure and the preoperative concerns. This video was well above the mean video length of 158.6 ± 128.1 s. The two videos with the highest number of views were rated as "poor" by all the 3 reviewers. Fourteen videos received a "very poor" rating by all reviewers and had a mean score of <5 thus questioning the true utility of YouTube videos as a reliable source of patient education and information.

The current medical practice is undergoing a change toward shared decision making for which patient's information and education constitutes a vital cornerstone. Social media outlets like YouTube, Twitter, and Facebook play an important role in dissemination and distribution of information, considering their huge number of subscribers and views per day. With widespread access to internet services, the patient and their attendants seek information regarding their symptoms, procedures, healthcare facilities, and the credentials of healthcare provider prior to scheduled appointment.

Recently, a myriad of studies pertaining to urological diseases and procedures have analyzed the reliability of YouTube videos as a source of medical information for patients (8–15). These studies, spanning across benign prostatic hyperplasia, stone treatment (15, 16), infertility (17), and erectile dysfunction (9) observed that YouTube videos had low quality of content, provided unreliable or false information and were subject to commercial bias. To best of our knowledge of English literature,

ours is the only study examining the role of such videos for ureteric stent placement and echoes the concerns raised by the existing studies. Only one study examining the quality and reliability of YouTube videos on pelvic floor muscle training observed most of the studies to be useful, albeit moderate in reliability, quality, and accuracy (18). Loeb (11) examined the existing literature for impact of social media on information about various benign and malignant urological conditions. They concluded that majority of the available information was biased, inadequate, misinformative, and commercially sponsored.

Comments, likes, and dislikes have also been found to have an important impact on the viewership, in turn influencing the viewers, irrespective of who comments on the videos and the authority/knowledge of the person. The median number of comments per video in the present study were 7 (range 0–219). A notable example of comments influencing public opinion is the human papillomavirus vaccination promotion on YouTube, where glaringly inaccurate information and propaganda was circulated in the form of negative commentary (19). Moreover, negative videos were liked more than positive ones by the viewers (20).

Popularity often measured in terms of view counts and/or public ratings is also an important concept in assessing the quality of YouTube videos. Unlike the focus on the assessment of the quality of content, which relies on human judgement and evaluation, view count, or video views per day are quantitative measures that are readily accessible for each video on YouTube. However, some videos have higher view counts due to marketing campaigns, viral effects, duration of availability of the video, or the video being linked from several webpages. Users need to be aware that frequency of views may be manipulated by parties with specific agendas to achieve its "perceived" popularity. Similarly, in the present study, 5 videos had more than 100,000 views each; all of them were qualified as "poor" source of information unanimously by the reviewers. The only study with a score >10, garnered 76,000 views, despite being around for over 2 years. This was probably due to its long duration (7 min 44 s) when compared to the rest of the videos.

The centers for disease control and prevention (CDC) has specified guidelines for publishing videos on its YouTube channel (21). However, these apply only to CDCs YouTube channel and are not uniformly followed. The Health on Net (HON) foundation also has attempted to standardize the information available online so that reliable, comprehensive, and trustworthy information is available to the public at large. The HON code of conduct (HONcode), which serves as a guarantee for reliable information, is accredited to websites ensuring basic ethical standards and where the source and purpose of data being presented in available and reliable (22). Unfortunately, no such system of accreditation exists for YouTube videos at present. This highlights the unexplored opportunities for medical professionals to produce high-quality, patient centered comprehensive informational videos online.

The present study has a few limitations. The results were limited to the first 100 videos only, which may have excluded some videos, but it is unlikely that viewers may go beyond first 100 videos of search results. Secondly, videos available only on YouTube were analyzed, and those on other VSP platforms were not included owing to the study design. YouTube, being a widely and openly available source of information was chosen as a source for the present study. Another drawback of the study is its restriction to English language videos only, leading to exclusion of a few high-quality videos.

YouTube provides an unparalleled resource of free and open access videos which may provide information to patients, aiding in education and decision making. However, they are often unregulated, biased and may contain insufficient information for patient education when compared to professional information such as EAU patient information platform. In summary, videos describing USP on YouTube should not be recommended for patient education as they fail to address a glaring majority of important aspects about ureteric stents. The results of this study underline the importance of thorough communication between the medical professional and the patient as well as calls out for regulation on the content available on such VSPs in order to provide comprehensive information to the patients. Promotion of well-balanced, unbiased and evidence-based online information platforms is the need of the hour.

CONCLUSION

Majority of the videos on ureteric stent placement available on YouTube are of poor overall quality and lack important information. This presents a risk of exposure to misinformation and calls for creation of unbiased and comprehensive videos for patient information on ureteric stent placement.

DATA AVAILABILITY STATEMENT

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

AUTHOR CONTRIBUTIONS

KC: protocol development, data collection, data analysis, manuscript writing, and editing. AC: data collection, data analysis, manuscript writing, and editing. SK and AS: protocol development, manuscript writing, and editing. ST: protocol development and data collection. SS: data analysis, manuscript writing, and editing. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2021.816222/full#supplementary-material

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Legal and Ethical Consideration in Artificial Intelligence in Healthcare: Who Takes Responsibility?

Nithesh Naik[1,2], B. M. Zeeshan Hameed[2,3], Dasharathraj K. Shetty[4], Dishant Swain[5], Milap Shah[2,6], Rahul Paul[7], Kaivalya Aggarwal[8], Sufyan Ibrahim[2,9], Vathsala Patil[10], Komal Smriti[10], Suyog Shetty[3], Bhavan Prasad Rai[2,11], Piotr Chlosta[12] and Bhaskar K. Somani[2,13]*

[1] Department of Mechanical and Manufacturing Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [2] International Training and Research in Uro-Oncology and Endourology Group, Manipal, India, [3] Department of Urology, Father Muller Medical College, Mangalore, India, [4] Department of Humanities and Management, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [5] Department of Instrumentation and Control Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [6] Robotics and Urooncology, Max Hospital and Max Institute of Cancer Care, New Delhi, India, [7] Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States, [8] Department of Computer Science and Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [9] Kasturba Medical College, Manipal Academy of Higher Education, Manipal, India, [10] Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Manipal, Manipal Academy of Higher Education, Manipal, India, [11] Department of Urology, Freeman Hospital, Newcastle upon Tyne, United Kingdom, [12] Department of Urology, Jagiellonian University in Krakow, Kraków, Poland, [13] Department of Urology, University Hospital Southampton National Health Service (NHS) Trust, Southampton, United Kingdom

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***Correspondence:**
Dasharathraj K. Shetty
raja.shetty@manipal.edu

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The legal and ethical issues that confront society due to Artificial Intelligence (AI) include privacy and surveillance, bias or discrimination, and potentially the philosophical challenge is the role of human judgment. Concerns about newer digital technologies becoming a new source of inaccuracy and data breaches have arisen as a result of its use. Mistakes in the procedure or protocol in the field of healthcare can have devastating consequences for the patient who is the victim of the error. Because patients come into contact with physicians at moments in their lives when they are most vulnerable, it is crucial to remember this. Currently, there are no well-defined regulations in place to address the legal and ethical issues that may arise due to the use of artificial intelligence in healthcare settings. This review attempts to address these pertinent issues highlighting the need for algorithmic transparency, privacy, and protection of all the beneficiaries involved and cybersecurity of associated vulnerabilities.

Keywords: artificial intelligence, machine learning, ethical issues, legal issues, social issues

INTRODUCTION

Increasing patient demand, chronic disease, and resource constraints put pressure on healthcare systems. Simultaneously, the usage of digital health technologies is rising, there has been an expansion of data in all healthcare settings. If properly harnessed, healthcare practitioners could focus on the causes of illness and keep track of the success of preventative measures and interventions. As a result, policymakers, legislators, and other decision-makers should be aware of this. For this to happen, computer and data scientists and clinical entrepreneurs argue that one of the most critical aspects of healthcare reform will be artificial intelligence (AI), especially machine learning (1).

Artificial intelligence (AI) is a term used in computing to describe a computer program's capacity to execute tasks associated with human intelligence, such as reasoning and learning. It also includes processes such as adaptation, sensory understanding, and interaction. Traditional computational algorithms, simply expressed, are software programmes that follow a set of rules and consistently do the same task, such as an electronic calculator: "if this is the input, then this is the output." On the other hand, an AI system learns the rules (function) through training data (input) exposure. AI has the potential to change healthcare by producing new and essential insights from the vast amount of digital data created during healthcare delivery (2).

AI is typically implemented as a system comprised of both software and hardware. From a software standpoint, AI is mainly concerned with algorithms. An artificial neural network (ANN) is a conceptual framework for developing AI algorithms. It's a human brain model made up of an interconnected network of neurons connected by weighted communication channels. AI uses various algorithms to find complex non-linear correlations in massive datasets (analytics). Machines learn by correcting minor algorithmic errors (training), thereby boosting prediction model accuracy (confidence) (3, 4).

The use of new technology raises concerns about the possibility that it will become a new source of inaccuracy and data breach. In the high-risk area of healthcare, mistakes can have severe consequences for the patient who is the victim of this error. This is critical to remember since patients come into contact with clinicians at times in their lives when they are most vulnerable (5). If harnessed effectively, such AI-clinician cooperation can be effective, wherein AI is used to offer evidence-based management and provides medical decision-guide to the clinician (AI-Health). It can provide healthcare offerings in diagnosis, drug discovery, epidemiology, personalized care, and operational efficiency. However, as Ngiam and Khor point out if AI solutions are to be integrated into medical practice, a sound governance framework is required to protect humans from harm, including harm resulting from unethical behavior (6–17). Ethical standards in remedy may be traced lower back to the ones of the health practitioner Hippocrates, on which the idea of the Hippocratic Oath is rooted (18–24).

Machine Learning-healthcare applications (ML-HCAs) that were seen as a tantalizing future possibility has become a present clinical reality after the Food and Drug Administration (FDA) approval for autonomous artificial intelligence diagnostic system based on Machine Learning (ML). These systems use algorithms to learn from large data sets and make predictions without explicitly programming (25).

APPLICATIONS OF AI FOR HEALTH RESEARCH

The use of data created for electronic health records (EHR) is an important field of AI-based health research. Such data may be difficult to use if the underlying information technology system and database do not prevent the spread of heterogeneous or low-quality data. Nonetheless, AI in electronic health records can be used for scientific study, quality improvement, and clinical care optimization. Before going down the typical path of scientific publishing, guideline formation, and clinical support tools, AI that is correctly created and trained with enough data can help uncover clinical best practices from electronic health records. By analyzing clinical practice trends acquired from electronic health data, AI can also assist in developing new clinical practice models of healthcare delivery (26).

ARTIFICIAL INTELLIGENCE IN DRUG DEVELOPMENT

In the future, AI is expected to simplify and accelerate pharmaceutical development. AI can convert drug discovery from a labor-intensive to capital- and the data-intensive process by utilizing robotics and models of genetic targets, drugs, organs, diseases and their progression, pharmacokinetics, safety and efficacy. Artificial intelligence (AI) can be used in the drug discovery and development process to speed up and make it more cost-effective and efficient. Although like with any drug study, identifying a lead molecule does not guarantee the development of a safe and successful therapy, AI was used to identify potential Ebola virus medicines previously (26).

ETHICAL CHALLENGES

There is a continuous debate regarding whether AI "fits within existing legal categories or whether a new category with its special features and implications should be developed." The application of AI in clinical practice has enormous promise to improve healthcare, but it also poses ethical issues that we must now address. To fully achieve the potential of AI in healthcare, four major ethical issues must be addressed: (1) informed consent to use data, (2) safety and transparency, (3) algorithmic fairness and biases, and (4) data privacy are all important factors to consider (27). Whether AI systems may be considered legal is not only a legal one but also a politically contentious one (Resolution of the European Parliament, 16 February 2017) (28).

The aim is to help policymakers ensure that the moral demanding situations raised by enforcing AI in healthcare settings are tackled proactively (17). The limitation of algorithmic transparency is a concern that has dominated most legal discussions on artificial intelligence. The rise of AI in high-risk situations has increased the requirement for accountable, equitable, and transparent AI design and governance. The accessibility and comprehensibility of information are the two most important aspects of transparency. Information about the functionality of algorithms is frequently deliberately made difficult to obtain (29).

Our capacity to trace culpability back to the maker or operator is allegedly threatened by machines that can operate by unfixed rules and learn new patterns of behavior. The supposed "ever-widening" divide is a cause for alarm, as it threatens "both the moral framework of society and the foundation of the liability idea in law." The use of AI may leave us without anyone to hold accountable for any sort of damage done. The extent of danger is

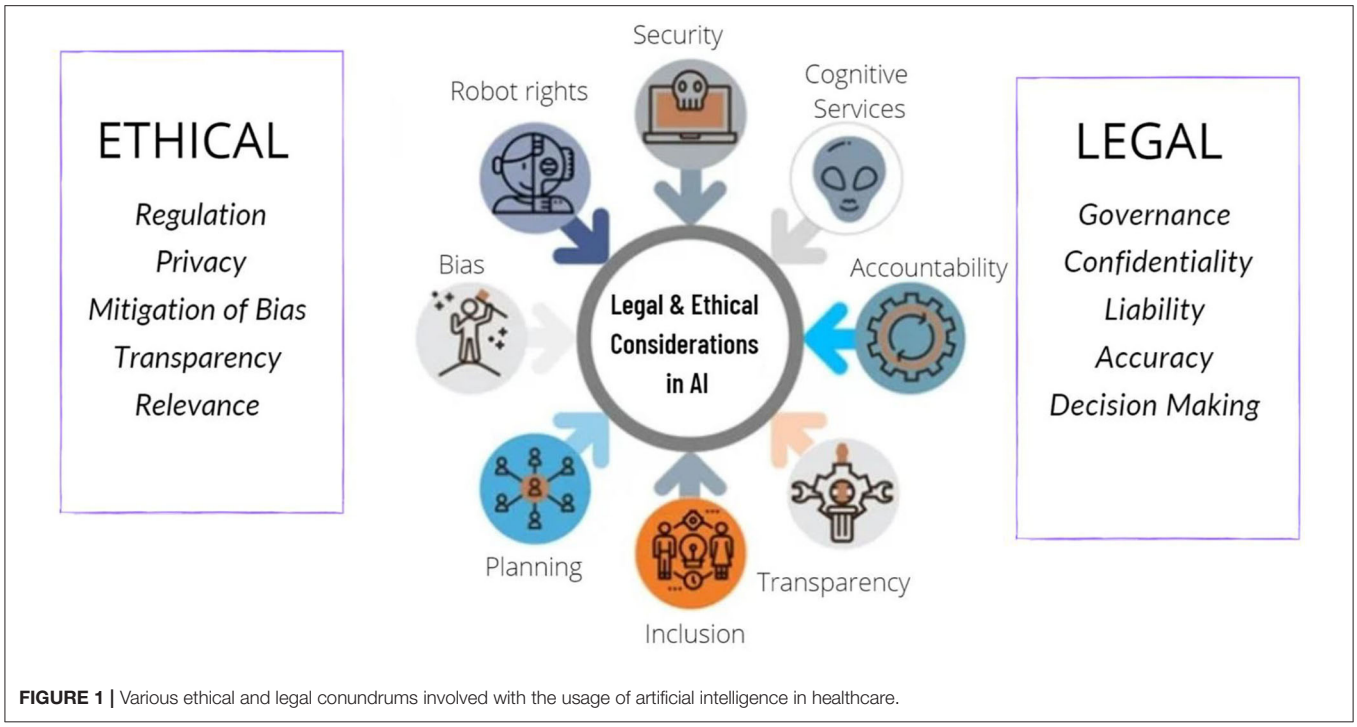

FIGURE 1 | Various ethical and legal conundrums involved with the usage of artificial intelligence in healthcare.

unknown, and the use of machines will severely limit our ability to assign blame and take ownership of the decision-making (30).

Modern computing approaches can hide the thinking behind the output of an Artificial Intelligent System (AIS), making meaningful scrutiny impossible. Therefore, the technique through which an AIS generates its outputs is "opaque." A procedure used by an AIS may be so sophisticated that for a non-technically trained clinical user, it is effectively concealed while remaining straightforward to understand for a techie skilled in that area of computer science (5).

AISs, like IBM's Watson for oncology, are meant to support clinical users and hence directly influence clinical decision-making. The AIS would then evaluate the information and recommend the patient's care. The use of AI to assist clinicians in the future could change clinical decision-making and, if adopted, create new stakeholder dynamics. The future scenario of employing AIS to help clinicians could revolutionize clinical decision-making and, if embraced, create a new healthcare paradigm. Clinicians (including doctors, nurses, and other health professionals) have a stake in the safe roll-out of new technologies in the clinical setting (5).

The scope of emerging ML-HCAs in terms of what they intend to achieve, how they might be built, and where they might be used is very broad. ML-HCAs range from entirely self-sufficient synthetic intelligence diabetic retinopathy prognosis in primary care settings, to non-self-sufficient death forecasts, to manual coverage and resource allocation (25). Researchers ought to describe how those outputs can be included in the research, along with predictions. This information is essential to setting up the cost of the scientific trial and guiding scientific research (31).

AI applied in healthcare needs to adjust to a continuously changing environment with frequent disruptions, while maintaining ethical principles to ensure the well-being of patients (24). However, an easy, key component of figuring out the protection of any healthcare software relies upon the capacity to check out the software and recognize how the software would fail. For example, the additives and physiologic mechanisms of medications or mechanical devices are comparable to the technique for software programmes. On the other hand, ML-HCAs can present a "black box" issue, with workings that aren't visible to evaluators, doctors, or patients. Researchers ought to describe how those outputs can be included in the research, along with predictions. This information helps assess the cost of the scientific trial and guides scientific research (25).

GLOBAL LEGISLATIONS

The Resolution of the European Parliament was based on research commissioned, supervised, and published by the policy department for "Citizens' Rights and Constitutional Affairs" in response to a request from the European Parliament's Committee on Legal Affairs. The report emphasizes the critical nature of a resolution calling for the immediate creation of a legislative instrument governing robots and AI, capable of anticipating and adapting to any scientific breakthroughs anticipated in the medium term (29). The various ethical and legal concerns associated with the use of AI in healthcare settings have been highlighted in **Figure 1**.

WHY IS RESPONSIBILITY NECESSARY?

When the setting or context changes, AI systems can fail unexpectedly and drastically. AI can go from being extremely intelligent to extremely naive in an instant. All AI systems

TABLE 1 | Considerations for ethical review for healthcare-based Machine learning research: procedural and conceptual changes (31).

Stage 1: Data access	
Group-based approval	Providing access to specific, qualified individuals who are grouped around a common governance structure, subject to certain conditions, and with a specific aim in mind.
PHI (Protected health information) protection	PHI that isn't required is deleted, leaving the option of examining raw or masked data.
Broad goal without pre-determined methodology	Allows comparison of alternative methodologies to help implementation and avoids biasing study outputs.
Data-access frameworks	A greater emphasis on data governance, with accountability gained by access and rationale records.
Pre-specified, frequent data retrieval without repeated amendments	Ascertains if the model is learning from the most recent patterns in health data.
Stage 2: Silent period	
Prospective non-interventional trial application as a template	Patients do not receive treatments, and machine learning results do not reach the treating team in time to influence decision-making or the trial's evaluation.
Goal of the trial	To see if the model is feasible and if it can be used in clinical settings.
Model validation	Technical performance and calibration were evaluated using ML best practices.
Clinical evaluation	By comparing quiet predictions to real-time patient labeling, evidence for the model's clinical usefulness is obtained.
Stage 3: Clinical trial	
Goal of the trial	To see if the model is more effective than the existing standard of treatment.
Generalizability	Rather than demonstrating the model's generalizability, the goal is to demonstrate the approach's generalizability.
Disaggregated performance metrics	Patient safety and justice depend on disaggregated performance indicators, which will guide clinical acceptance.
Clinically relevant evaluation	Disaggregated performance measures will guide clinician acceptance, ensuring patient safety and justice. • The model was investigated in the context of its planned application in decision-making. • The outputs of the model were recorded. • Clinical decisions are kept track of. • Determining the cause of a disparity in output and decisions.

will have limits, even if AI bias is managed. The human decision-maker must be aware of the system's limitations, and the system must be designed so that it fits the demands of the human decision-maker. When a medical diagnostic and treatment system is mostly accurate, medical practitioners who use it may grow complacent, failing to maintain their skills or take pleasure in their work. Furthermore, people may accept decision-support system results without questioning their limits. This sort of failure will be repeated in other areas, such as criminal justice, where judges have modified their decisions based on risk assessments later revealed to be inaccurate (32).

The use of AI without human mediation raises concerns about vulnerabilities in cyber security. According to a RAND perspectives report, applying AI for surveillance or cyber security in national security creates a new attack vector based on "data diet" vulnerabilities. The study also discusses domestic security issues, such as governments' (growing) employment of artificial agents for citizen surveillance (e.g., predictive policing algorithms). These have been highlighted as potentially jeopardizing citizens' fundamental rights. These are serious concerns because they put key infrastructures at risk, putting lives and human security and resource access at risk. Cyber security weaknesses can be a severe threat because they are typically hidden and only discovered after the event (after the damage is caused) (28).

In recent years, there has been an uptick in the feasibility, design, and ethics of lethal autonomous weapon systems (LAWS). These machines would have AI autonomy's vast discretion combined with the power to murder and inflict damage on humans. While these advancements may offer considerable advantages, various questions have been raised concerning the morality of developing and implementing LAWS (33).

The problem of selection bias in datasets used to construct AI algorithms is a typical occurrence. As established by Buolamwini and Gebru, there is bias in automated facial recognition and the associated datasets, resulting in lower accuracy in recognizing darker-skinned individuals, particularly women. A huge number of data points are required for ML, and the majority of frequently utilized clinical trial research databases come from selected populations. As a result, when applied to underserved and consequently probably underrepresented patient groups, the resulting algorithms may be more likely to fail (34).

WHO BEARS THE RESPONSIBILITY?

Unlike doctors, technologists are not obligated by law to be accountable for their actions; instead, ethical principles of practice are applied in this sector. This comparison summarizes the dispute over whether technologists should be held accountable if AIS is used in a healthcare context and directly affects patients. If a clinician can't account for the output of the AIS they're employing, they won't be able to appropriately justify their actions if they choose to use that data. This lack of accountability raises concerns about the possible safety consequences of using unverified or unvalidated AISs in clinical settings. Some scenarios show how opacity affects each stakeholder. **Table 1** shows the necessary considerations for procedural and conceptual changes to be taken for ethical review for healthcare-based Machine learning research. It is

indeed a challenging aspect of technology. We think that new framework and approach is needed for approval of AI systems but practitioners and hospitals using it need to be trained and hence have the ultimate responsibility of its use. Medical devices based AI will facilitate the decision making too carry out treatment and procedures by the individuals, and not to replace them in entirety. There is dearth of literature in this regard and a detailed frame-work needs to be developed by the highest bodies of policy makers.

AISs should be evaluated and validated, according to the Association for the Advancement of Artificial Intelligence. It is critical to establish, test, measure, and assess the dependability, performance, safety, and ethical compliance of such robots and artificial intelligence systems logically and statistically/probabilistically before they are implemented. If a clinician chooses to employ an AIS, verification and validation may help them account for their activities reasonably. As previously mentioned, clinical rules of professional conduct do not allow for unaccountable behavior. It has been suggested, however, that AIS is not the only thing that may be opaque, and doctors can also be opaque. If AIS cannot be punished, it will be unable to take on jobs involving human care. Managers of AIS users should make it clear that physicians cannot evade accountability by blaming the AIS (5).

Assistive ML-HCAs provide resources to healthcare providers by providing "ideas" for treatment, prognosis, or control while relying on individual interpretation of any suggestions to make judgments. Autonomous ML-HCAs provide direct prognostic and control statements without the intervention of a clinician or any other human. Because the developer's preference for an ML-autonomy HCA's stage has clear implications for the assumption of responsibility and liability, this autonomy stage must be visible (25). Instead of asking if they were aware of the hazards and poor decision-making, the question should be asked if they could grasp and recognize those risks (35).

BIAS IN THE USE OF AI

Evidence suggests that AI models can embed and deploy human and social biases at scale. However, it is the underlying data than the algorithm itself that is to be held responsible. Models can be trained on data which contains human decisions or on data that reflects the second-order effects of social or historical inequities. Additionally, the way data is collected and used can also contribute to bias and user-generated data can act as a feedback loop, causing bias. To our knowledge there are no guidelines or set standards to report and compare these models, but future work should involve this to guide researchers and clinicians (36, 37).

AI is moving beyond "nice-to-have" to becoming an essential part of modern digital systems. As we rely more and more on AI for decision making, it becomes absolutely essential to ensure that they are made ethically and free from unjust biases. We see a need for Responsible AI systems that are transparent, explainable, and accountable. AI systems increase in use for improving patient pathways and surgical outcomes, thereby outperforming humans in some fields. It is likely to meager, co-exist or replace current systems, starting the healthcare age of artificial intelligence and not using AI is possibly unscientific and unethical (38).

CONCLUSION

AI is going to be increasingly used in healthcare and hence needs to be morally accountable. Data bias needs to be avoided by using appropriate algorithms based on un-biased real time data. Diverse and inclusive programming groups and frequent audits of the algorithm, including its implementation in a system, need to be carried out. While AI may not be able to completely replace clinical judgment, it can help clinicians make better decisions. If there is a lack of medical competence in a context with limited resources, AI could be utilized to conduct screening and evaluation. In contrast to human decision making, all AI judgments, even the quickest, are systematic since algorithms are involved. As a result, even if activities don't have legal repercussions (because efficient legal frameworks haven't been developed yet), they always lead to accountability, not by the machine, but by the people who built it and the people who utilize it. While there are moral dielemmas in the use of AI, it is likely to meager, co-exist or replace current systems, starting the healthcare age of artificial intelligence, and not using AI is also possibly unscientific and unethical.

AUTHOR CONTRIBUTIONS

NN, DSh, BH, and BS contributed to the conception and design of the study. MS, SI, DSw, SS, and KA organized the database. DSw, KA, VP, KS, SS, and SI wrote the first draft of the manuscript. NN, DSh, KS, BR, VP, and BH wrote sections of the manuscript. PC, BR, and BS critically reviewed and edited the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Application of Virtual Reality, Augmented Reality, and Mixed Reality in Endourology and Urolithiasis: An Update by YAU Endourology and Urolithiasis Working Group

B. M. Zeeshan Hameed[1,2,3], *Shraddha Somani*[4], *Etienne Xavier Keller*[5], *R. Balamanigandan*[6], *Satyasundara Mahapatra*[7], *Amelia Pietropaolo*[2,8], *Şenol Tonyali*[9], *Patrick Juliebø-Jones*[10,11], *Nithesh Naik*[3,12]*, *Dilip Mishra*[13], *Sarvesh Kumar*[14], *Piotr Chlosta*[15] *and Bhaskar K. Somani*[2,8]

[1] *Department of Urology, Father Muller Medical College, Mangalore, India,* [2] *European Association of Urology—Young Academic Urologists Urolithiasis and Endourology Working Group, Arnhem, Netherlands,* [3] *International Training and Research in Uro-oncology and Endourology Group, Manipal, India,* [4] *Department of Computer Science and Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India,* [5] *Department of Urology, University Hospital Zurich, University of Zurich, Zurich, Switzerland,* [6] *Department of Artificial Intelligence, Institute of Computer Science and Engineering, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India,* [7] *Computer Science and Engineering, Pranveer Singh Institute of Technology, Kanpur, India,* [8] *Department of Urology, University Hospital Southampton National Health Service (NHS) Trust, Southampton, United Kingdom,* [9] *Department of Urology, Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey,* [10] *Department of Urology, Haukeland University Hospital, Bergen, Norway,* [11] *Department of Clinical Medicine, University of Bergen, Bergen, Norway,* [12] *Department of Mechanical and Manufacturing Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India,* [13] *Department of Urology, Global Rainbow Healthcare, Agra, India,* [14] *Department of Computer Science and Engineering, Babu Banarasi Das University, Lucknow, India,* [15] *Department of Urology, Jagiellonian University in Kraków, Kraków, Poland*

The integration of virtual reality (VR), augmented reality (AR), and mixed reality (MR) in urological practices and medical education has led to modern training systems that are cost-effective and with an increased expectation toward surgical performance and outcomes. VR aids the user in interacting with the virtual environment realistically by providing a three-dimensional (3D) view of the structures inside the body with high-level precision. AR enhances the real environment around users by integrating experience with virtual information over physical models and objects, which in turn has improved understanding of physiological mechanisms and anatomical structures. MR is an immersive technology that provides virtual content to interact with real elements. The field of urolithiasis has adapted the technological advancements, newer instruments, and methods to perform endourologic treatment procedures. This mini-review discusses the applications of Virtual Reality, Augmented Reality, and Mixed Reality in endourology and urolithiasis.

Keywords: virtual reality, augmented reality, mixed reality, endourology, urolithiasis (urinary stones)

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***Correspondence:**
Nithesh Naik
nithesh.naik@manipal.edu

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INTRODUCTION

The surgical industry seeks out modern and cost-effective training systems with an increased expectation toward surgical performance and outcome with greater reactivity to medico-legal considerations (1, 2). Recent advancements in technologies have led to the integration of Virtual Reality (VR), Augmented Reality (AR), and Mixed Reality (MR) with medical tools, equipment, and training kits into medical education. The simulation in surgical education and healthcare applications is strongly influenced by industries like aviation, automobile, the military for real-world training, and experience (3, 4). The studies and investigations from the literature validate that simulation training for medical students and residents to prepare for hands-on procedures has become an effective and reliable approach (5, 6).

VR aids the user in interacting with the virtual environment realistically by providing a three-dimensional (3D) view of the structures inside the body with high-level precision. VR is proven to be an effective method of training students and residents alike with hands-on procedures due to the recent advancements made in haptics, high-resolution audio-visual effects, motion detection, and display systems. With the use of VR, skills like suturing can be practiced on robotic consoles, simulation tools can recreate mid-stages of surgeries with high and low accuracy dry labs, animal models, wet-lab cadaveric organs, thus providing an optimal experience and learning (1–5).

AR enhances the real environment around users by integrating experience with virtual information over physical models and objects, which in turn has improved understanding of physiological mechanisms and anatomical structures (1). Simulation-based training can be performed in isolation or a "full immersion simulation" where operating conditions are mimicked for maximum experience to increase technical and non-technical skills in return for improved patient results and team performance (7). MR is the most recent form of immersive technology, wherein the virtual contents interact with real elements. This is typically achieved by translucent glasses on which the virtual content is projected. MR requires considerably more sensors and processing power in comparison with VR and AR. **Figure 1** shows the differentiation of immersive experience (Virtual Reality, Augmented Reality, and Mixed Reality) medical simulation tools.

An endoscopic method or examination executed using a percutaneous approach from the urethra to the kidney is referred to as "endourology" (17). The traditional "hands-on" training approach does not lend itself well to minimal access surgery, which results in a fragmented approach to surgical education that lacks consistency and is both time and labor-intensive. Thus, paving a path for exploring newer technologies that aid improved experience in clinical practices, surgical education, patient counseling, diagnosis, and treatment. The field of urolithiasis and endourology has progressed immensely in the past three decades and has adapted the technological advancements, newer instruments, and methods to perform endourologic treatment procedures.

ROLE OF VR/AR/MR IN ENDOUROLOGY AND UROLITHIASIS

Renal stone is a common urological disease encountered irrespective of gender, ethnicity, or age (18). Percutaneous nephrolithotomy (PCNL) is a crucial component of the treatment of renal stones and is the most developed procedure for large or numerous kidney stones. With the growth of technology, procedures like stone removal treatments have become more technologically driven (18). PCNL delivers stone-free rates of over 90% while significantly reducing the risk of complications due to advanced technological equipment (19–21). Percutaneous renal access (PCA) is one of the hardest steps during PCNL since the kidney is surrounded by very important body parts, such as the spleen, the colon, and the liver which can be accidentally punctured while trying to establish the kidney due to inaccurate needle placement and insertion. Studies conducted in the past reported that almost 70% of the percutaneous procedures were performed by practicing urologists, however, only 11% could achieve PCA themselves with the reason stated as the lack of practice during training (22–25).

The PERC Mentor is a VR simulator specially developed for percutaneous kidney access training. The study included 56 participants to test the varying validity of VR training for PCA. During the study, a standardized questionnaire was submitted to the expert group to evaluate the validity of the simulation. The beginner group received two 30 min supervised training sessions on the PERC Mentor to facilitate learning of the percutaneous kidney access skill (8). A total of 24 participants were fully evaluated who completed the process including two cohorts of 15 beginners and 9 experts (clinical experience of performing PCNL in more than 50 cases). A subgroup of five beginners underwent training on pigs before PERC Mentor training. Five beginners (who initially performed the task on the pig) repeated the same task on the pig. After the PERC mentor training, they showed a statistically significant improvement in the reduction in total surgical time.

The ideal teaching aid for beginners is manual training on living patients which unfortunately carries various ethical issues. The ease by which basic endourological procedures like PCA could be performed using virtual reality simulators resulted in improved operating room performance. This study has also concluded that simulation can be used to refine techniques and tactics of new medical students. **Table 1** lists the recent studies and their outcomes related to the application of virtual reality (VR), augmented reality (AR), and mixed reality (MR) in endourology and urolithiasis.

Symbionix's Uro Mentor^{TM} is a virtual reality ureteroscopy simulator that can potentially support the teaching and evaluation of surgical residents. Matsumoto et al. (9) conducted a study in which 16 residents were evaluated on their competence to execute various tasks like guidewire insertion, performing cystoscopy, and extraction of a ureteric stone on a VR simulator. A blinded checklist was used by the examiner with a global rating scale, and a Pass/Fail rating to evaluate the subject's performance. Computer-generated characteristics such

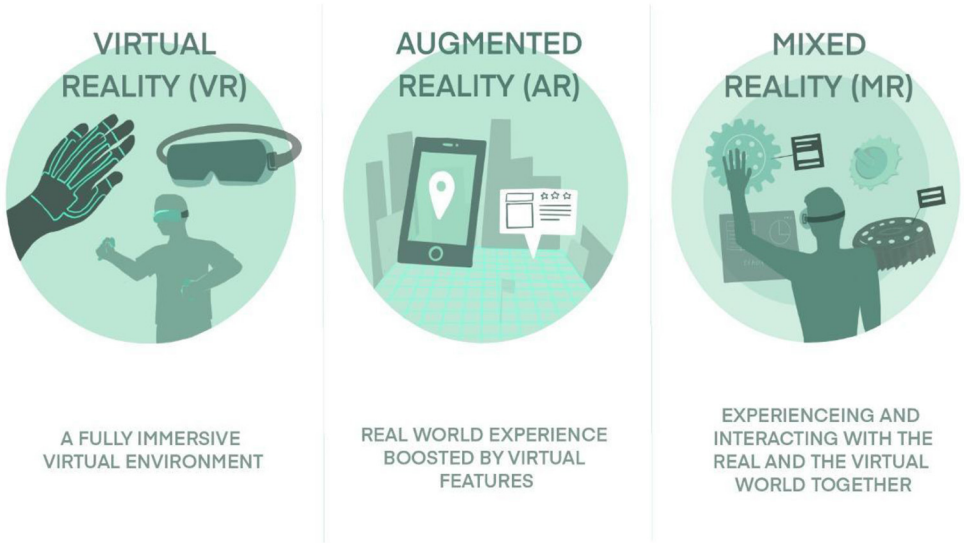

FIGURE 1 | Differentiation of immersive experience (Virtual Reality, Augmented Reality, and Mixed Reality) medical simulation tools.

as task completion time, scope and instrument trauma, and the attempts to introduce a guidewire were also examined. A performance comparison between the high-fidelity ureteroscopy bench model and VR simulator was carried out. The senior residents trained on the VR simulator, scored considerably higher on their global rating scale, checklist, pass/fail rating, and required a significantly lesser time to complete the task whereas the junior residents showed a higher rate of trauma than senior residents. A ureteroscopy simulator proved to be a great tool for evaluating endourological skills in residents.

Noureldin et al. conducted a study to evaluate the skills of urology postgraduate trainees in percutaneous renal access (PCA) using Objective Structured Clinical Examinations (OSCEs) to observe the impact of previous percutaneous nephrolithotomy (PCNL) experience on outcomes. A brief questionnaire was used to assess the previous experience of trainees in endourology. The PERC Mentor^{TM} is a device that is used to teach the operator how to perform the percutaneous renal collecting system access puncture. After a 3-min briefing on this simulator at Simbionix, Cleveland, OH, the trainees then demonstrated their ability to access the renal calyces in a model of a normal left kidney and pop the balloons present. The data collected from the completed simulations' performance report and the questionnaires were thoroughly analyzed. The PERC Mentor simulator can be used to examine the PCA abilities of urology trainees during OSCEs. The trainees with prior PCNL knowledge performed better and had fewer problems (10).

Knudsen et al. conducted a study that included 63 trainees to evaluate and establish face, content and construct validation of the PERC Mentor simulator. The subjects were then randomly assigned to one of two groups: intervention (underwent two 30-min training sessions on the simulator) or control (no further training). When compared to their baseline performance and the untrained control group, subjects who received simulator training showed significant improvements in objective and subjective parameters. The study concluded that training on simulators may enable trainees to gain the fundamental skills required for PCA since practicing on live models always comes with a handful of ethical restrictions and complications (11).

The study conducted by Nayahangan et al. (12) aimed to incorporate urological procedures into simulation training conducted during the residency period. Delphi method was used to conduct a national wide need assessment involving 56 experts having significant roles in urology education. The assessment was carried out in three rounds wherein, Round 1 involved sorting the relevant procedures to decide the tasks that can be performed by the newly qualified urologists. Round 2 involved investigations wide a survey with a need assessment formula to identify the following: procedure frequency, how important the procedure is and how many physicians should be able to carry it out, the patient response and associated risks when a procedure is performed by a beginner physician, and the feasibility of simulation training. The ranking based on the importance of procedure, elimination of unsuitable candidates was carried out in Round 3. Cystoscopy, transrectal ultrasound-guided prostate biopsy, ureteral stent placement, urethral and suprapubic catheter insertion, and transurethral resection of the bladder were the five urological procedures with the highest priority that qualified to be converted to simulations to create and develop a training program for the new urologists (12).

TABLE 1 | Summary of studies related to the application of virtual reality (VR), augmented reality (AR), and mixed reality (MR) in endourology and urolithiasis.

References	Objective	Tool used	Method	Results
Mishra et al. (8)	Validity and performance testing of virtual reality-based training for PCA	PERC Mentor	To test the varying validity of VR training for PCA −56 participants	Beginners with PERC Mentor training showed statistically significant improvement in the reduction of total surgical time during PCA
			Participants fully evaluated and completed the process −24 participants	
			Two cohorts: 15 beginners and 9 experts	
			Five beginners were trained on pigs before PERC Mentor training	
Matsumoto et al. (9)	Testing and performance comparison Symbionix model versus high fidelity ureteroscopy guide model	Uro Mentor	Sixteen residents in urology were evaluated on their competence to execute various tasks on a VR simulator	Senior residents scored higher (statistically significant) and overall took less time to complete the task in comparison to the junior residents
			The evaluation was based on a global rating scale, and a Pass/Fail rating to evaluate the subject's performance	The tool is good to assess the skills of surgical residents
Raison et al. (10)	Skill assessment of urology postgraduate trainees in percutaneous renal access (PCA)	PERC Mentor	Objective Structured Clinical Examinations (OSCEs) to study the impact of previous percutaneous nephrolithotomy (PCNL)	The postgraduate trainees with previous experience in PCNL performed significantly better and faster
Knudsen et al. (11)	Evaluate and establish face, content and construct validation of the PERC Mentor simulator	PERC Mentor	Total 63 participants were divided into two groups: (a) Intervention group (underwent two 30-min training sessions on the simulator) (b) Control group (no further training)	Intervention group participants had improved and better performance
Nayahangan et al. (12)	Integration of urological procedures into simulation-based training for resident trainees	–	The Delphi method was used to conduct a national needs assessment	The qualified experts have chosen in three rounds created and developed a simulation-based training program for the new urologists
			The study involved a total of 56 experts with significant roles in urology education	
Aydin et al. (13)	Evaluating current training methods and soliciting feedback on the potential role of AR simulation in urological training	–	A cross-sectional survey containing three sections: (a) Introduction (b) Technical skills in urology (c) Non-technical skills in urology	Both trainees and specialists advocate simulation, as the solution for safe and effective urological procedural training
Hu et al. (14)	Comparison of post-training ureteroscopy and cystoscopy competency	Uro-scopic trainer	The study involved 36 participants divided into three groups, was assessed on the Objective Structured Assessment of Technical Skills (OSATS) scale: (a) Trained with the transparent simulator (b) Trained with the non-transparent simulator (c) Trained with verbal instructions	Students improved their ureteroscopy and cystoscopy proficiency with simulator training
	Unique transparent anatomic simulator vs. no simulator training			Transparent simulators were more successful than other methods
Cai et al. (15)	Investigating the effectiveness of VR simulator training in the treatment of kidney stones using retrograde flexible ureteroscopy	Uromentor	Participants underwent 4-h training and practice sessions on VR simulators	Significant improvement ($P < 0.01$) made by trainees in procedure times, etc., after training on the VR simulators
			The participants were assessed on procedure time, techniques, and ability to perform specific tasks	
Zhang et al. (16)	Validating the use of PERC Mentor in percutaneous renal access training	PERC mentor	Total participants −21 urologists	Participants who had simulation-based training performed considerably faster
			The instructional video was shown, then the PERC Mentor was used to conduct percutaneous renal access	VR simulator offers high-quality training to accurately assess trainees' abilities in fluoroscopy-guided PCA
			Participants were judged based on the global rating scale	

Aydin et al. evaluated the effectiveness and limitations of simulation in urology training and assessment. Types of simulations (synthetic, VR, and animal models) with participant experience levels and the number of tasks completed were considered in the assessment process. For the early stage of training and testing, current simulation tools are credible and accurate. Modalities can be used to teach intermediate and expert level techniques, but their availability is limited due to supply shortages and ethical concerns. Over the last few decades, several medical institutes have readily accepted simulation-based training as a supplement to conventional operating theater experience for improved technical and non-technical skill training (13).

Huet al. (14) compared post-training ureteroscopy and cystoscopy competency with a unique transparent anatomic simulator, an opaque model, vs. no simulator training. Ten experienced urologists conducted a preliminary review of the models as teaching materials. Thirty-six first-year medical students who received the same theoretical training, were rated on a 50-point scale on their theoretical knowledge. The students were placed into three groups: those who received training with a transparent simulator (Group 1), those who received training with a non-transparent simulator (Group 2), and those who only received comprehensive verbal instruction (Group 3). The trainee's ability to insert and remove ureteral stents was assessed using the Uro-scopic Trainer and rated on an Objective Structured Assessment of Technical Skills (OSATS) scale after 12 days of training. All 10 urologists who evaluated the devices agreed that they were anatomically correct, that either version was simple to use, and that they were good ureteroscopy and cystoscopy training tools. Students improved their ureteroscopy and cystoscopy skills with simulator training, and transparent simulators were shown to be more effective than their counterparts (14).

The effectiveness of virtual reality simulator training in the treatment of kidney stones using retrograde flexible ureteroscopy was investigated by Cai et al. The results revealed a considerable improvement in the management of renal stones using retrograde flexible ureteroscopy after completing the 4-h special-purpose training using VR simulators. Between the first and second assessments, there were several statistically significant differences ($P < 0.01$). Finally, the virtual reality simulator training program can assist trainees in quickly improving their retrograde flexible ureteroscopy skills for the treatment of renal stones (15).

Zhang et al. conducted a study to establish the effectiveness of the PERC Mentor simulator in percutaneous renal access training. A fluoroscopy-guided percutaneous kidney accessing technique was introduced to 21 urologists. Ten of the 21 students had never performed percutaneous nephrolithotomy under ultrasound guidance earlier. Thus, the trainees were divided into two groups: those with primitive experience and those with no experience. When comparing the primitive experience group to the inexperienced group, the amount of contrast material used, and overall operating time were significantly lower in the primitive experience group ($P = 0.03$ and 0.02, respectively). The PERC Mentor simulator allows trainees with no prior expertise in fluoroscopy-guided PCA to complete the virtual manipulation of the process independently. This VR simulator is essential for offering high-quality training and may be used to accurately assess trainees' abilities in fluoroscopy-guided PCA (16).

Checcucci et al. evaluated surgeons' perception of mixed reality for partial nephrectomy. Attendees were given the opportunity to try MR for themselves and share their opinion on its application using a Likert scale (1–7, 17–19) questionnaire. A total of 172 participants shared their opinion. Both the surgical planning and anatomical accuracy scores (8 and 9, respectively) were excellent. This technology's potential role in preoperative planning and comprehension of surgical complexity (both rated 9/10) was expressed with high satisfaction by the participants. A more selective approach was chosen by 64.4% of surgeons and 44.4% after using HoloLens and MR technology for the first time in the field of surgery instead of just using CT images for guidance. According to the findings of the study, surgeons believe holograms and MR imaging to be a useful and interesting preoperative tool before partial nephrectomy (26).

Checcucci et al. summarized the most recent research on PCNL's use of virtual imaging guidance. Surgery training and surgical planning in urology were the first applications for PCNL 3D virtual navigation technology, which was later expanded into the field of surgical navigation using various modalities. Tools that focus on surgery have proven to be beneficial to both surgical planning and surgical navigation by using augmented or mixed reality systems that assist the surgeon in real time during an intervention (27).

Francesco Porpiglia et al. evaluated the feasibility of 3D MR holograms for establishing the point of access and directing the needle during percutaneous kidney puncture. Ten patients underwent 3D MR endoscopic combined intrarenal surgical procedure (ECIRS) for kidney stones were included in the study. A matched pair analysis was performed on a group of patients who had previously undergone a standard procedure. Different patient characteristics were compared between groups prior to and following surgery. Statistical tests for continuous and categorical variables was performed. Using 3D MR guidance for renal puncture is safe and effective, according to the study results. As a result of the MR guidance, the inferior calyx was punctured correctly in all cases, and the procedure was found to be safe and effective (28).

CONCLUSION

Numerous methods are introduced and practiced by students in medical education to make their learning and practice easier before hands-on experience. Researchers have cumulatively agreed that simulation-based training as being one of the effective modalities for teaching and training. AR in medicine enables trainees to experience full operating conditions, but VR and MR allow them to practice and improve on skills like suturing, which otherwise would be performed on animal models and raise various ethical issues. Additionally, tools like the PERC Mentor and Uromentor have shown a remarkable impact in the field of endourology with several studies evaluating

and proving their effectiveness. The results have proven that students often perform better after being trained on these simulators. Moving forward, surgical education is bound to improve as medical technology advances and simulation-based training becomes a permanent and vital part of a medical student's curriculum.

FUTURE DIRECTIONS

Several studies have been conducted on the application of VR/AR in urology, however, they have only been limited to training simulators and performing surgery. Their clinical use in endourology has been limited to pilot studies in PCNL puncture but a wider adoption of this is still lacking in the clinical field of endourology. These simulators have usages such as flexible ureteroscopy, laparoscopic surgery, robotic surgery, and detecting prostate cancer. While these applications have been proven useful, to further advance the field of urology, usage of AR/VR must broaden as well. AR/VR technology can be used to reflect symptoms of patients when they are going on with their daily lives—not only would this give a greater insight to the assigned doctor, but the treatment will have high accuracy and be more effective. To conclude, the growing field of AR/VR technology has opened a door to various opportunities to improve patient care in endourology.

AUTHOR CONTRIBUTIONS

BH, NN, AP, and BS contributed to the conception and design of the study. EK, ŞT, AP, PJ-J, and DM organized the database and wrote the first draft of the manuscript. NN, SK, ŞT, RB, SM, and BH wrote sections of the manuscript. PC, AP, EK, and BS critically reviewed and edited the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Telemedicine and Telehealth in Urology—What Do the 'Patients' Think About It?

Nithesh Naik[1,2], B. M. Zeeshan Hameed[2,3], Sanjana Ganesh Nayak[4], Anshita Gera[4], Shreyas Raghavan Nandyal[5], Dasharathraj K. Shetty[6], Milap Shah[2,7], Sufyan Ibrahim[2,8], Aniket Naik[8], Nagaraj Kamath[8], Delaram Mahdaviamiri[9], Kenisha Kevin D'costa[10], Bhavan Prasad Rai[2,11], Piotr Chlosta[12] and Bhaskar K. Somani[2,13]*

[1] Department of Mechanical and Manufacturing Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [2] iTRUE (International Training and Research in Uro-oncology and Endourology) Group, Manipal, India, [3] Department of Urology, Father Muller Medical College, Mangalore, India, [4] Department of Computer Science and Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [5] Gandhi Medical College, Kaloji Narayana Rao University of Health Sciences, Secunderabad, India, [6] Department of Humanities and Management, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [7] Robotics and Urooncology, Max Hospital and Max Institute of Cancer Care, New Delhi, India, [8] Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India, [9] Manipal College of Pharmaceutical Sciences, Manipal, Manipal Academy of Higher Education, Manipal, India, [10] Department of Biomedical Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, India, [11] Department of Urology, Freeman Hospital, Newcastle upon Tyne, United Kingdom, [12] Department of Urology, Jagiellonian University in Krakow, Kraków, Poland, [13] Department of Urology, University Hospital Southampton NHS Trust, Southampton, United Kingdom

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***Correspondence:**
B. M. Zeeshan Hameed
zeeshanhameedbm@gmail.com

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Telemedicine is the delivery of healthcare to patients who are not in the same location as the physician. The practice of telemedicine has a large number of advantages, including cost savings, low chances of nosocomial infection, and fewer hospital visits. Teleclinics have been reported to be successful in the post-surgery and post-cancer therapy follow-up, and in offering consulting services for urolithiasis patients. This review focuses on identifying the outcomes of the recent studies related to the usage of video consulting in urology centers for hematuria referrals and follow-up appointments for a variety of illnesses, including benign prostatic hyperplasia (BPH), kidney stone disease (KSD), and urinary tract infections (UTIs) and found that they are highly acceptable and satisfied. Certain medical disorders can cause embarrassment, social exclusion, and also poor self-esteem, all of which can negatively impair health-related quality-of-life. Telemedicine has proven beneficial in such patients and is a reliable, cost-effective patient-care tool, and it has been successfully implemented in various healthcare settings and specialties.

Keywords: telemedicine, telehealth, urology, patients perspective, COVID-19

INTRODUCTION

Telehealth is a rapidly developing healthcare that entails electronic communication between patients and clinicians, and telemedicine is a subset of telehealth (1). The WHO defines telemedicine as "the delivery of healthcare services, by all healthcare workers using the information and communication technologies for the exchange of dependable data for the diagnosis, treatment, and prevention of disease and injuries, research and evaluation, and continuing education of healthcare providers, where distance is an important aspect" (2). The telephone utilization to

minimize office visits was first documented in the Lancet in 1879. Telemedicine has evolved into a wide range of forms and uses electronic devices to improve healthcare delivery in various contexts (3). Video visits (VVs) have provided a real-time audio–visual substitute to traditional in-person appointments. Such an interactive communication model has allowed clinicians, patients, and families to communicate in real-time (4). Teleclinics have been reported to be successful in post-surgery and post-cancer therapy follow-up and provide consultation services for diagnosing patients with urolithiasis (5, 6). Recent research has looked into the usage of video consulting in urology centers for hematuria referrals and follow-up appointments for a variety of illnesses, including benign prostatic hyperplasia (BPH), kidney stone disease (KSD), and urinary tract infections (UTIs), having greater levels of acceptability as well as fulfillment (7–9). Telemedicine has shown to be dependable and successful as a patient-care technique and has been effectively deployed in various healthcare settings and specialties (10–13). **Figure 1** shows the process flow of telehealth/telemedicine tools that are used in patient consultation.

Benefits of Telemedicine in Healthcare

Telehealth has piqued the interest of clinicians and decision-makers, particularly since the expanded usage of the internet, with its potential to reduce healthcare costs and improve convenience (14). It uses advanced telecommunication technology to improve healthcare accessibility and availability (15). Telemedicine has a favorable impact on patients and offers cost-saving (4, 16). Enhancements in the patients' well-being, increased healthcare access in under-served areas, reduced travel time and expenses, shorter wait times, and fewer admissions in hospitals are a few of the benefits (17–19). Telemedicine has the potential to improve healthcare outcomes in the remote areas by lowering costs and boosting access to specialized treatments (20). It also ensures better information access (21). Other indirect advantages include increased adaptability in scheduling, increased availability of space in clinics and parking lots, reduced traffic, and reduced greenhouse gas emissions (22, 23).

Shin et al. (24), in their study, examined the patient contentedness and savings and clinical results of televisits in female pelvic medicine and reconstructive surgery at an urban educational center and identified that the patients reported a variety of savings, such as 88 (48.1%) of them saved at least 1 h in travel time and 54 (28.9%) saved more than $25 on transportation costs. The patient and family burden was reduced because 43 (23%) had a healthcare issue that made it hard to go for face-to-face appointments, 37 (19.8%) said that traveling for face-to-face appointments was grueling, and 41 (21.9%) said that doing a televisit allowed them to avoid taking time off work. More than half of all patients 94(51.4%) indicated they generally spend more than half an hour in the waiting area for face-to-face sessions (24).

Importance of Telemedicine During COVID-19

On March 20, 2020, the WHO proclaimed novel coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), an epidemic (25). The SARS-CoV-2 infection and the burden of urgent and challenging healthcare situations and needs took varied forms around the world (26, 27). Before the pandemic, telemedicine was infrequently used for follow-up visits rather than new appointments (28). The pandemic provided an exceptional chance to evaluate the efficacy of telemedicine for both new and follow-up patient consultations, as most of these appointment sessions were conducted over the phone (29).

As the epidemic enters a more chronic phase (30), with possible peaks in the future, it is critical to strike a balance between virtual treatment and a secure environment for in-person appointments. The approach of conducting telephone interviews with approved clinical tools such as checklists and questionnaires has the potential to be widely used to manage the COVID-19 pandemic's growing limitations successfully. It is a cost-effective and resource-efficient approach that protects both patients and healthcare providers while ensuring the care of vulnerable patients. (31). In addition, telephone interviews have the potential to provide social support to patients who are lonely, worried, and afraid of abandonment as a result of the pandemic (32).

Cancer remains the leading cause of death, and individuals are unwilling to compromise on their care. When there is a need for social separation, rapid introduction of telehealth is tolerated well, with a clear "red line" for alterations in the current interactions of patients and physicians. Human dignity in uro-oncology will be preserved by balancing future telemedicine implementation with the patients' demands for personal contacts (33). Because of the immunosuppression and numerous routine hospital visits, the patients of cancer having systemic treatment may be at increased possibility of developing a critical case of COVID-19(27). Telehealth can safeguard cancer patients and healthcare providers from infections during face-to-face encounters, given the existing necessity for social and patient–physician separation (33).

Urology, Telemedicine, and COVID-19

Telemedicine in urology can reduce patient contact, lower infection rates among staff, allow isolated urologists to continue providing care (34). It can help with urological conditions such as monitoring kidney stones, renal cysts, and long-term lower urinary tract symptoms (LUTSs) management. Ureteric colic can also be diagnosed *via* phone appointment because its clinical setting is comparatively unharmful. Symptoms and scan results can be evaluated and relayed over the phone without a requirement for physical evaluation at a follow-up appointment (35, 36).

Despite the apparent advantages of telehealth, the long-term patient outcomes of urological telehealth are unknown (37). Some urologic oncology patients, mainly those with prostate cancer, have reported high satisfaction with telemedicine. Telemedicine visits were used as a consequent endpoint in a study of metformin in prostate cancer patients (38). Patients with prostate cancer who had undergone prostatectomy were highly satisfied with telemedicine (39). Apart from the prostate cancer population, the research on remote care in urologic oncology is still lacking (40). The COVID-19 epidemic has forced major

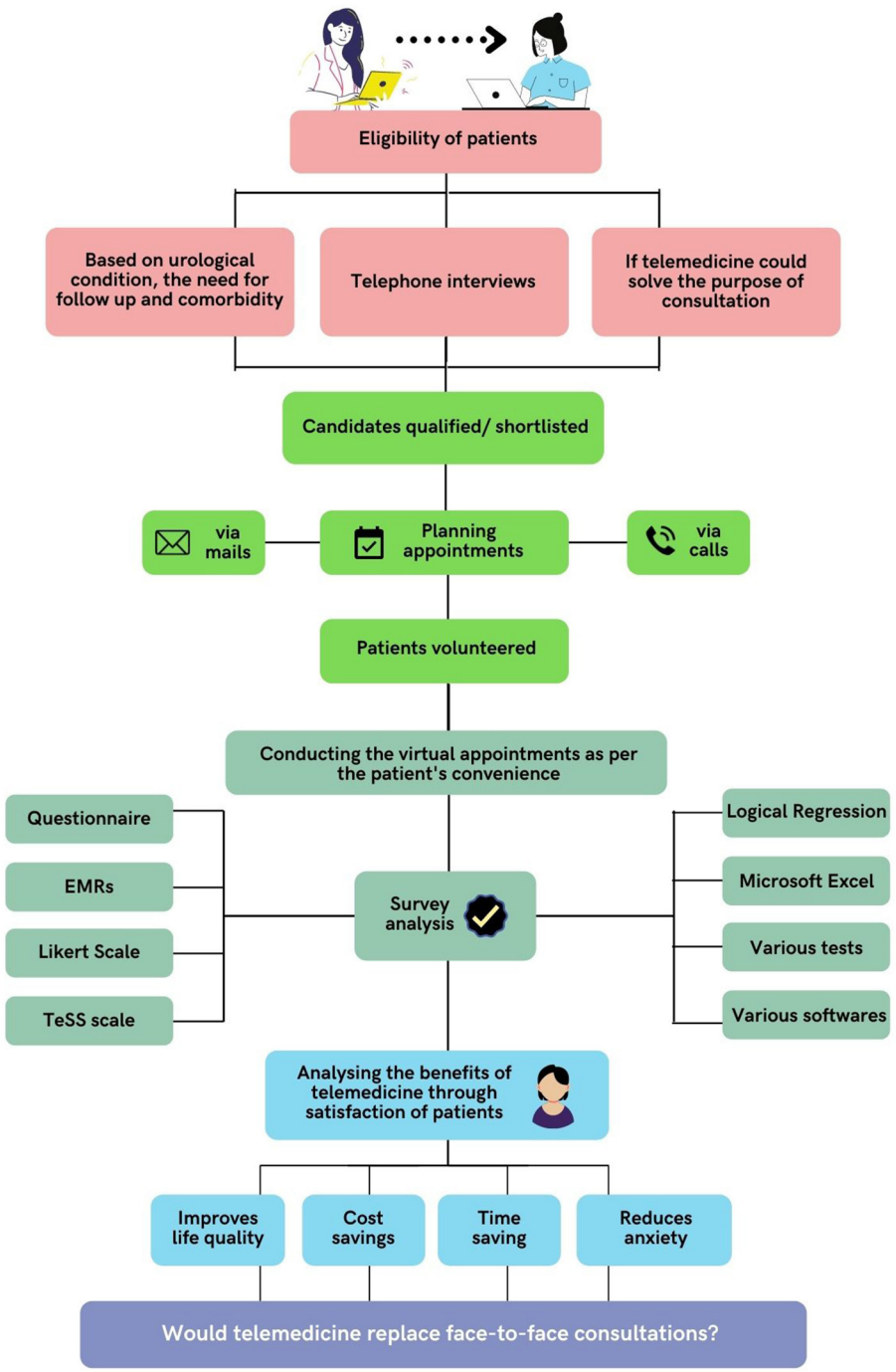

FIGURE 1 | Process flow of telehealth/telemedicine tools for patient consultation.

changes in the healthcare worldwide, including urology (41). The pandemic has put a significant strain on hospital resources (42). As hospitals pose a substantial infection exposure through COVID-19 positive patients and asymptomatic exposed medical workers, deferred access for patient care has been suspended chiefly (43). In the COVID-19 scenario, urology is regarded as a non-essential clinical service by the international healthcare delivery system, even though the patient's quality-of-life is significantly impacted by urological disease (44, 45).

Stay-at-home policies restricted the clinic visits, including urological visits (46). In such cases, telemedicine was a practical solution for providing patients with follow-up care (47, 48).

The COVID-19 pandemic has paved way for the technological advancements in the field of healthcare. Technology assisted consultation is proven to be beneficial for the patients (40, 49, 50). "Does the National Health Service (NHS) future lie in telephone consultations?" The results and experiences of the patients using NHS urology service's with telemedicine for various urological issues included clinic types ranging from post-radical prostatectomy to PSA surveillance, general, functional, and andrology followup. Patients with lower urinary tract symptoms, hematuria, and stones were observed in the general urology clinic. Patients were not evaluated individually for telephone clinic eligibility. As a result, phone calls were used to discuss difficult management decisions and deliver bad news. During the pandemic, they discovered high levels of overall contentment with the usage of telephone appointments for urology patients. Patients in the PSA surveillance and post-radical prostatectomy clinics, on the other hand, reported significantly higher levels of satisfaction (50).

In a study for outpatient hematuria referrals, involving the implementation of teleurology with the help of teleconsultation to gather clinical information using a standardized algorithm, patients reported higher overall satisfaction and acceptance rates as an expedited evaluation strategy (7). Teleconsultation-based services increase urologic access by enabling asynchronous web-based consults and patient co-management between primary care providers and urologists. Patients in the neuro-urology unit frequently have disabilities that make travel difficult and necessitate the appearance of caregivers during medical appointments. Furthermore, these patients' follow-up generally involves multiple visits, with all of the recognized effects regarding medication adherence, contentedness in general, personal uneasiness, and general and medical healthcare expenses.

Telemedicine could be beneficial in patients attending neuro-urology appointments (51). In a recent report, clinicians used telemedicine to ensure patient follow-up at the neuro-urology department dealing with problems such as persisting urine incontinence, vesicoureteric reflux, and repetitive urinary tract infections, which are pretty common in neuro-urologic patients. Telephone consultation was used because of a delay in implementing telephone consultation (using video equipment) and cognitive impairment of a few of the patients. In conclusion, telemedicine in the area of neuro-urology was related to a significant level of patient satisfaction (52). **Table 1** summarizes the recent studies on telemedicine and telehealth in urology based on patient's perspectives.

The Perspective of Different Communities/Groups

It was observed in the studies that the patients' age, gender, ethnicity, race, and distance from the hospital did not seem to be related to contentment associated with telephone consultations (52, 53). However, every healthcare system includes groups at risk of bad news, who may now face increased challenges due to a lack of digital literacy or access. Rural communities, elderly persons, ethnic/racial minority populations, people with low-socioeconomic positions, inadequate health education, and little English proficiency are more likely to face this obstacle (54–56).

Gender

Certain health conditions can cause feelings of disgrace, social separation, and low self-esteem, all of which can affect health-related quality-of-life (HRQoL) (57–59). Many women are affected by urgent urinary incontinence (UUI) and mixed urinary incontinence (MUI), significantly influencing their QoL. As a result, it is critical to provide effective treatment alternatives that can reach many patients, and eHealth technologies are fresh new ways to assist self-management. Wadensten et al. (60), in their study, examined the usefulness of the mobile application Tät II for self-monitoring of women having UUI and MUI and concluded that it was effective as the majority of the women who were present in the therapy group were happy with their treatment (60).

In their study, Shin et al. (24) attempted to assess the patient satisfaction and cost savings and analyzed visit outcomes using a main complaint of women for a televisit to the FPMRS clinic at an urban educational center. They did a cross-sectional review of all the women who finished a televisit to an FPMRS specialist at their institution and found out that 187 out of 290 (64.5%) women who were called completed the survey, and 168 (89.8%) of them were satisfied with the televisit. In total, 88 (48.1%) ended up saving at least 1 hour, and 54 (28.9%) saved more than $25 on transportation. In total, 99 (52.9%) televisits resulted in face-to-face follow-up, with chief complaint of prolapse (odds ratio [OR] = 4.2 (1.7–10.3); $p = 0.002$), new patient (OR = 2.2 (1.2–4.2); $p = 0.01$), and Hispanic ethnicity (OR = 3.9 (1.2–13.6); $p = .03$) as considerable determinants. Because many participants were comfortable with FPMRS televisits at their urban academic center, telemedicine could become a main treatment within the FPMRS specialty even after the epidemic is gone. As more healthcare institutions adopt telemedicine, further research needs to be conducted to determine which patients will benefit the most from it (24).

Age

During the COVID-19 pandemic, Efthymiadis et al. surveyed patient satisfaction with telephone consultations, which was evaluated using an adaptation of the Telehealth Satisfaction Scale (TeSS). Patients who received a telephone appointment during 1 month were asked to fill out a survey. The patients' responses were compared by the clinic type, age, and gender. Patients in post-radical prostatectomy and PSA surveillance clinics responded with more 'Excellent' or 'Agree' comments. A considerably higher number of 'Agree' responses to one item was associated with older age. Gender had no bearing on the responses. The study found that urologist patients were quite satisfied with the utilization of telephone consultations. (50). However, older age was independently associated with lesser completed telemedicine visits.

TABLE 1 | Summary of recent studies on telemedicine and telehealth in urology based on patient's perspectives.

Author	Objective	Patient sample	Software/tests/data analysis	Outcomes
Shin et al. (24)	To assess patient satisfaction and cost-effectiveness, as well as to compare the results of women who came in for a tele visit to a female pelvic medicine and reconstructive surgery (FPMRS) clinic at an urban educational center based on their chief complaint (CC).	• Cross-sectional research on women who had a telephone consultation with an FPMRS specialist	• Survey analysis • Telephone questionnaire, • Electronic medical records	• 64.5% of the women polled had completed the survey. • 89.8% were satisfied with the television visit.
Shiff. (29)	To assess the satisfaction of patients with telemedicine consultations as a substitute for in-person consultations at Andrology-focused academic urology practice during COVID-19 epidemic.	• Appointments over the phone • Telephone questionnaire	• Survey analysis • Likert scale	• As an alternative to in-person visits, patients were mostly satisfied with telephone consultations.
Barba et al., (31)	To see patients' satisfaction with the alternate strategy as deferred access, including non-urgent outpatient consultations, were suspended during the COVID-19 pandemic.	• To explore pelvic floor symptoms, telephone interviews were held with the help of a standardized questionnaire.	• JMP 9.0 (SAS, Cary, NC, USA)	• All patients were satisfied with the telephone interview. They thought it was an acceptable tool to replace routine hospital appointments during the COVID-19 lockdown.
Rodler et al. (33)	To ascertain patients' perspectives on the use of telehealth as a pandemic response and its long-term viability.	• Discussion on virtual multidisciplinary tumor boards by means of video conference.	• 10-item Likert scales • Wilcoxon matched-pair signed-rank test • Mann-Whitney U test • Chi-square test • Software: Prism 8 (GraphPad Software)	• Patients' perceptions of COVID-19 and cancer anxiety, perspectives on means of telehealth in response to the current epidemic, and long-term acceptance were employed.
Boehm et al. (42)	To evaluate the patients' eligibility for telemedicine and examine their perspective by accessing their readiness for telemedicine during the COVID-19 epidemic.	• Patients were eligible if telemedicine could entirely solve their primary purpose for consultation. • In all, 216 patients (54.1%) qualified for telemedicine and requested a telemedical visit.	• RStudio v0.98.953 (R Project for Statistical Computing, www.R-project.org)	• Risks for a serious course of COVID-19 are usual in urology patients (94.5%). • Many patients expressed an interest in having a telemedicine consultation (84.7%).
Efthymiadis et al., (50)	To assess the satisfaction of urologist patients using telephone appointments during the COVID-19 epidemic.	• A questionnaire was sent to all patients who received a phone appointment within 1 month. • In the first instance, patients were not offered face-to-face appointments.	• A seven-question adaptation of the Telehealth Satisfaction Scale (TeSS) • Likert scale • Microsoft Excel • R statistical environment • Univariable logistic regression.	• Urologist patients are generally satisfied with the usage of telephone consultations. • Telephone consultations are better suitable for some patients and may be used more frequently in the future.
Chesnel et al. (52)	To evaluate the effectiveness and contentment of telephone consulting in neuro-urology since Patients' appointments to the department of neuro-urology were limited owing to the COVID19 outbreak.	• Scheduled medical appointments were replaced by telephone consultations during the epidemic.	• Software: R and RStudio software • Means • Percentages • Standard deviations • Univariate analysis with *t*-test or variance analysis • Linear regression model in multivariate analysis • Weight kappa (wkappa)	• In neuro-urology, telemedicine was connected to high patient satisfaction and was specified as efficient by physicians. • However, patient's satisfaction was harmed by cognitive impairment, the humiliating aspect of teleconsultation, and an inclination toward physical appointment.

(Continued)

TABLE 1 | Continued

Author	Objective	Patient sample	Software/tests/data analysis	Outcomes
Heeno et al. (53)	To gather review from patients about their telemedicine experience.	• Patients for appointments in telemedicine were selected based on their urological condition, need for follow-up, and illness.	• Study-specific questionnaire	• Patients' age, sex, and distance from the hospital weren't related to satisfaction with telephone consultations. • 85% of urological patients were generally satisfied with telephone appointments.
Margolin et al. (62)	To find out how patients and doctors feel about using telemedicine to treat genitourinary cancer. The effectiveness of telemedicine for the treatment of patients having urologic malignancies was evaluated from both the patient and provider perspectives.	• Patients who had telemedicine sessions with urology, medical oncology, or radiation oncology for the treatment of genitourinary cancers were studied in a prospective cross-sectional study.	• 5-point Likert scale • Spearman correlation coefficient • ordinal logistic regression • Stata 16.1 (StataCorp, College Station, TX) • Software: MyChart (Epic, Verona, WI) or Doximity software (San Francisco, CA).	• Patients and physicians showed high levels of satisfaction with telemedicine consultations for management of genitourinary cancers.
Bell et al. (61)	To investigate the factors that led to non-attendance at a urology telehealth appointment at a large metropolitan safety-net hospital after COVID-19 obliged the institution to switch to telehealth.	• All telehealth appointments after March 17, 2020, and for the next 8 weeks were recognized.	• Stata SE 16.1 • Logistic regression • Mean • Standard deviation • Median • interquartile range • Frequency tables • Proportions • *T*-test • Chi-square statistics	• Non-attendance at outpatient telehealth urological encounters at an urban safety-net hospital in initial phases of COVID-19 epidemic was linked to various social factors like social support and drug usage.
Kim et al. (64)	To check if non-medical professionals performing Post-Operative Check-in Phone Calls (POPC) before 48 h of outpatient pediatric urological surgeries could improve patient/family content and reduce emergency department consultations within 30 days of the procedure by increasing email/telephone communication.	• Over the course of 8 weeks, families of children receiving ambulatory pediatric urology surgeries were included.	• Likert scale • Fisher's exact test • Mann–Whitney U test • Software: Statistical Package for Social Sciences (version 20.0.0)	• POPC by an NMP in 48 h of surgery might not have an effect on perioperative satisfaction of families of patients who underwent same-day pediatric urological surgery. • But it can help to reduce postoperative anxiety.
Gan et al. (66)	To expand telemedicine for initial and follow-up pediatric urology patient visits efficiently while meeting the expectations of both patients and parents.	• Video Visits expanded in March 2020 when the epidemic was gaining traction. • Patients who had technical reasons were excluded.	• Electronic medical record • Standardized questionnaire • Software: NVivo software (launched March 2020) (13)	• Families expressed high levels of overall satisfaction with the video visits, believing that the visit addressed the medical needs of their children.
Warda et al. (83)	To see if a phone call prior to a urodynamic study (UDS) reduced test-related stress in comparison to normal care.	• Survey of patients of at least 18 years who had lesser urinary tract dysfunction was done.	• X2 • Fisher exact • Wilcoxon rank-sum tests	• The phone call before UDS did not reduce anxiety but it improved satisfaction with pre-UDS counseling.
Vallasciani et al. (84)	To use the digital clinic approach for new recommendations to Riyadh's pediatric urology clinic, the city's major tertiary care center.	• Retrospective review of the expenditures and timing associated with the VC practice • 15-question survey	• Survey analysis	• Cost savings can be achieved through telemedicine without compromising patient safety or negatively impacting patient management.

(Continued)

TABLE 1 | Continued

Author	Objective	Patient sample	Software/tests/data analysis	Outcomes
Finazzi et al. (85)	To find out the patients' sayings regarding telephone-based urological appointments during the COVID-19 epidemic.	• A cross-sectional telephone survey among some Italian patients who were scheduled for a urological appointment.	• A four-question patient questionnaire.	• In a very stressful circumstance, a telephone consultation was shown to give high levels of satisfaction, reassure urology patients, and improve their quality of life.
Wadensten et al. (60)	To see how effective the mobile software Tät II is in helping women control their Urgent Urinary Incontinence and Mixed Urinary Incontinence	• This randomized controlled experiment consisted of women of at least 18 years old having UUI or MUI and at least 2 leakages per week. • The women who displayed red flag signs weren't allowed to participate.	• Incontinence episode frequency • Intention-to-treat analysis • ICIQ-UI SF • ICIQ-LUTSqol Module • ICIQ-OAB Module • IC scale (Incontinence Catastrophizing) • Linear mixed-model analysis • Mann-Whitney U test • Paired *t*-test • Wilcoxon signed-rank test • Chi-square test • SPSS (version 25; IBM Corp)	• Women's urgency and mixed incontinence were both improved by using the treatment app. • This application may be a useful substitute to pharmaceutical care or other conservative management when self-management is appropriate, thereby boosting access to care.
Ong et al., (86)	To see how effective a telemedicine service for ureteric colic patients is at minimizing unwanted face-to-face consultations and reducing appointment wait times	• Patients with ureteric colic that did not have elevated symptoms such as fever, acute discomfort, or hydronephrosis were involved in the study, and face-to-face appointments to review scan data were replaced with phone sessions.	• SQUIRE (Standards for Quality Improvement Reporting Excellence) quasi-experimental, interrupted time series analysis	• The enrolled patients were mostly satisfied with the new service as it saved them money and time. • Without compromising patient safety, the ureteric colic telemedicine service successfully lowered the number of face-to-face visits and review time.

Vulnerable Groups

Remarkably, common sociodemographic characteristics such as race/ethnicity, country of birth, and primary language were not linked to the chances of attending a telehealth appointment (61). Margolin et al., in their study, found no significant differences in patient satisfaction among vulnerable groups (e.g., elderly patients, Hispanic/Latino ethnicity, non-White race patients). The negative consequences of technology hurdles may be felt disproportionately by vulnerable communities, thus aggravating existing healthcare gaps (62). The usage of video for telemedicine appointments was shown to be less common in black and Latinx ethnicity people creating further disparity (63).

When the racial factor was taken into account, more than three-quarters (77%) of encounters were attended by ethnic/racial minorities, and the attended and non-attended encounters had similar racial/ethnic compositions. When other considerations were taken into account, homelessness/unstable housing had no impact on the chances of attending a telehealth visit ($p = 0.13$) (61). Less video-based telemedicine consultations were connected with the black race, lower household salary, and Latinx ethnicity (63).

Other Factors

Bell et al. (61), in their study, indicated that the married/partnered patients were in a higher percentage of attended encounters (88, 38.6%) than non-attended encounters (18, 19.2%, $p = 0.001$). Being single/widowed/divorced, having an active substance use problem, and having a new patient consultation were all linked to decreased attendance rates in multivariable analysis. The use of a language other than English as the patient's chosen language and having Medicaid insurance were both linked to independently lesser completed telemedicine appointments (61).

Family Satisfaction

In a prospective study, Kim et al. (64) examined whether non-medical professionals (NMPs) performing post-operative check-in phone calls within 48 h of outpatient pediatric urological operations could improve patient/family contentment and reduce superfluous service utilization by increasing telephone/email communication and minimizing emergency department visits in 30 days of the process. This study suggested that well-defined perioperative guidelines and protocols can be

the more significant factor in influencing patient and family happiness during the perioperative process. Moreover, it was concluded that the patient families undergoing same-day pediatric urology surgery might not be affected by a POPC made within 48 h of surgery. However, a 48-h post-operative consultation with a non-medical professional may help to alleviate post-operative anxiety. The POPCs provided improved educational and emotional assistance to most families in the pediatric age group receiving same-day tonsillectomies (65). Moreover, Gan et al. (66), in their study (66), identified that the families were generally satisfied with video visits (median score of 10/10), indicating that they met their child's medical requirements satisfactorily. A telehealth visit was strongly recommended by 90% of families. Only 15.6% of the families reported visual or hearing problems, and 7.6% reported internet connectivity problems, suggesting that the great majority of families had no technical concerns.

Challenges

Telemedicine came with its own sets of difficulties, such as software flaws, a lack of video-compatible devices, a lack of high-speed internet, and individual technological fluency (67). Users and service providers alike experienced a variety of technical and connectivity challenges, including the visit's poor audio and/or video quality and problems in logging into the mobile application (68). Some patient-facing health apps are difficult to use for people with little health literacy (69). Furthermore, in their design and user interface, some digital health products expressly take into consideration digital literacy, age, health literacy, and English proficiency (70, 71).

Recently introduced procedures and workflows such as mandating enrolment in an online patient website have artificially created further hurdles to telehealth, even though vulnerable people are less inclined to utilize patient portals (72, 73). Even though these are excellent techniques to ensure uptake, many healthcare systems do not supply training, teaching, or guidance to patients on using these technologies (72, 74). Moreover, according to some facilitators, the outside technical aspects associated with the technique of teleconsultation include the patient's motivation, confidentiality, and familiarity with staff, and previous experience (52).

While a video visit is appropriate for most of the visits, the restrictions of remote diagnosis pose a difficulty for specific diagnoses. For example, the testing of an undescended testicle was inconsistent, and clinicians would prefer an in-person review in the future. The necessity for radiographic imaging is yet another issue that arises but is more easily solved. In this situation, some families received studies and mailed or had them transmitted electronically to the clinical team before the scheduled video consultation, facilitating inspection. Coordination of this procedure can be time-demanding for all the parties involved (66).

Furthermore, given the COVID-19 pandemic, the patient's satisfaction during the telephone consultation may be overrated (52). The encounter was deemed to have had significant technological challenges if the patient or physician reported on the survey that they had the visit over the phone without video or that the platform did not perform well enough to complete the visit as intended (62). Despite having access to the technology of mobiles, elderly patients, those from poorer socio-economic backgrounds, and those who do not speak English fluently are less inclined to use the health technologies (75, 76).

Barriers to Telemedicine

Despite being shown to be beneficial and successful in healthcare settings, telemedicine has limitations and obstacles. It has yet to gain widespread acceptance in the urological community because of various restrictions including patient and physician acceptability, licensure and responsibility, costs, safety, and concerns with ethical issues. A systematic review of the global challenges to telemedicine adoption found that technology-specific concerns were the major barriers to telemedicine usage, with technically challenged employees being the most commonly identified impediment (77).

The pandemic period was difficult for healthcare delivery and resulted in legislative reforms that acted as a spur for us to better comprehend this previously untapped resource. Despite regulatory and legislative improvements aimed at encouraging the use of telemedicine, the financial expense of adopting it may remain a barrier for small practices (78). This implementation will continue to need careful planning, procedures and processes, and rigorous assessment to maintain the long-term viability of telemedicine and telehealth beyond the COVID-19 pandemic. Critics of telehealth use are also concerned that it will have a negative impact on the continuity of care, stating that online interactions are impersonal and unsafe since the virtual physician lacks the advantage of a comprehensive history and physical examination to help in diagnosis and treatment (79, 80).

This is particularly true in cases of chronic illnesses and malignant diseases where a thorough physical examination is of paramount importance even from the perspective of a clinician to guide the investigations and management. Ease of access, ability to use, and the design of interface being used to provide telehealth services continue to be the major technological factors limiting the use of telemedicine.

Future Predictions of Usage of Telemedicine in the Post COVID-19 Situation

The rapid digitalization of our communities has resulted in higher levels of mobile connectivity, including in emerging economies, so a higher uptake of telemedicine is anticipated (81). Telemedicine is better suited for long-term follow-up as well as reports on chronic illnesses, as evidenced by the findings. Moreover, as telemedicine becomes more common in the specialty, validated tools for urology patients and specific patient populations will be helpful in upcoming studies. Patients in the post-radical prostatectomy and PSA surveillance clinics reported considerably higher satisfaction levels. This suggests that telemedicine will be used to some extent when the COVID-19 epidemic is over (50). Telemedicine can be used effectively in pediatric urology for various visit types, including unfamiliar,

return, and post-operative consultations, with comprehensive favorable feedback from the families (66).

However, face-to-face consultations are essential in some circumstances for a safe and full clinical assessment. So, face-to-face appointments, which are superior for breaking bad news and checking acutely ill patients, cannot be replaced by telemedicine. Telemedicine should not be used to treat diseases that require a medical assessment or extensive discussions. Due to privacy concerns, people with sexual health disorders may be less eager to participate in telemedicine (8). Many patients prefer face-to-face appointments over phone consultations for personal reasons, and this should be acknowledged while keeping patient's and practitioner's safety in mind. So, as part of a patient-centered approach, the choice of telephone and remote consultations must be made available to the relevant patients (50).

Moreover, to avoid increasingly existing disparities, recognizing people at greater possibility of non-attendance because of reasons such as inadequate digital literacy, insecure housing, or substance use disorder is critical (82). As a result, healthcare organizations will need to minimize technological barriers to increase telehealth availability and acceptance among vulnerable groups. To achieve fair access to telemedicine, physicians and healthcare institutions will need to make informed, integrated, and intentional efforts (61).

CONCLUSION

Telemedicine, which refers to delivering healthcare to the patients who are not at the physician's exact location, is associated with many benefits and overall patient engagement and satisfaction. It is better suited for long-term follow-up and assessment of long-standing conditions and has played a vital part in the present global COVID-19 pandemic, delivering timely patient service while simultaneously ensuring the social distancing required to avert the transmission of infectious diseases. Being a cost-effective and resource-efficient solution, it also provides additional social support to lonely and anxious patients due to the pandemic.

However, telemedicine presents its own set of potential hurdles such as software faults, a shortage of video-compatible devices, a lack of high-speed internet, and individual expertise. Besides, the rural section, elderly, ethnic/racial minority populations, and people having minor socioeconomic status, poor-health literacy, and narrow proficiency in English are more susceptible to the technological barriers. But, the choice of having telephone and remote consultations must be made accessible to appropriate patients as part of a patient-centered strategy. Healthcare organizations will need to develop strategies to eliminate technological barriers to improve telehealth accessibility and acceptance among everyone. To achieve fair access to telemedicine, physicians and healthcare institutions will need to make informed, coordinated, and intentional efforts.

AUTHOR CONTRIBUTIONS

NN, DS, BH, and BS contributed to the conception and design of the study. MS, SI, SN, AG, AN, and NK organized the database. SN, AG, AN, DM, KD, and SI wrote the first draft of the manuscript. NN, DM, DS, BR, SN, and BH wrote sections of the manuscript. PC, BR, and BS critically reviewed and edited the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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BRIEF RESEARCH REPORT
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3D Imaging Segmentation and 3D Rendering Process for a Precise Puncture Strategy During PCNL – a Pilot Study

Otaš Durutović[1,2], Aleksandar Filipović[1,3], Katarina Milićević[4], Bhaskar Somani[5], Esteban Emiliani[6], Andreas Skolarikos[7] and Milica M. Janković[4]*

[1]Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [2]Clinic of Urology, University Clinical Centre of Serbia, Belgrade, Serbia, [3]Center for Radiology and Magnetic Resonance Imaging, University Clinical Centre of Serbia, Belgrade, Serbia, [4]Laboratory for Biomedical Instrumentation and Technologies, Department of Signals and Systems, University of Belgrade, School of Electrical Engineering, Belgrade, Serbia, [5]Faculty of Medicine, University Hospital Southampton, Southampton, United Kingdom, [6]Department of Urology, Fundacion Puigvert, Autonomous University of Barcelona, Barcelona, Spain, [7]National and Kapodistrian University of Athens, 2nd Department of Urology, Sismanoglio Hospital, Athens, Greece

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****Correspondence:***
Aleksandar Filipović
aleksandar.filipovic11@gmail.com

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Percutaneous nephrolithotomy (PCNL) is frequently used as the first-line treatment of large and complex stones. The key point for successful complex stone removal with minimal risk of complications is to establish the most appropriate access route. Understanding the three-dimensional (3D) relationship of kidney stones and renal collecting systems is crucial for planning and creating an optimal access route. By using a 3D volume segmentation tool a more accurate approach to the renal collecting system and stone treatment could be planned. The objective of this study was assessing the impact of 3D software in getting the desired access.

Keywords: 3D reconstruction, 3D rendering, PCNL, puncture guidance, kidney stone

INTRODUCTION

During renal stone treatment planning, non-contrast computerized tomography (NCCT) is a highly recommended examination, used for assessing the stone size, number, and location. Non-excretory phases do not provide precise insight into detailed stone distribution inside the renal collecting system. With the use of an additional excretory phase scan, the urologist can study in-depth the relationship between the stone and the occupied pelvicalyceal system.

European Association of Urology (EAU) Urolithiasis Guidelines recommend percutaneous nephrolithotomy (PCNL) as the first-line treatment of large stones, more than 2 cm (1). Urologists usually define a renal stone as being complex based on the complicated and difficult pelvicalyceal anatomy, branching of the stone into the pelvicalyceal system, or the existence of multiple stones in various calyces. PCNL treatment of complex renal stones frequently require several access tracts and clear out the stone completely (2–4). However, the overall complication rate, as well as the transfusion rate, is higher when using multiple tracts (5–7). The key point for successful complex stone removal with minimal risk of complications is to establish the most appropriate access route (8). That means that the urologist should select and puncture

that calyx(s) which will lead to complete stone extraction, while they will not increase perioperative complication rate.

Understanding the three-dimensional (3D) relationship of kidney stones and renal collecting systems is crucial for planning and creating an optimal access route. In recent years the use of advanced imaging and 3D reconstruction of CT data in the treatment of kidney stones is increasing (8). Advanced imaging systems have been shown to provide the 3D perception of target organs, surrounding anatomic structures, depth perception, and spatial orientation during endoscopic and minimally invasive surgery (9, 10).

There is a continuous search for new and improved methods that could help and refine the course of the PCNL procedure by achieving a more accurate approach to the renal collecting system and stone treatment while decreasing the risk of complications (11).

For the purpose of this study an elective semi-automated instrument was created for a more exact and quantitative evaluation of the renal collecting system and the stone by using a 3D volume segmentation tool. This could help for preoperative comprehensive PCNL access route planning but is also viable for real-time use in the operating room. The aim of this study was to assess the impact of 3D software in getting the desired access.

METHODS

In this pilot case study, we enrolled 5 patients, which were selected with kidney stones, planned for PCNL procedure. CT scans were performed using a 64 multi-detector row CT scanner (General Electric) with 0.625 mm axial plane reconstruction. The scan was performed before and after contrast administration and both phases (plain and excretory) were used for the segmentation process and fusion of the 3D images into a single semi-transparent model demonstrating the stone distribution in the collecting system. While NCCT was used for stone segmentation, the excretory phase was used for collecting system segmentation. The scan delay time for excretory phase after i.v. contrast administration was 10–15 min, depending on the kidney excretion and degree of obstruction if present. The data set was routinely analyzed in Advantage Workstation Software V 4.6. The contrast medium used was Ultravist 370 mg J/mL, approximately 70–100 mL depending on the patient's weight.

After NCCT acquisition DICOM images were used for segmentation and 3D reconstruction of the renal stones using the *3D Gastro CT Ex tool*. The same software was used for segmentation and 3D reconstruction of pelvicalyceal system images obtained at the excretory phase scan. The reconstructed 3D model represented the interrelation between the pelvicalyceal system and stone with the greater anatomical details. Visualization is achieved by adjusting the scanned object transparency. Segmentations were performed to obtain stone volume (SV) and pelvicalyceal system volume (PSV). After volume rendering of the collecting system and renal stone, the stone volume (SV) was analyzed and compared with the pelvicalyceal system (PS) volume. The volumetric ratio of the stone and collecting system (SV/PS) was also analyzed.

Software Environment

3D Gastro CT Ex tool is an open-source tool developed on Python 3. This tool is the extended version of the *3D Gastro CT* tool that was previously introduced (12). The previous software version supports segmentation and 3D rendering of abdominal CT scans for individual phases (native and vein phase). The new software version, whose advantages in the planning of PCNL treatment are illustrated through this paper, offers the option for 3D hybrid visualization of native and delayed phase, which will be described in detail. The following libraries and toolkits were used in the tool development process: matplotlib (13), ndimage (14), SimpleITK (15–17), and VTK (Visualization Toolkit) (18). PyQt5 binding for Qt v5 was used for designing an intuitive and user-friendly graphical interface (19). The tool offers options for reading and viewing different image formats that are supported by SimpleITK reader (e.g., *Dicom*, *MetaImage*, etc.). Export options for saving rendering results in.stl and .jpg formats are available. The source code of *3D Gastro CT Ex* is available for download from the Github repository: https://github.com/milicevickatarina/3D-Gastro-CT-Extended.

Image Preprocessing

Image preprocessing of axial CT slices (512×512) included band shifting on a histogram, image noise re-movement, and co-registration process. First, the band [−548, 800] was shifted to [0,255] using a linear intensity transfer function. Second, image noise removal was performed by median filtering. Finally, Mattes mutual information was used as a criterion for the co-registration of native and delayed phase using the *SimpleITK* class *Image Registration Method* (sitkLinear was used as interpolator and gradient descent was used for the optimization process) (20).

Segmentation and 3D Rendering

The overall segmentation process on native and delayed phases is presented in **Figure 1**. First, the segmentation procedure implies the calculation of histograms for the whole CT volume of both phases. Skeleton segmentation includes the following steps:

1. Volume binarization from the native phase based on the histogram thresholding method (default threshold values: lower = 117 and upper = 180, light green line and light red line on native phase histogram in **Figure 1** respectively)
2. Particle removal from the volume extracted in step 1 based on opening and closing of the volume (cube structural element with the dimension 3)
3. Dilatation of the volume extracted in step 2
4. Volume binarization from the delayed phase based on the histogram thresholding method (default threshold values: lower = 130 and upper = 255, light green line and light red line on delayed phase histogram in **Figure 1** respectively)
5. Particle removal from the volume extracted in step 3 based on opening and closing of the volume (cube structural element with the dimension 3)
6. The intersection of volumes obtained in step 3 and step 5.

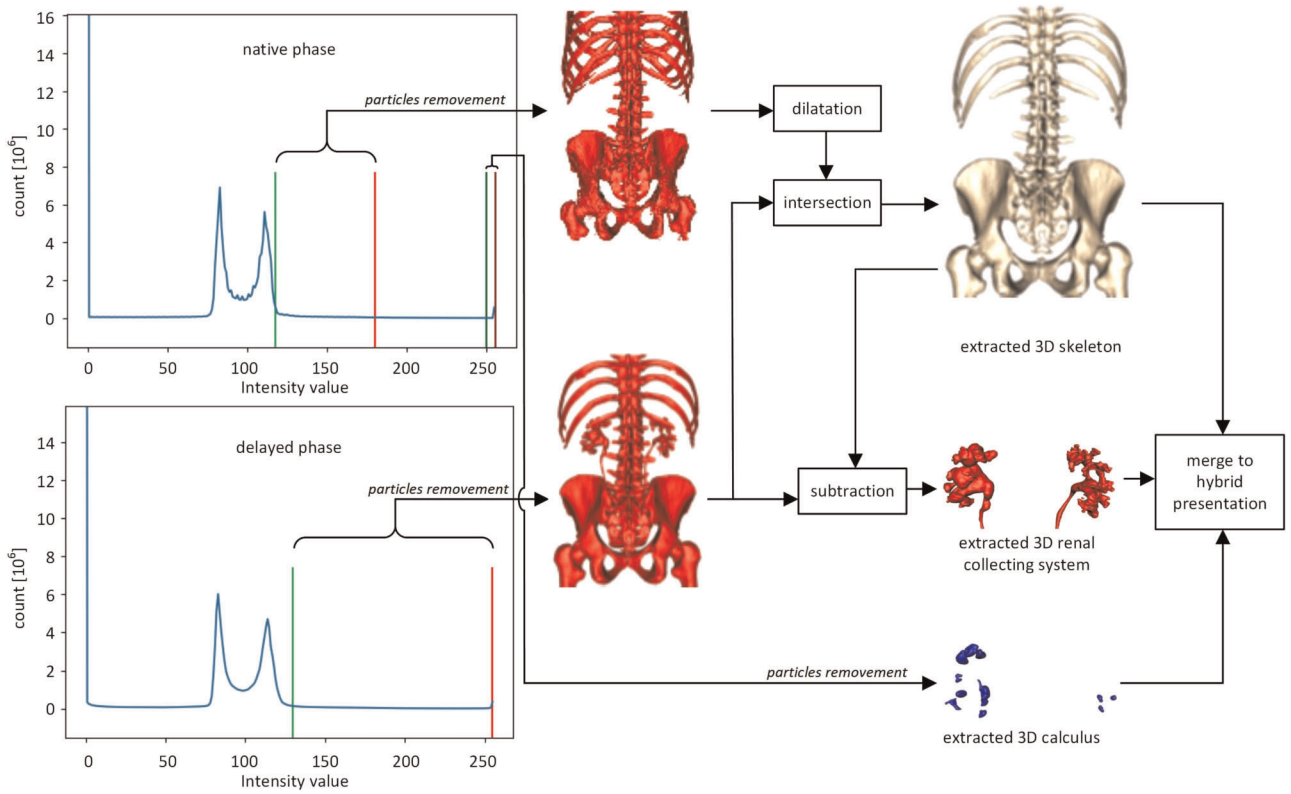

FIGURE 1 | The flow chart of the segmentation and 3D rendering process.

A renal collecting system is extracted by the subtraction of volumes archived in steps 6 and 5.

Calculus segmentation includes the following steps:

1. Volume binarization from the native phase based on the histogram thresholding method (default threshold values: lower = 250 and upper = 255, dark green line and dark red line in **Figure 1** respectively)
2. Particle removal from the volume extracted in the previous step is based on the opening and closing of the volume (cube structural element with the dimension 2).

3D rendering was performed by Marching Cubes algorithm (21, 22). VTK renderer was used for the implementation of rotation and zoom options (**Figure 1**). The processing time of DICOM files required to obtain a semi-automatic 3D image is from 45 to 90 min on a computer with the following features: processor Intel (R) Core (TM) i7-8565U CPU@1.80 GHz, 8GB RAM, graphics card NVIDIA GeForce MX250

At the operating room, the patient was positioned on the table in a prone position with all the coordinates and measurements taken out from both conventional CT evaluation and 3D model translated on the skin of the lumbar area to enable the planned access route. Puncture was performed under ultrasound and pulsed fluoroscopy control after retrograde contrast injection through the ureteral catheter. Tract was dilated up to 30 Fr Amplatz sheath (standard PCNL) with the use of 26 Fr nephroscope.

RESULTS

All patients were completely investigated by conventional protocols proposed by guidelines. After confirming the indication for surgery, an additional puncture strategy was made after 3D reconstruction using the 3D Gastro CT Ex tool. Images from conventional CT scanners were compared with new images and an optimal axis for percutaneous puncture was made upon case characteristics. Due to the 3D reconstructed semi-transparent images, it was possible to analyze volumetric datasets in both anterior and posterior view (**Figures 2 and 3**). Patients from the study group had complex renal stones (Guy stone score 3 and 4) (23). All cases were treated by using a single puncture (**Figure 4**). The use of flexible nephroscope was indicated by case characteristics and surgery flow. Stone-free status was achieved in all cases, confirmed by follow up imaging. No perioperative complication occurred. In our series there was no unsuccessful outcome of PCNL procedures performed regardless the use of the 3D software for puncture planning.

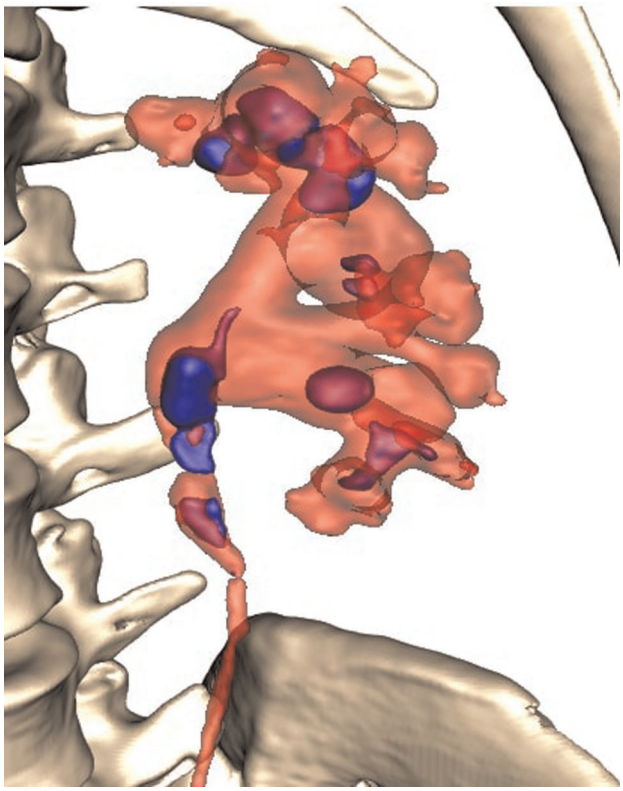

FIGURE 2 | Anterior view.

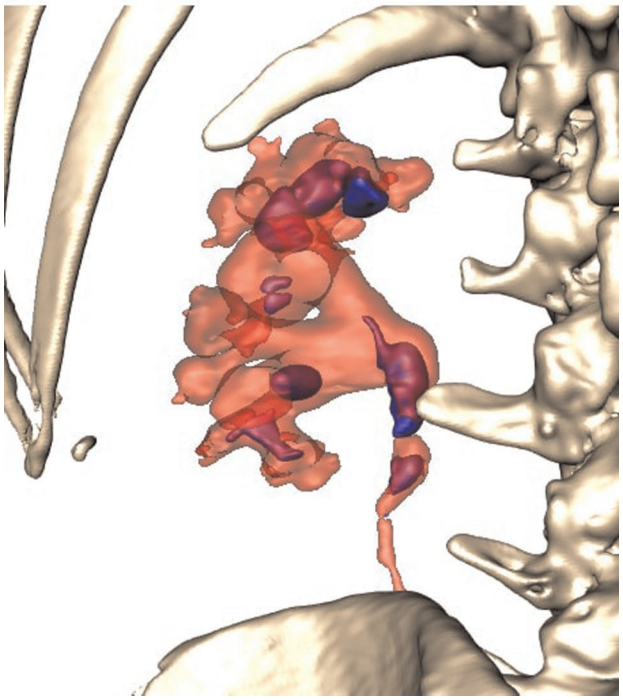

FIGURE 3 | Posterior view.

DISCUSSION

The pelvicalyceal system with a complex stone represents a complex 3D structure. Thus, for accurate access route planning, the semi-transparent 3D model representing the correlation between the collecting system and stone seems to be very useful.

Rendering of the CT images with the ability to adjust the transparency of different tissue layers allowed the operator to see the stone through the renal collecting system, locate the stone and navigate the puncture needle. This semi-transparent 3D model could provide additional information during endourological procedures and therefore raise the possibility of achieving one-stage clearance of complex renal stones. The greatest advantage of using a 3D software is in creating a clear preoperative plan and selecting a target access route. Once having a clear preoperative puncture plan further steps of puncture guidance and control can be performed very precisely, usually with less fluoroscopy use. In this way the total fluoroscopy time can be reduced. As the total fluoroscopy time is a surrogate for radiation exposure, we assume that preoperative planning is a good way to also achieve the goal of reducing the use of fluoroscopy to a minimum in accordance with ALARA principles.

It has been proven that the surgeon is more comfortable with the initial puncture due to the 3D preoperative planning (24, 25). PCNL is routinely performed under 2D visualization with ultrasound and/or fluoroscopy guidance. In our technique the use of flexible nephroscope is not mandatory but flexible nephroscope should always be available during PCNL in aim to clear all stones from the pelvicalyceal system but also upper ureter.

By using a 3D model of CT images in planning the route and controlling the needle path, we would be able to use all the advantages of multidetector CT (MDCT) without raising the risk of radiation dose as it would be the case with CT fluoroscopy or Cone-beam CT guidance. 89% of success rate for percutaneous kidney access has been reported when using Cone-beam CT for guidance, but it comes with a higher radiation dose than conventional fluoroscopy guidance (26).

An accurate preoperatively defined puncture trajectory may also contribute to decreasing total fluoroscopy time to the lowest possible level. Once the operator has a clear preoperative puncture plan during fluoroscopy and ultrasound-guided PCNL procedures, fluoroscopy can be used only for access tract formation and wire position confirmation. Shortening of fluoroscopy time during PCNL is an important technical requirement to ensure safety and efficiency in PCNL while also reducing the radiation exposure of the patient and surgical team (11).

Our puncture technique involves ultrasound guidance with the assistance of pulsed fluoroscopy. Compared with our initial cases which were performed by ultrasound and continuous fluoroscopy we have already achieved significant reduction in fluoroscopy time from 155.4 s (median value) to 76.8 s (27).

If we compare the total fluoroscopy time values of PCNL procedures performed without the use of 3D software already

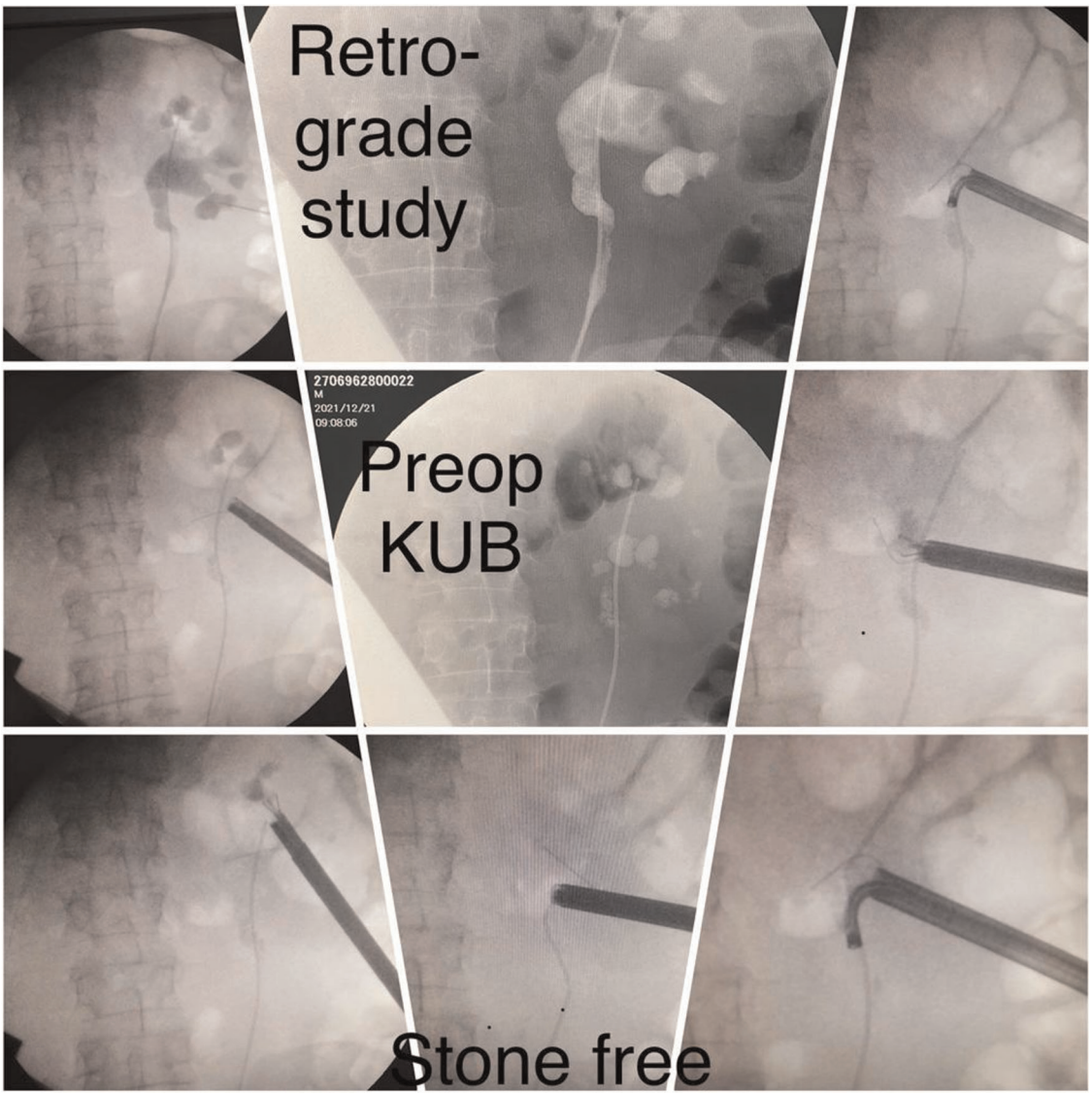

FIGURE 4 | Images from surgery.

reported in our larger series (27) with the total fluoroscopy time values of the PCNL procedures performed in this study (after creating the semi-transparent 3D model of pyelocaliceal system and stone) a significant reduction in the total fluoroscopy time is noted when 3D software was used (76.8 s vs 27.7 s).

Bearing in mind that in this study the results obtained on a small sample of five patients are presented, we cannot speak from the relevance of the statistically obtained data. This reduction can also be a result of an increased experience and skills of surgeon (OD), as his volume increased during the years.

To this study, CT images were segmented by focusing on renal stone, collecting system, and bone structures serving as a landmark for translation of measurements on the patient's skin. Contrast is not absolutely mandatory for MDCT examination, especially in cases with damaged renal function. As the majority of patients have normal renal function the use of contrast offers a huge benefit in term of detail determination and distinction between stone and pelvicalyceal system.

Measurements of puncture angles and distances from the referent points were collected from a 3D model and translated in the operating room with accuracy. Vascular structures' segmentation was not taken into consideration because the initial puncture of the renal collecting system was performed by an experienced urologist with real-time ultrasound guidance. The vessel segmentation process could take additional time before the procedure starting point without any substantial decrease in the rate of vascular injuries.

From the point of PCNL safety, avoidance of unnecessary puncture(s) is crucial. A greater rate of complications has been reported during calyceal stones treatment in comparison

with the treatment of pelvic stones (28). When planning treatment with rigid instruments, the access route should be as straight as possible from the skin through the calyx in the axial line of the calyx through the infundibulum of the certain calyx and into the renal pelvis. Any additional intraoperative angulation of the access sheath would increase the risk of renal injury and bleeding. Every percutaneous kidney puncture is associated with a risk of bleeding. With the need for tract formation and dilatation, this risk is increased. The transfusion rate is higher in cases where multiple tracts were used during PCNL. Therefore, a decrease in access tracts is one of the goals of endourologists. The use of flexible nephroscope can decrease the need for additional puncture. In our opinion, even with flexible nephroscope the importance of optimal access axis remains of huge importance. Optimal access offers two biggest benefits: avoidance of torqueing and in that way less possibility of bleeding and better visibility during the procedure, especially in complex cases with stone distribution in different calices. Another benefit of detailed preoperative planning and selection of an optimal access route is in possibility to easily approach to all other calices that contain stones (such as in parallel calices, that sometimes can not easily be approached, even with flexible nephroscope from the punctured calyx) or might be a possible place of stone migration (usually upper calyx).

Stone burden and volume distribution in the renal collecting system is proven to be a significant determinant of the stone-free rate (SFR) (24), which was defined as no residual fragments larger than 3 mm in diameter (29, 30). In our initial experience and case series, the use of this tool helped significantly in preoperative planning and surgical strategy, allowing access to secondary calices from the main axis tract more easily.

There were no additional costs for this kind of evaluation, the software is free for use and its utilize was simple and intuitive. Collaboration with radiologists and software engineers was necessary, especially as the program offers the opportunity of rotation of the image and creating a picture in all positions used for PCNL, whether prone or supine or Valdivia modified used for retrograde intrarenal surgery (RIRS).

The limitation of the study was a shift and change in the position of the stone that can happen with the positioning of the patient. This was especially the case with smaller stones in the dilated collecting system. After 3D model calculation and taking measurements in a few cases the stone had changed its position most likely due to patient positioning. The CT scan was routinely performed while the patient was in the supine position and the PCNL procedure was performed in a prone position.

CONCLUSION

Having a clear and precise preoperative puncture plan is the key point to ensure efficiency in PCNL. Optimal access according to stone distribution and renal collecting system anatomy may contribute to both PCNL procedure efficacy and safety. This semi-automated segmentation tool for 3D visualization of the collecting system and stone interrelation is proven to be very useful for preoperative PCNL access planning. Currently, this might be a time-consuming process, but in the future, it should be a completely automated process with widespread use and adoption for all complex stone procedures.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article.

AUTHOR CONTRIBUTIONS

OD is responsible for study design, data collection, data interpretation, manuscript preparation, funds collection; AF for data collection, data interpretation, manuscript preparation, literature search; KM for data interpretation, manuscript preparation, literature search; BS for manuscript preparation, data interpretation, literature search; EE for study design; AS for study design, manuscript preparation, literature search; MJ for study design, data interpretation, manuscript preparation, literature search. All authors contributed to the article and approved the submitted version.

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Transurethral Incision of the Bladder Neck at Three Points with a Needle-Type Electrode for Bladder Neck Contracture

*Guihua Cao[1], Liangcheng Liu[1], Jianping Du[1], Wei Li[1], Qiang Li[1], Na Luo[1], Xun Liu[2], Junjie Zhou[3] and Tao Wu[3]**

[1]Department of Urology, People's Hospital of Leshan, Leshan, China, [2]Department of Pathology, People's Hospital of Leshan, Leshan, China, [3]Department of Urology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China

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***Correspondence:**
Tao Wu
alhawking@163.com

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Purpose: This study aims to evaluate the efficacy of transurethral incision of the bladder neck (TUIBN) at three points with a needle-type electrode for treatment of bladder neck contracture (BNC).

Materials and Methods: Between January 2016 and April 2021, the bladder necks of 53 patients with BNC after surgery were incised by the needle-type electrode at the 5, 7, and 12 O'clock positions. Patient's preoperational characteristics, peri- and postsurgical outcomes, such as time of operation, postoperative bladder irrigation, and postoperative hospital stay, and data of the international prostate symptom score (IPSS), maximum flow rate (Qmax), and postvoid residual (PVR) were recorded 3 and 6 months after surgery.

Results: All 53 cases of BNC were successfully treated in 35.00 (25.00, 45.00) min with 18.00 (14.00, 21.00) h for postoperative bladder irrigation with little intraoperative bleeding (less than 50 mL). The postoperative hospital stay ranged from 2 to 8 days, a mean of 3.50 (3.00, 5.00) days. No major intraoperative or postoperative complications were observed. All cases that underwent follow-up assessment at 3 and 6 months after the surgery showed significantly decreased IPSS and PVR and increased Qmax compared to preoperation ones ($p \leq 0.001$). Of these 53 patients, there was no recurrence in severe BNC patients, but 5 of 53 (9.4%) BNC patients developed BNC again within 6 months and required repeated TUIBN. Thirty patients comprised five recurrent cases with a follow-up period of more than 1 year.

Conclusions: TUIBN at three points provides a safe, effective, and reliable option in treating patients with BNC.

Keywords: bladder neck contracture, transurethral incision of the bladder neck, needle-type electrode, benign prostatic hyperplasia, transurethral endoscopic treatment

INTRODUCTION

Benign prostate hyperplasia (BPH) is a common disease among the elderly (1), which is the major cause of lower urinary tract symptoms. Surgical treatment is often the most effective intervention for such a disease. It has been reported that in transurethral resection of prostate (TURP), different energy laser sources and prostatic tissue ablation, such as photoselective vaporization of the prostate (PVP) with a green light laser, holmium laser enucleation or ablation of the prostate, and thulium vapoenucleation laser, are widely used in the clinical setting (2). However, complications of urethral stricture and BNC occur postoperation, which cause poor quality of life in patients. The reported incidence range of BNC is from 0.3% to 9.6% (3–6). Risk factors of BNC include a low adenoma volume, excessive electrocoagulation, resection of the bladder neck, and long operative time (7–9). Bladder neck incision (BNI), laser vaporization, balloon dilatation, and stent placement are applied for the treatment of BNC with overall high recurrence rates (10).

In recent years, new techniques such as T-plasty, a modified YV-plasty, and robot-assisted laparoscopic YV plasty have been performed in the treatment of BNC and have achieved satisfactory outcomes with a success rate of 83.3%–90% (11, 12). However, transurethral endoscopic treatment is still widely accepted as the initial treatment of BNC because of little trauma, low complications, and quick recovery. The present study aims to perform TUIBN at three points with a needle-type electrode for the treatment of bladder neck contracture and evaluate the efficacy of the procedure.

MATERIALS AND METHODS

Study Population

A total of 53 patients between January 2016 and April 2021 were included in the present study, following approval by The Ethics Committee of the People's Hospital of Leshan (approval no. LW2022-01-01). These patients participated in this study between 3 and 120 months after TURP, PVP, or suprapubic prostatectomy. The mean time to diagnose BNC was 22.9 months; 20 patients (37.7%) developed BNC within 6 months and 13 (24.5%) within 3 months. All patients were diagnosed with BNC under cystoscopy. The severity of BNC was classified into three grades (13): grade 1, the mild-17F cystoscopic sheath can pass through the bladder neck by force but 22F cystoscopic sheath cannot (diameter of the bladder neck between 5 and 7 mm); grade 2, the moderate-17F cystoscopic sheath cannot pass through the bladder neck (diameter of the bladder neck between 2 and 5 mm); and grade 3, severe pinpoint-like hole (less than 2 mm). There were 24, 19, and 10 patients with mild, moderate, and severe BNC, respectively.

Assessment Parameters

Patient's preoperational properties, pre- and postsurgical data, including age, the volume of prostate before the first surgical procedure for the treatment of BPH (the volume of the prostate was assessed by transrectal ultrasonography and obtained as height × length × width × 0.52), previous surgical procedures, weight of excised scar tissue, surgical complications, and time of operation, occurrence of BNC, postoperative bladder irrigation, and postoperative hospital stay, and data of the international prostate symptom score (IPSS), postvoid residual (PVR), and maximum flow rate (Qmax) were recorded 3 and 6 months after TUIBN.

Instruments and Surgical Procedures

All patients provided informed consent before transurethral surgery. A team of urologists with similar experience performed all transurethral surgeries. Combined spinal and epidural anesthesia was performed on each patient in the lithotomy position. Major equipment and instrument for surgery included the following: an Olympus Plasmakinetic system generator (Olympus, Japan), a needle-type electrode (Olympus, Japan), a resectoscope (Olympus, Japan), a ureteroscope (Wolf, Germany), and a zebra guidewire (Boston Scientific, MA, USA). The generator settings for treating BNC were 240 and 120 W for cutting and coagulation, respectively. Normal saline was used for irrigation.

Transurethral insertion of the Olympus 26F resectoscope was under direct vision. For a mild or moderate BNC case, a cutting loop was pushed retrogradely to enter the bladder. For the severe BNC case, a zebra guidewire was inserted into the bladder under the direct vision of the ureteroscope through the urethra to determine the right pathway. If failed in the retrograde course, suprapubic cystostomy was performed and the ureteroscope was inserted by the tract of cystostomy to enter the bladder. The zebra guidewire was inserted into the urethra from the bladder neck, which contracted as a pinpoint-like hole. The bladder neck could be expanded along the guidewire by using a dilator (**Figure 1**), and the resectoscope was then inserted along the zebra guidewire to enter the bladder. Following that, the incisions were performed at 5, 7, and 12 O'clock positions using an Olympus needle-type electrode to create an incisional pathway from the bladder neck to the proximal verumontanum, which reached the adipose layer; the bladder neck opened wider and wider as the fibrous rings leading to contracture were completely cut off. Finally, the redundant scar tissues of the bladder neck and prostatic urethra were excised with the cutting loop, making the bladder neck parallel to the vesical trigone (**Figure 2**). The 22F urethral catheter was retained after surgery for continuous irrigation of the bladder (14).

Statistical Analysis

The normal distribution data were represented by mean ± standard deviation; non-normal distribution data were represented by median and quartile. The comparison of indexes before and after surgery was self-paired (self-paired design, using a paired *t*-test or a paired rank-sum test according to whether the difference was normally distributed); Z was the Z-value of the paired rank-sum test, t was the paired t-test value, and $p < 0.05$ was statistically significant based on SPSS25.0 statistical analysis software.

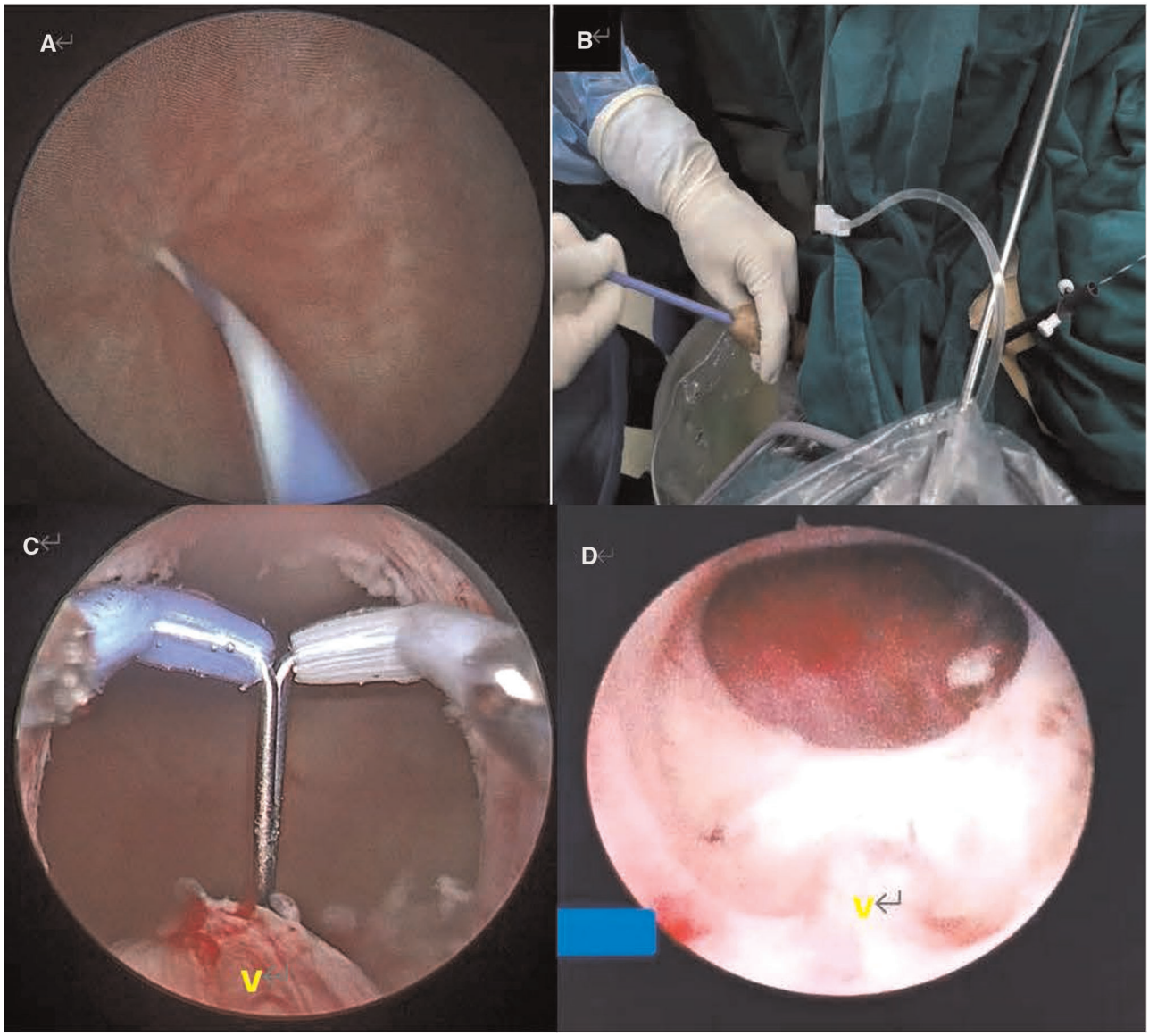

FIGURE 1 | (**A**) Intraoperative ureteroscopic view of a pinpoint-like bladder neck; (**B**) suprapubic cystostomy and dilation of the bladder neck; (**C**) immediate resectoscopic view of a bladder neck after TUIBN; (**D**) cystoscopic view of a bladder neck 18 months after TUIBN.

RESULTS

The patients' baseline characteristics and perioperative results are shown in **Table 1**. The previous mean prostate volume was 30.05 (24.95, 37.18) mL. Of the 53 patients, 44 underwent TURP once or PVP before the development of BNC, 3 underwent TURP twice, and 6 underwent suprapubic prostatectomy once. All surgeries went smoothly, with the time of TUIBN varying from 15 to 70 min, 35.00 (25.00, 45.00) min. There was little intraoperative bleeding (less than 50 mL). The excised mean weight of redundant scar tissue of the bladder neck and prostatic tissue was 2.10 (0.65, 8.35) g. The mean time of postoperative bladder irrigation was 18.00 (14.00, 21.00) h. The postoperative hospital stay ranged from 2 to 8 days, mean 3.50 (3.00, 5.00) days. During perioperation, no patients had serious bleeding. Three cases of venous sinus hemorrhage were resolved by continuous balloon compression with catheterization. One patient was with hydroabdomen. One case of dysuria following the catheter removal 4 days after surgery, however, resolved completely in the further course of catheterization. Another case of dysuria was due to the presence of a large bladder diverticulum, but there was no recurrent BNC by the cystoscopic view at a follow-up of 18 months (**Figure 1**). One case of urethral stricture was resolved by regular urethral dilation in 2 months. There were two cases of retrograde ejaculation.

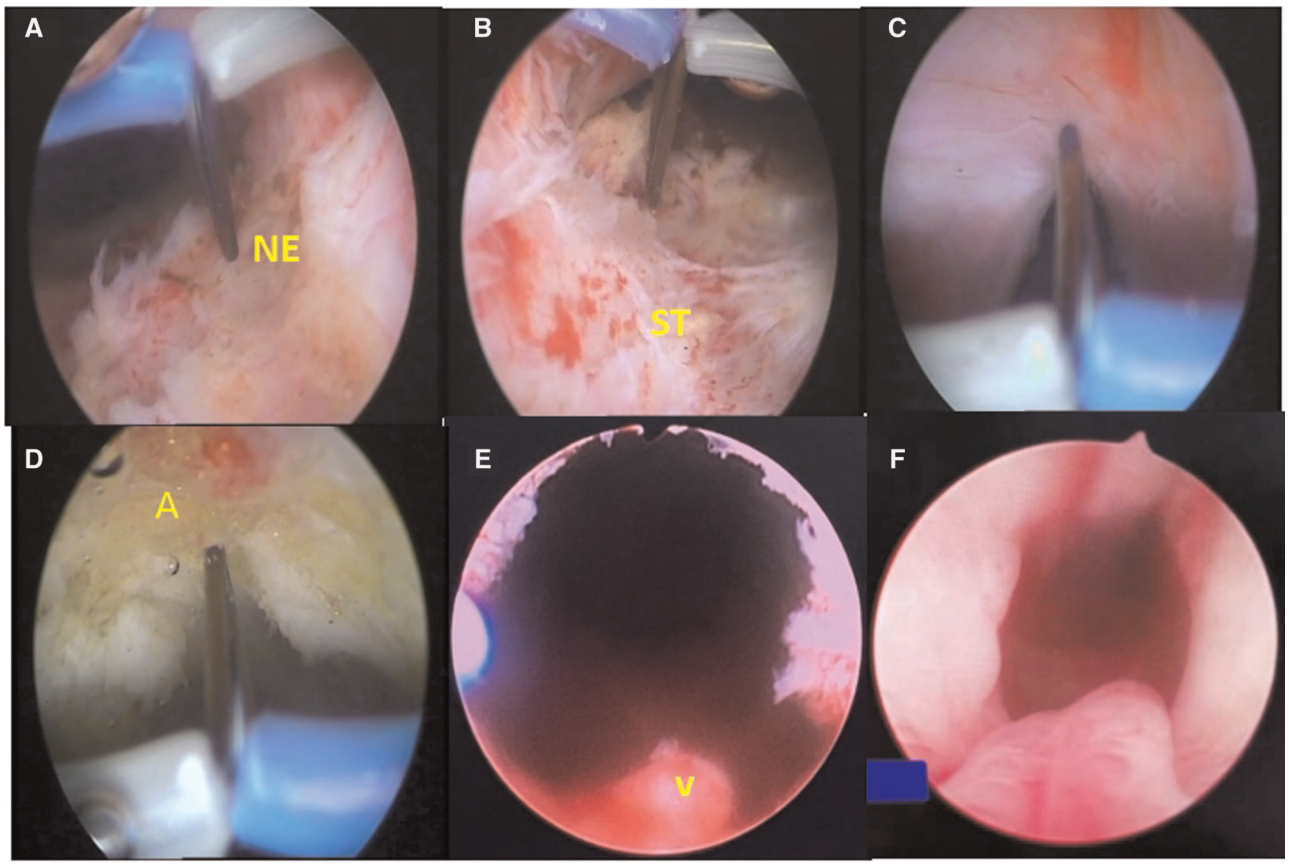

FIGURE 2 | (**A–D**) The incisions were performed at 5, 7, and 12 O'clock positions using a needle electrode (NE) to create an incisional pathway from the bladder neck to the proximal verumontanum (V), which reached the adipose layer (A); (**E**) immediate resectoscopic view of the bladder neck after TUIBN; (**F**) cystoscopic view of the bladder neck 1 month after TUIBN.

All cases that underwent follow-up assessment (**Table 2**) at 3 and 6 months after the surgery showed significantly decreased IPSS and PVR and increased Qmax compared to preoperation ($p \leq 0.001$). All cases that underwent follow-up assessment 3 months after the surgery showed no significantly decreased IPSS ($p = 0.331$) and PVR ($p = 0.297$) and increased Qmax ($p = 0.373$) compared to 6-month data. Of these 53 patients, there was no recurrence of BNC in severe BNC patients, but a total 5 of 53 (9.4%) BNC patients developed BNC again within 6 months and required repeat TUIBN. Thirty patients comprised five recurrent cases with a follow-up period of more than 1 year and five patients with a follow-up period of more than 2 years, and there was no recurrence of BNC. However, routine and periodic cystoscopy for each patient is not ethical and is unnecessary in clinical practice. So, only two patients followed by the view of cystoscopy. An example of a severe BNC patient, whose bladder neck contracted to a pinpoint-like hole preoperatively and obtained a persistent wide bladder neck at 18 months after TUIBN, is presented in **Figure 1**. According to the modified Clavien–Dindo classification, there are two postoperative complications to patients, which were graded as grade II. The rest of the postoperative complications to patients were graded as grade I.

DISCUSSION

BNC is a relatively severe complication after endoscopic surgery for BPH. It usually develops within 60 days after transurethral resection (15). Lee (13) reported that the mean time to diagnose BNC after surgery was 18.5 months; however, half of patients developed BNC within in 6 months. If there is no significant improvement in dysuria after urethral dilation, a necessary cystoscopy can confirm the diagnosis due to the possibility of BNC. So far, the exact mechanisms of BNC after TURP remain unclear, and the proposed predisposing factors have been stated as extensive resection of the bladder neck, excessive fulguration at the bladder neck, or a large resecting loop that generates excessive heat to produce a hypertrophic scar in a small intraurethral adenoma (16). Treatment options for BNC remain controversial; urethral dilation 18F followed by a 3-month period of intermittent self-catheterization, cold

TABLE 1 | Baseline characteristics and perioperative and follow-up results of patients ($n = 53$).

Parameter	Mild BNC (>5 mm) ($n = 24$)	Moderate BNC (2–5 mm) ($n = 19$)	Severe BNC (<2 mm) ($n = 10$)
Age (year)	74.96 ± 8.01	74.06 ± 7.08	69.0 (65.75, 78.50)
Previous prostate volume (mL)	32.49 ± 10.52	32.86 ± 8.06	29.20 ± 6.69
Occurrence time of BNC (month)	7.50 (3.00, 33.00)	11.00 (4.75, 39.00)	9.50 (4.75, 24.00)
Previous surgical procedure			
TURP	15	8	5
PVP	7	8	4
Other	2	3	1
IPSS	26.46 ± 4.85	28.44 ± 5.10	29.30 ± 4.69
PVR (mL)	71.00 (48.00, 93.00)	124.00 (65.00, 227.75)	234.60 ± 189.11
Qmax (mL/s)	6.73 ± 3.29	4.72 ± 3.70	2.26 ± 1.87
Operative time (min)	32.67 ± 11.50	39.67 ± 14.99	43.00 ± 18.59
Bladder irrigation time (h)	17.88 ± 5.61	17.50 (13.50, 20.00)	20.50 (15.00, 32.00)
Postoperative hospital stay (day)	3.50 (3.00, 5.00)	3.00 (2.75, 5.00)	4.40 ± 1.96
Excised scar tissue (g)	1.25 (0.35, 4.73)	2.85 (0.73, 11.05)	8.06 ± 4.35
Complications			
Blood loss (mL)	5.00 (5.00, 13.75)	10.00 (10.00, 15.00)	10.00 (5.00, 21.25)
Dysuria	0	1	1
Incontinence	0	0	0
Urethral stricture	1	0	0
Retrograde ejaculation	1	1	0
BNC recurrence	3	2	0

TABLE 2 | Data at baseline and 3- and 6-month after surgery.

Parameter	Baseline ($n = 53$)	3-Month ($n = 53$)	6-Month ($n = 53$)	F	p^a	F	p^b	F	p^c
IPSS	28.00 (23.00, 32.00)	15.00 (10.00, 21.00)	15.00 (10.00, 25.00)	Z = 5.848	<0.001	Z = 0.972	0.331	Z = 3.399	0.001
PVR	86.00 (63.50, 179.00)	5.00 (3.00, 6.00)	4.00 (3.00, 5.50)	Z = 6.334	<0.001	Z = 1.043	0.297	Z = 6.334	<0.001
Qmax	4.90 (2.20, 7.85)	20.75 ± 4.93	21.46 ± 5.07	t = 19.852	<0.001	t = 0.898	0.373	t = 21.400	<0.001

The normal distribution data were represented by mean ± standard deviation, and non-normal distribution data were represented by median and quartile. The comparison of indexes before and after surgery was self-paired (self-paired design, using paired t-test or paired rank-sum test according to whether the difference was normally distributed), Z was the Z-value of paired rank-sum test, T was the T-value of paired t-test, and $p < 0.05$ was statistically significant.

[a]*3-Month compared with baseline data.*

[b]*6-Month compared with 3-month data.*

[c]*6-Month compared with baseline data.*

knife incision, and transurethral resection have been proposed with varying success rates. Regular long-term urethral dilation contributes to a false urethral pathway, hemorrhage, infection, and poor quality of life. About 90% of patients may have to repeat urethral dilation within the first 2 years (17). Eltahawy et al. demonstrated a success rate of 83% after stricture site irrigation with triamcinolone following BNC ablation with a holmium laser (18). Redshaw et al. showed a success rate of 75% after mitomycin C (MMC) injection following a radial cold-knife incision of BNC. However, for MMC utilization, adverse events were described, such as anaphylaxis, extravasation, or bladder neck necrosis, that need to be noticed (19).

Patients with refractory BNC are advocated for more invasive procedures such as YV-plasty, TV-plasty, T-plasty (a modified YV-plasty) (11), and even robot-assisted laparoscopic Y-V plasty (RAYV) (12). The analysis of subjective satisfaction showed that patient satisfaction was very high, high, and undecided in 70%, 20%, and 10%, respectively, with the T-plasty procedure; however, the mean time of operation was 112 min, and the mean hospital stay was 13 days. Musch et al. presented a success rate of RAYV of more than 80%, with a median follow-up of 23.2 months. However, the surgical time ranged from 140 to 360 min, and the blood loss was more than 50 mL. Therefore, these complicated procedures are not accepted among BNC patients initially but for the refractory BNC.

It appeared that a prophylactic bladder neck incision could protect against the formation of bladder neck contracture and reduce the incidence of BNC (4, 20). According to these results, BNI may be beneficial for the treatment of BNC. Ramirez et al. reported a success rate of 72% at a mean follow-up of 12.9 months after Collings knife (the same as the

needle-type electrode) incision of BNC at 3 and 9 O'clock positions, an overall success rate of 86% after two procedures (21). Rosenbaum et al. showed that the success rate after TUIBN at 4, 8, and 12 O'clock positions was 45%, and the risk factors associated with recurrent BNC were >10 pack/year history of smoking and patients who had undergone more than two previous TUIBN procedures (22). In the present study, the incision of BNC was carried out at 5, 7, and 12 O'clock positions, resulting in 48 (90.6%) successful cases.

Our present study showed scar tissue of prostatic urethra (**Figure 2**) formed in patients, which combined with BNC promoted dysuria. That is why we performed the incision not only at the bladder neck but also extended the incision from the bladder neck to the proximal verumontanum. The mechanism of TUIBN for the treatment of BNC may be lowering the pressure by destroying a part of the adrenergic receptors of the prostatic fascia (13). A greater degree of destruction of the sympathetic innervation can be obtained through deep trilateral incisions.

The needle-type electrode has the advantage of precise hemostasis and cutting to avoid urinary extravasation or incontinence. If venous sinus hemorrhage occurs, 1 h of compression by F22 catheterization with 45 mL water injection in a balloon was performed for hemostasis. In the present study, several cases of venous sinus hemorrhage were treated with this method efficiently, and the total blood loss was within 50 mL in each case. For those severe BNC cases, especially patients with false urethral pathways caused by incorrect urethral dilation, it is very difficult to find the right urethral pathway under a resectoscope. So, a guidewire should be used to identify a correct pathway under the ureteroscope through the urethra or bladder (14).

From our point of view, this approach brings more advantages compared to the previous endoscopic incision and reanastomosis for BNC. A short operative time, less blood loss, fewer complications, and a higher success rate (90.6%) were also presented. It is noteworthy that TUIBN seemed more likely to treat the severe BNC without recurrence of BNC in the present study. Specifically, this easy method will benefit the surgeon who holds the essential TURP skills for the treatment of BNC.

Limitations of this study are that it is a retrospective study and a relatively small number of patients for follow-up are included. Thus, the incidence of recurrent BNC could have been underestimated in this study.

CONCLUSIONS

This method was reported on TUIBN at three points with a needle-type electrode for BNC. As performed, the method was feasible for all patients and easy to perform. At the same time, no major intraoperative or postoperative complications were observed. Certainly, more clinical data with a longer follow-up are needed to reveal the actual efficacy and relevance of TUIBN for BNC.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional national research committee at The People's Hospital of Leshan and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethics Committee of The People's Hospital of Leshan approved the protocol (approval no. LW2022-01-01). Given that this was a retrospective analysis, all patients' informed consent was not required. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

GHC and TW did project development and obtained public funding. JPD, WL, and LCL collected the data. GHC, QL, NL, and XL performed data analysis. JJZ wrote/edited the manuscript. All authors contributed to the article and approved the submitted version.

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

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CASE REPORT
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Renal Pseudoaneurysms after Flexible Ureteroscopy and Holmium Laser Lithotripsy: A Case Report

Xin-xi Deng[1,2], Wensheng Zhang[1], Delai Fu[3] and Bin Fu[2]**

[1]Department of Urology, Jiu Jiang NO.1 People's Hospital, Jiujiang, China, [2]Department of Urology, The First Affiliated Hospital of Nanchang University; Jiangxi Institute of Urology, Nanchang, China, [3]Department of Urology, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

Background: Flexible ureteroscopy (FURS) and holmium laser lithotripsy is considered one of the most minimally invasive and safe surgical methods for the treatment of renal calculi. Renal pseudoaneurysm is a rare complication after FURS holmium laser lithotripsy. We report a case of renal pseudoaneurysm after FURS and holmium laser lithotripsy and review the relevant literature to analyze the possible etiology and summarize the treatment.
Case presentation: A 29-year-old male with a 2-year history of diabetes was admitted to the hospital because of right back pain for 5 days. A doppler ultrasound demonstrated bilateral renal calculi with bilateral mild hydronephrosis. The patient underwent one-stage right FURS and holmium laser lithotripsy and bilateral ureteral stent implantation. The urine was clear on the second day after the operation, and he was discharged from the hospital. Due to severe gross hematuria, he had to be hospitalized 28 days after the operation. A CT scan showed multiple blood clots in the right renal pelvis and bladder. An emergency blood transfusion and removal of the bladder blood clots and bilateral double J tubes were performed. His urine was clear for one week, and he was discharged from the hospital. He was hospitalized again 47 days after the operation because of fever and hematuria. A CT scan demonstrated blood clots in the bladder and right renal pelvis. Angiography showed a pseudoaneurysm in a small branch of the right renal artery, and hematuria stopped after selective renal artery embolization with microcoils.
Conclusion: FURS and holmium laser lithotripsy is safe, but we should be aware of the possibility of renal artery pseudoaneurysms (RAP). Through careful operation during the surgery, avoiding kidney injury, reducing intrarenal pressure and controlling the time of operation may prevent the occurrence of this complication. Vascular embolization is the first choice for the treatment of pseudoaneurysms.

Keywords: flexible ureteroscopy (FURS), holmium laser, pseudoaneurysm (PA), renal calculi, vascular embolization

Abbreviations: FURS, Flexible ureteroscopy; SWL, shock wave lithotripsy; PCNL, Percutaneous nephrolithotripsy; RAP, Renal artery pseudoaneurysm; NR, Not Reported; NSTEMI, Non-ST elevation myocardial infarction; HBP, Hypertension; CHD, Congenital valvular heart disease; DM, Diabetes mellitus; CKD, Chronic kidney disease; EHL, Electrohydraulic lithotripsy; HLL, Holmium laser lithotripsy.

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Edited by:
Bhaskar K. Somani, Faculty of Medicine, University of Southampton, United Kingdom

Reviewed by:
Senol Tonyali, Istanbul University, Turkey
Julien Renard, Ente Ospedaliero Cantonale (EOC), Switzerland
Sarwar Mahmood, College of Medicine, University of Sulaimani, Iraq

***Correspondence:**
Bin Fu
urofbin@163.com
Delai Fu
fudelai@126.com

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INTRODUCTION

FURS and holmium laser lithotripsy is widely used for the treatment of renal calculi with minimal trauma and rapid recovery. The treatment is suitable for renal stones less than 2 cm and residual stones after shock wave lithotripsy (SWL) or percutaneous nephrolithotripsy (PCNL). Compared with FURS lithotripsy, PCNL has some disadvantages, such as a high risk of bleeding and slow recovery after the operation (1). Therefore, there are an increasing number of reports about FURS lithotripsy in the treatment of renal calculi larger than 2 cm (2). However, RAP caused by FURS lithotripsy is rare. We report a case of pseudoaneurysm after FURS and holmium laser lithotripsy, and the related literature was reviewed by PubMed and other databases (3–7) (**Supplementary Table S1**). The clinical characteristics of the patient were analyzed, and the possible etiology and exact treatment of the pseudoaneurysm have been summarized.

CASE PRESENTATION

The patient was a 29-year-old male with a 2-year history of diabetes. He was admitted to the hospital because of right back pain for 5 days. A doppler ultrasound showed bilateral renal calculi and bilateral mild hydronephrosis. The size of the right kidney stone was approximately 2.5*2.2 cm, and the size of the left kidney stone was approximately 2.2*2.3 cm. A CT scan showed double renal calculi with mild hydronephrosis, double renal pelvis and upper ureteral inflammation (**Supplementary Figure S1**). Routine examinations were basically normal before the operation. The patient underwent one-stage right FURS and holmium laser lithotripsy and double ureteral stent implantation under general anesthesia. During the operation, an ultraslippery hydrophilic guide wire (0.35 mm, Cook, USA) and a ureteral access sheath (inner diameter: 12 Fr, length: 46 cm, Laikai Medical, China) were inserted into the right ureteropelvic junction. Using hand-pump irrigation, a flexible ureteroscope (8.5 Fr, Karl Store, Germany) showed a yellowish-brown stone in the right renal pelvis approximately 2.0*2.5 cm in size. The holmium laser energy was adjusted to 0.8 J, and the frequency was 25 Hz. The stone was crushed into powder, and the double J tube was indwelled. The operation time was approximately 60 min, and no active bleeding was observed during the operation. The patient's urine was clear, and he was discharged on the second day after the operation.

The patient came to the emergency department of our hospital 28 days after the operation due to severe gross hematuria with urinary retention. A CT scan indicated multiple stones in the bilateral kidneys with mild hydronephrosis, and massive blood clots were considered in the right renal pelvis and bladder (**Supplementary Figures S2A,B**). The hemoglobin level decreased sharply from 165 to 68 g/L. First, 8 units of red blood cells were transfused to maintain the patient's vital signs, and the bladder blood clots and bilateral double-J tubes were removed in emergency surgery. A large amount of blood clots in the bladder and intermittent bloody urine in the bilateral ureteral opening could be seen. After the operation, the bladder was continuously irrigated with three cava balloon urinary catheters, the urine was clear, and the hemoglobin level was not further decreased. This patient refused angiography and was discharged after the operation for one week.

He was hospitalized again 47 days after the operation due to complaints of fever and hematuria. A CT scan demonstrated a large amount of blood clots in the right renal pelvis and bladder and right perirenal fascia thickening (**Supplementary Figures S2C,D**). Considering the recurrence of active bleeding, angiography showed a pseudoaneurysm of a small branch of the right renal artery (**Figure 1**). After selective arterial embolization with microcoils, the patient recovered and was discharged one week later. No obvious abnormality was found during the 2-month follow-up, and the patient did not consider the operation for a left kidney stone for the time being.

DISCUSSION

RAP is a pulsatile hematoma formed by blood outflow from the rupture of the renal artery wall and is wrapped by perirenal soft tissue (5). The wall of an RAP tumor is not a real blood vessel wall but a cystic wall formed by the organization of tissue around the hematoma. With the progressive increase in bleeding, the pulling force on the cyst wall gradually increases, resulting in the sudden rupture of the cyst wall, causing massive bleeding, and even endangering the lives of patients. The occurrence of RAP is often caused by abdominal trauma or kidney injury after renal surgery (8). For example, after PCNL, the incidence of intrarenal pseudoaneurysm or arteriovenous fistula is approximately 0.6%–1.0% (9). However, this complication is extremely rare after FURS and holmium laser lithotripsy. In total, we obtained 6 cases of pseudoaneurysm after FURS, of which 5 cases were retrieved by PubMed and 1 case was reported by us. There were 2 cases of electrohydraulic lithotripsy and 4 cases of holmium laser

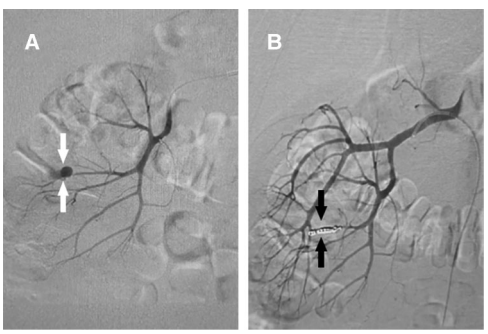

FIGURE 1 | (**A**) An angiogram showing a right interlobar RAP (white arrows). (**B**) Microcoils embolizing the pseudoaneurysm in the right kidney (dark arrows).

lithotripsy. The ages of the patients ranged from 29 to 79 years, including 5 males and 1 female. Four patients had diabetes, high blood pressure or cardiovascular diseases, and 2 patients had no reported underlying diseases. No obvious active bleeding was found in any patient during the operation, and the operations were completed successfully. All patients showed delayed gross hematuria, which was cured by renal angiography and vascular embolization. However, the specific causes of its formation are still unclear, and it is considered that the possible causes include intraoperative thermal injury, mechanical injury, irrigation pressure, operation time and some underlying diseases affecting renal vessels, resulting in the formation of postoperative pseudoaneurysms.

RAP often manifests as delayed hematuria in the clinical setting. After vascular injury during the operation, there was no obvious bleeding in the short term because the compression of the surrounding tissue covers the injury of diseased blood vessels. When blood pressure rises, the wall of the damaged artery will rupture and bleed (10). In all cases, the bleeding time ranged from 6 days to 46 days. It was previously reported that this is related to the method of lithotripsy (11). For example, electrohydraulic hydroelectricity is more likely to damage the kidney than the holmium laser during lithotripsy, but with the widespread use of holmium laser, 4 cases of pseudoaneurysm after holmium laser lithotripsy have been reported. Both lithotripsy methods may lead to renal vascular injury and the formation of pseudoaneurysms. The thermal damage caused by the holmium laser energy should not be ignored. Tiplitsky et al. (12) proposed that laser thermal injury can avoid direct renal injury by maintaining a distance between the optical fiber and the mucous membrane of at least 0.5 mm, while the use of low energy levels can minimize renal vessel damage (4).

Second, mechanical damage to the kidney during the use of guide wires has also attracted more attention. If an inappropriate guide wire with hard or poor flexibility is chosen, the wire may damage the kidney. However, with the development of technology and materials, super-slippery guide wires have appeared, and the possibility of kidney damage caused by guide wires is lessened (5); however, they cannot be completely avoided. This may be related to the improper use of the guide wire during the operation or the pathological changes of the kidney itself. In our case, a super-slippery hydrophilic guide wire was selected, and there was no renal parenchyma injury during the operation. The position of the double-J tube was normal after the operation, and the possibility of a guide wire injury was not considered. Some related diseases lead to pathological changes in the kidney, making it easier for guide wires to penetrate the renal parenchyma, especially in patients with long-term vascular diseases such as diabetes, high blood pressure and coronary heart disease. In addition, due to long-term severe hydronephrosis, the renal cortex is thinner and prone to kidney damage.

At the same time, the intrarenal perfusion pressure and operation time are also issues that should be considered during FURS. These two factors are very important for septic shock, but they may also be related to the formation of postoperative pseudoaneurysms. As we all know, the normal physiologic intrarenal pressure is approximately 10 mmHg. When a hand-pump rather than an intelligent pressure pump is used during the operation, it is easy to increase the intrarenal pressure and lead to rupture of the renal parenchymal or fornix and renal hemorrhage (13). For pathological renal damage, renal hemorrhage may occur even when the intrarenal pressure is normal. In addition, if the ureteroscope sheath is not inserted or if there is a size mismatch between the ureteroscope sheath and the flexible ureteroscope, it can still lead to an increase in intrarenal perfusion pressure (14). This leads to renal dilatation and parenchyma thinning during the operation, which aggravates the damage to blood vessels. For example, long-term operation (15) will lead to renal ischemia, affect the elasticity of the blood vessel wall, and aggravate vascular injuries. To date, 6 cases have been reported, of which 4 cases were not given close attention to the operation time and pumping method. One patient was operated on for more than 90 min, and the water pressure was controlled within 80 cm of H_2O. In another case, the operation time was less than 90 min, and the water pressure was controlled by artificial water injection. Therefore, the risk may be reduced by controlling the appropriate intrarenal pressure and operation time during the operation.

Vascular embolization is currently considered to be the first-line treatment of renal pseudoaneurysms in patients with hemodynamic stability because it is efficient and safe and has little effect on renal function (6). In all 6 cases reported, the patients were discharged from the hospital after vascular embolization and recovered well after the operation. Therefore, vascular embolization should be the first choice for the treatment of intrarenal artery pseudoaneurysms.

CONCLUSION

In summary, although the occurrence of pseudoaneurysms after FURS and holmium laser lithotripsy is very rare, it should not be ignored. For example, patients with obvious hematuria, severe back pain or hemodynamic instability, pseudoaneurysms need to be highly suspected. During the operation, a clear field of vision, as far as possible, should be maintained, laser damage to the kidney should be avoided, the laser energy should be reduced, mechanical injuries caused by the guide wire should be avoided, and the operation time and intrarenal pressure should be controlled, especially in patients with potential diseases that affect the integrity of renal vessels. Once pseudoaneurysms happen, renal arteriography and vascular embolization should actively be performed.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The present study was approved by the Research Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University (Xi'an, China). Written informed consent was obtained from the participant for the publication of any potentially identifiable images or data included in this article. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

X-xD: Investigation, Writing - original draft, review & editing. WZ: Data curation, Methodology, Investigation. DF and BF: Supervision, Funding acquisition. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/article/10.3389/fsurg.2022.896548/full#supplementary-material.

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ORIGINAL RESEARCH
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Preliminary Outcomes of Different Tactics of Ureteral Stent Placement in Patients with Ureteral Stricture Undergoing Balloon Dilatation: Experience from a Large-Scale Center

Xiao Hu[†], *Dechao Feng*[†] *and Xin Wei**

[1]*Department of Urology, Institute of Urology, West China Hospital, Sichuan University, Chengdu, China*

Purpose: Our aim is to demonstrate the optimal number of ureteral stent placements in patients with a ureteral stricture (US) after balloon dilatation (BD).

Methods: A retrospective analysis of 213 patients who underwent BD from 2011 to 2019 was conducted. All statistical analyses were completed by software SPSS 25.0.

Results: Of the patients enrolled, 119 were males and 94 were females. The average age was 44.71 years. One month after stent removal, the overall success rate of ureteral stent placement was 76.99%, and the success rates of single, double, and triple stent groups were 81.7%, 70.3%, and 79.3%, respectively. Six months after stent removal, the overall success rate was 61.9%, and the success rates of the three groups were 61.7%, 52.7%, and 74.1%, respectively. Twelve months after stent removal, the overall success rate was 55.9%, and the success rates of the three groups were 51.9%, 48.6%, and 70.7%, respectively. During indwelling of the stents, the proportions of severe bladder irritation symptoms in the three groups were 13.6%, 16.2%, and 20.7%, respectively. Multivariate analysis indicated the length of US and the time and number of ureteral stent placements were independent risk factors of the treatment effect at 6 months and 12 months after stent removal. Patients in the triple stent group had a better prognosis when compared to those in the single or double stent group.

Conclusion: The long-term effect of three stents was better than that of single and double stents, but the success rate of treatment reduced gradually over time.

Keywords: ureteral stricture, balloon dilatation, single ureteral stent, double ureteral stents, triple ureteral stents

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Edited by:
Bhavan Prasad Rai,
Freeman Hospital, United Kingdom

Reviewed by:
Alberto Parente, Spain Consultant
Federico Soria,
Jesús Usón Minimally Invasive Surgery Center, Spain

***Correspondence:**
Xin Wei
xweiwch@126.com

[†]*These authors have contributed equally to this work and share first authorship*

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INTRODUCTION

Ureteral stricture (US) is one of the most commonly encountered problems in the clinical practice of urology, and ureteral reconstruction remains a challenge in the field of reconstructive urology. The US is a common sequela after endoscopic procedures for urinary stones and invasive diagnostic, with an incidence of approximately 3.5% (1). Besides, iatrogenic urinary tract injuries are frequent in pelvic surgeries, like obstetrical and gynecologic surgery, which might

contribute to US (2). An increasing number of the US has been observed due to increased endoscopic procedures for kidney and ureteral stone treatment, radiation therapy, and pelvic surgery (3).

Conservative treatment of the US is highly associated with hydronephrosis, urinary tract infection, and deterioration of renal function (4). Conventional open approaches are limited by the risk of larger trauma, bleeding, restricture, longer operation time, and length of stay. With the development of endoscopic techniques, such as incision through endoscopy and balloon dilatation (BD), endoscopic treatment for the US might serve as an alternative to open surgery. The success rate of BD reported in the literature was about 13%−80%, but US might recur over time (5, 6). A study reported that endoscopic BD has a high success rate in the treatment of benign USs, but some points remain controversial such as balloon type, dilatation pressure, expansion number, postoperative ureteral stent type, and stent retention time for the BD technique (7). Another treatment such as laser endoureterotomy provides favorable results, and double ureteral stents benefit more than a single stent in the long-term patency rate (8). Endourological therapy is a cost-effective and minimally invasive method for the treatment of benign short-segment USs (<2 cm). Thus, we proposed whether the number of ureteral stent placements (USPs) exerts an impact on the effect of BD.

METHODS

Study Design

The study was conducted according to the Declaration of Helsinki (as revised in 2013). A retrospective analysis of 213 patients who underwent BD in our hospital from 2011 to 2019 was conducted. Patients were eligible if they met the following criteria: (1) age ≥18 years; (2) the US was diagnosed by retrograde pyelography; and (3) the diameter of the US was less than 2 mm, which was about double the width of a guidewire. Exclusion criteria are the following: (1) ureteral atresia; (2) the length of US was more than 5 cm; (3) the guidewire or balloon failed to pass through the stricture segment; and (4) the US was derived from exogenous compression, uncontrolled cancers, and oncologic invasion.

Procedures

Retrograde BD was performed transurethrally with lithotomy position under general anesthesia. Two hydrophilic coated guidewires were passed through the US under the vision of a ureteroscopy, and subsequently, a balloon dilator (21F, Bard Medical, Covington, GA, United States) was placed over the narrowed segment. We confirmed the position of the guidewire or balloon dilator with the C-arm of an X-ray machine. An iodine contrast agent was injected into the high-pressure balloon, and the pressure was maintained at 25 atmospheres for several minutes. The definition of expansion completion was that the pressure did not decrease with time and was stable at 25 atmospheres. We would perform ureteropyelography to ensure that the stenosis was fully expanded after dilatation. After the operation, one to three 4.7 Fr or 6 Fr ureteral double J stents (Bard Medical) were indwelled for 1–6 months according to the degree of ureteral dilatation and injury. There was no intraoperative complication that needed further interventions.

Follow-Up

Color Doppler ultrasound, diuretic renogram, or abdominal computerized tomography was used to assess the hydronephrosis at 1 month after stent removal. The success of the operation is defined as no increase in hydronephrosis and deterioration of renal function after removing the USP. Demographic data, the position and length of the US, time of USP, serum creatinine, and follow-up time were collected to compare the effect of different numbers of USPs.

Statistical Analysis

Quantitative data with normal distribution were described as mean ± standard deviation; otherwise, median and interquartile range were used. When the quantitative data were normally distributed and the variance was homogeneous, analysis of variance or independent sample *t*-test was used for comparison between groups, and the SNK-q test was used for pairwise comparison between groups. Kruskal–Wallis rank-sum test was used between different stent groups when the data did not follow a normal distribution or the variance was uneven. The Mann–Whitney rank-sum test was used between the two groups. The categorical variables were expressed as proportion and percentage, and the comparison between groups was performed by the χ^2 test. The test level of comparison between the two groups was $\alpha = 0.05$. All statistical analyses were completed by software SPSS 25.0.

RESULTS

A total of 213 individuals met the criteria for inclusion, including 119 males and 94 females. The average age was 44.71 years. The average length of the US was 1.52 cm, and the average time of indwelling stent was 4.78 months. Besides, the patients were followed up for at least 12 months. The numbers of patients indwelling a single stent, double stents, and triple stents were 81, 74, and 58, respectively. The causes of US included stone-related operations (ureteroscopic lithotripsy or ureterolithotomy and extracorporeal lithotripsy, 59.6%), ureteropelvic junction obstruction (12.7%), other surgical injuries (10.8%), and unclear etiology (16.9%).

The overall success rate of BD was 51.1% until the last follow-up. The patients who failed to BD underwent surgical ureteral reconstruction, nephrostomy, placement of allium metal stent, and even nephrectomy. One month after stent removal, the overall success rate of USP was 76.99%, and the success rates of single, double, and triple stent groups were 81.65%, 70.3%, and 79.3%, respectively. Six months after stent removal, the overall success rate of USP was 61.9%, and the success rates of single, double, and triple stent groups were

61.7%, 52.7%, and 74.1%, respectively. Twelve months after stent removal, the overall success rate of USP was 55.9%, and the success rates of single, double, and triple stent groups were 51.9%, 48.6%, and 70.7%, respectively. We divided the bladder irritation symptoms into three levels after placing the stents: mild, moderate, and severe. We evaluated the irritation of the stent to the bladder based on the overactive bladder symptom score (OABSS). If OABSS ≤ 5, or symptoms are not sufficient to meet the OAB diagnostic criteria, we consider that the stent has mild irritation to the bladder; if OABSS ranges from 6 to 11, we classify it moderate; if OABSS ≥ 12, we classify it severe. The proportions of severe bladder irritation symptoms in the three groups were 13.6%, 16.2%, and 20.7%, respectively. The basic characteristics of the patients included in this study are summarized in **Table 1**.

Supplementary Table S1 and **Table 2**, respectively, showed the risk factors related to the prognosis of patients, and the multivariate analysis of surgical success at 1 month after stent removal was negatively correlated with the length of the US and the time of USP but not with the number of USP. However, the length of the US, the time of USP, and the number of USPs were independent risk factors of the treatment effect at 6 months (**Supplementary Table S2** and **Table 3**) and 12 months (**Supplementary Table S3** and **Table 4**) after stent removal. Furthermore, patients in the triple stent group had a better prognosis when compared to those in the single or double stent group.

DISCUSSION

Regarding the number of stents placed in patients, at the early stage of starting BD treatment in our hospital, only one stent was placed in the ureter of all patients. In the middle stage, two stents were placed in all patients after BD. In the last 4 years, the placement of the three-bracket strategy was widely applied.

The use of stents after ureteral dilation or incision might contribute to ureteral healing, prevention of urine extravasation, and avoiding restenosis (9). However, the management of optimal USP following endourologic treatment of US remains controversial (10). It is noticeable that there is no positive correlation between the stent size and the therapeutic effect of US. Several studies indicated that the use of a 14F stent provided no advantage over the use of a smaller, more easily positioned 7F stent (11, 12). Currently,

TABLE 1 | Baseline characteristics of enrolled patients in this study.

Features	Single stent	Double stents	Triple stents	X/F	*p*-value
Male/female	31/50	40/34	23/35	4.555	0.103
Age (years)	41.44 ± 13.56	46.81 ± 14.09*	46.59 ± 12.32*	3.870	0.022
BMI (kg/m^2)	22.81 ± 3.04	23.34 ± 3.12	23.40 ± 2.87	0.864	0.423
SCR (umol/L)	80 (67, 99)	78 (67, 88)	84 (65, 100)	0.641	0.726
Length of US (cm)	1 (0.5, 1)	1 (1, 2)	1.5 (1, 2)*	10.035	0.007
Side				3.002	0.223
Left	49	35	29		
Right	32	39	29		
1 m after UTR				2.985	0.225
Valid	66	52	46		
Invalid	15	22	12		
6 m after UTR				6.343	0.042
Valid	50	39**	43		
Invalid	31	35	15		
12 m after UTR				7.262	0.026
Valid	42	36**	41		
Invalid	39	38	17		
Last follow-up				8.444	0.015
Valid	38	32**	39		
Invalid	43	42	19		
Level of BIS				6.370	0.173
Mild	51	45	25		
Moderate	19	17	21		
Severe	11	12	12		

SCR, serum creatinine; US, ureteral stricture; UTR, ureteral stent removal; IS, bladder irritation symptoms.
**Compared to a single stent, $p < 0.05$; **Compared to three stents, $p < 0.05$.*

TABLE 2 | Risk factors related to the prognosis of patients at 1 month after stent removal using multivariate analysis.

Variables	Regression coefficients	Standard error	Wald test	*p*-value	OR	95% CI
Length of US	−0.474	0.144	10.810	0.001	0.622	0.469–0.826
Time of USP	−0.232	0.082	8.230	0.004	0.791	0.674–0.929
Single stent			1.109	0.574		
Double stents	0.056	0.442	0.016	0.899	1.058	0.444–2.517
Triple stents	0.452	0.476	0.904	0.342	1.5572	0.619–3.994
Constant	3.029	0.511	35.091	<0.001	20.680	

US, ureteral stricture; USP, ureteral stent placement; OR, odds ratio; CI, confidence interval.

TABLE 3 | Risk factors related to the prognosis of patients at 6 months after stent removal using multivariate analysis.

Variables	Regression coefficients	Standard error	Wald test	*p*-value	OR	95% CI
Length of US	−0.372	0.135	7.612	0.006	0.689	0.529–0.898
Time of USP	−0.162	0.072	5.036	0.025	0.851	0.739–0.980
Single stent			7.545	0.023		
Double stents	0.112	0.373	0.091	0.763	1.119	0.539–2. 323
Triple stents	1.050	0.416	6.355	0.012	2.857	1.263–6.463
Constant	1.528	0.400	14.599	<0.001	4.610	

US, ureteral stricture; USP, ureteral stent placement; OR, odds ratio; CI, confidence interval.

TABLE 4 | Risk factors related to the prognosis of patients at 12 months after stent removal using multivariate analysis.

Variables	Regression coefficients	Standard error	Wald test	*p*-value	OR	95% CI
Length of US	−0.373	0.138	7.291	0.007	0.689	0.525–0.903
Time of USP	−0.145	0.071	4.138	0.042	0.865	0.752–0.995
Single stent			10.357	0.006		
Double stents	0.327	0.369	0.785	0.376	1.387	0.673–2. 859
Triple stents	1.265	0.405	9.741	0.002	3.542	1.601–7.839
Constant	1.043	0.385	7.324	0.007	2.838	

US, ureteral stricture; USP, ureteral stent placement; OR, odds ratio; CI, confidence interval.

evidence assessing the effect of the number of USP on US after BD is still deficient.

In most cases, the number of stents depends on the preference of surgeons and the degree of the US. In 1998, Liu et al. (13) found the use of two ipsilateral ureteral stents was beneficial in relieving flank pain and persistent azotemia in four patients who failed the single stent due to ureteral obstruction secondary to non-urinary tract malignancies. Subsequently, several clinical studies indicated that placing two parallel stents simultaneously provides a more favorable effect than a single stent after endoureteral treatment of the ureter (14–16). Endourological treatments have been tried for benign short-segment USs (<2 cm). Thus, increased stents had potential advantages in drainage effect, and a better drainage effect is conducive to local tissue healing. Our study observed that three parallel stents were better than a single stent and double stents, but no significant difference was detected between the single stent and double stents. We believed that the urine drainage of the ureteral stent did not depend on the lumen of the stent but on the peritubular space. The increased stiffness of three stents reduced kinking and luminal compression, and the potential space between the stents likely preserved flow around as well as through them (13). Additionally, some researchers proposed that the relative motion between ureteral stents might provide a continuous dilation effect and preclude the formation of stenosis (17). However, plethoric stents could lead to local ischemia in the US segment, affecting tissue healing. Despite the obvious success rate of three stents over single or double stents, further studies on the effect of the number of stents on local tissue are warranted.

The length of the US is also an essential factor for urologists. Some studies showed that the success rate of BD for a benign US < 2 cm was higher (18, 19), and some studies had more strict requirements on the length of the US. They believed that a US < 1.5 cm had a higher success rate of BD, and open surgery

should be considered for longer US (20). We suggested that the short stricture is more beneficial to increasing the success rate of BD according to our results. There is also no uniform standard for the placement time of the stent. Some complications follow indwelling stents such as low back pain, hematuria, bladder irritation, and so on. Long-term indwelling stents can cause local inflammation, promote the proliferation of scar tissue, and affect incision healing (21). Our studies showed that the indwelling time of stents in the effective group was significantly shorter than that in the ineffective group. How to choose the placement time needs further research. The reported study indicated that the success rate of BD gradually decreased over time (22). This trend was consistent with our study, but the decline of multiple stents was slower.

In the results, there was no significant difference in prognosis between patients with a single stent and double stents, but prognosis in the triple stent group was conspicuously different from the other two groups. We guess the supporting effect of one and two stents was not enough to be reflected in patients after BD in the ureter because the injury or healing method of BD may be different from endoureterotomy and discontinuous anastomosis in the ureter.

There is no denying that our study had the following limitation. First, the inherent limitations of a retrospective study and limited sample size preclude us from making a definite and robust conclusion. Second, complications and quality of life are also absent. Besides, whether complications, like urinary tract infection, could exert a significant impact on renal function could not be further evaluated. Despite these limitations, our study does provide some evidence for the management of such patients.

CONCLUSIONS

The long-term effect of three stents is better than that of single and double stents, but the success rate of treatment reduces gradually over time. Further large, well-designed trials are warranted to confirm our findings.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

XH and DF: conception and design, provision of study materials or patients, collection and assembly of data, data analysis and interpretation; XW: administrative support; XH: manuscript drafting. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/article/10.3389/fsurg.2022.847604/full#supplementary-material.

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METHODS
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Robot-Assisted Laparoscopic Radical Cystectomy and Modified Y-Shaped Ileal Orthotopic Neobladder Reconstruction

Weipu Mao[1,2,3†], Shuqiu Chen[1†], Lijie Zhang[1†], Tao Li[1†], Si Sun[1], Bin Xu[1], Weidong Zhu[1], Guangyuan Zhang[1], Lei Zhang[1], Jianping Wu[1]* and Ming Chen[1,2,3]**

[1]Department of Urology, Affiliated Zhongda Hospital of Southeast University, Nanjing, China, [2]Surgical Research Center, Institute of Urology, Southeast University Medical School, Nanjing, China, [3]Department of Urology, Nanjing Lishui District People's Hospital, Zhongda Hospital Lishui Branch, Southeast University, Nanjing, China

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Bhaskar K. Somani,
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United Kingdom

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Maria Chiara Sighinolfi,
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Qingwen Li,
The First Affiliated Hospital of Bengbu Medical College, China

***Correspondence:**
Ming Chen
mingchenseu@126.com
Jianping Wu
doctorwujianping@126.com
Lei Zhang
lei198711@163.com

†These authors have contributed equally to this work

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Background: Orthotopic neobladder reconstruction has become the preferred method of urinary diversion after radical cystectomy in major medical centers. We performed modified Y-shaped ileal orthotopic neobladder reconstruction and presented the functional results and postoperative complications of the modified surgery.

Methods: We included 21 patients with bladder cancer who underwent radical cystectomy at our center between February 2019 and December 2019. All patients underwent robotic-assisted laparoscopic radical cystectomy and lymph node dissection plus modified Y-shaped ileal orthotopic neobladder reconstruction. We collected the demographic and pathological history of the patients, and perioperative and postoperative functional outcomes and postoperative complications were recorded.

Results: All surgeries were successful and no serious postoperative complications occurred. The mean operative time was 321.43 ± 54.75 min, including 101.67 ± 10.88 min required for neobladder reconstruction. Liquid intake was encouraged about 5 days after surgery, stent and catheter were removed after 13.52 ± 3.28 days, and the patients were discharged 1–2 days after removing the catheter. No ureteral anastomotic and neobladder urethral anastomotic strictures occurred. The volume of the neobladder at 1-year post-surgery was 195.24 ± 16.07 mL and the maximum urinary flow rate was 20.64 ± 2.22 mL/s.

Conclusion: We describe the robotic-assisted modified Y-shaped ileal orthotopic neobladder reconstruction performed at our center, which requires a simple suture and short neobladder construction time, minimizes the occurrence of anastomotic stenosis, facilitates smooth patient emptying, and is clinically scalable and applicable.

Keywords: bladder cancer, robot-assisted laparoscopic, radical cystectomy, modified Y-shaped ileal orthotopic neobladder, urinary diversion

BACKGROUND

According to the 2020 global cancer statistics, bladder cancer (BCa) is the 12th most common cancer with 573,278 new cases, accounting for 3.0% of all new cancers, and 212,536 deaths, approximately 2.1% of all deaths (1). As the second most common malignancy of the genitourinary system, BCa can be categorized into non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC). BCa also shows a high recurrence rate and aggressiveness (2, 3). Surgery is the treatment of choice for patients with BCa. Transurethral resection of bladder tumors (TURBT) combined with postoperative intravesical infusion chemotherapy is the main treatment for NMIBC patients (4, 5). For patients with MIBC or high-grade recurrent T1 and/or carcinoma in situ, radical cystectomy (RC) is the best surgical intervention (6, 7). RC can significantly improve tumor control rates and patient survival time.

Urinary diversion after RC is a core treatment for improving patient quality of life and the methods of urinary diversion include an ileal conduit (IC), orthotopic neobladder reconstruction (ONB), and cutaneous ureterostomy (CU) (8, 9). Because ONB can significantly improve patients' long-term quality of life compared to IC and CU, ONB is now gradually becoming the preferred urinary diversion method after RC in major medical centers (10, 11). Based on the study of Massimo et al (12), our center explored robot-assisted laparoscopic RC and modified Y-shaped ileal ONB in 2019. Here, we report our initial clinical experience, surgical procedures, complications thereof, and oncologic and functional outcomes.

PATIENTS AND METHODS

Patients Selection

A total of 21 patients with bladder cancer who underwent RC at our center between February 2019 and December 2019 were included in the current study. All patients underwent preoperative pelvic magnetic resonance imaging (MRI) or enhanced computed tomography (CT), and preoperative cystoscopic biopsy and the postoperative pathological test confirmed whether it was MIBC or refractory NMIBC. Patients with locally advanced or metastatic disease, stress urinary incontinence, impaired external urethral sphincter, impaired renal function (serum creatinine > 200 μmol/L), severe hepatic impairment, severe small bowel disease, positive prostatic urethral biopsy, and psychiatric disease were excluded. The basic preoperative information of the patients is summarized in **Table 1**. All patients were followed up until December 2021. The study was approved by the Ethics Committee of the Southeast University Zhongda Hospital (Nanjing, China), and all patients signed written informed consent.

TABLE 1 | Preoperative characteristics.

Variable	Result
Patients (*n*)	21
Age (years)	65.76 ± 7.35
Sex (male/female)	21/0
Body mass index (Kg/m^2)	23.48 ± 2.87
Clinical stage (*n*)	
cTis	1
cT1	13
cT2	5
cT3	2
Serum creatinine, μmol/L	72.65 ± 11.57

Data for continuous variables are presented as mean ± standard deviation.

Surgical Technique

Position and Operation Hole

The surgery was performed with the patient in the steep Trendelenburg position and a five-port transperitoneal approach was used: the first 12-mm trocar was placed 5 cm above the umbilicus along with the laparoscopic camera; an 8-mm trocar was placed along the lateral aspect of the rectus abdominis muscle where the No. 1 and No. 2 robotic arms were placed; an 8-mm trocar was placed medial to the left iliac spine where the No. 3 robotic arm was placed. In addition, a 12-mm trocar was placed medial to the right iliac spine and at the midpoint of the No. 1 robotic arm and the camera hole where the assistant instruments were placed (**Figure 1**).

A surgeon (MC) experienced in laparoscopic and robotic-assisted surgery for kidney, prostate and bladder cancers performed all the procedures.

"Procedural" Cystectomy

Cystectomy was performed according to our center's programmed optimization protocol, in the following general order: (1) separation of the right ureter; (2) separation of the bilateral seminal vesicle glands; (3) removal of the right lymph nodes; (4) separation of the right lateral bladder ligament; (5) separation of the left ureter; (6) removal of the left lymph nodes; (7) separation of the left lateral bladder ligament; (8) separation of the retropubic bladder space; (9) opening the pelvic floor and suture ligation of the dorsal deep vein complex (DVC); (10) separation of the lateral prostatic ligament and disconnecting the urethra. After disconnection of the urethra, the prostatic urethral stump is clamped shut using a surgical clip to prevent urine spillage from the bladder. The bladder was then placed in the endobag and finally removed from the incision.

The obturator, internal iliac, external iliac and presacral lymph nodes were cleared during extended pelvic lymph node dissection. Intraoperative frozen sections were used to assess whether the ureteral stump margin and urethral stump margin were positive.

Neobladder Preparation and Reconstruction

The ileocecal portion was first located and the ONB was performed starting at 20 cm from the ileocecal flap, isolating approximately 45 cm of the ileum for ONB (**Figure 2A**). The

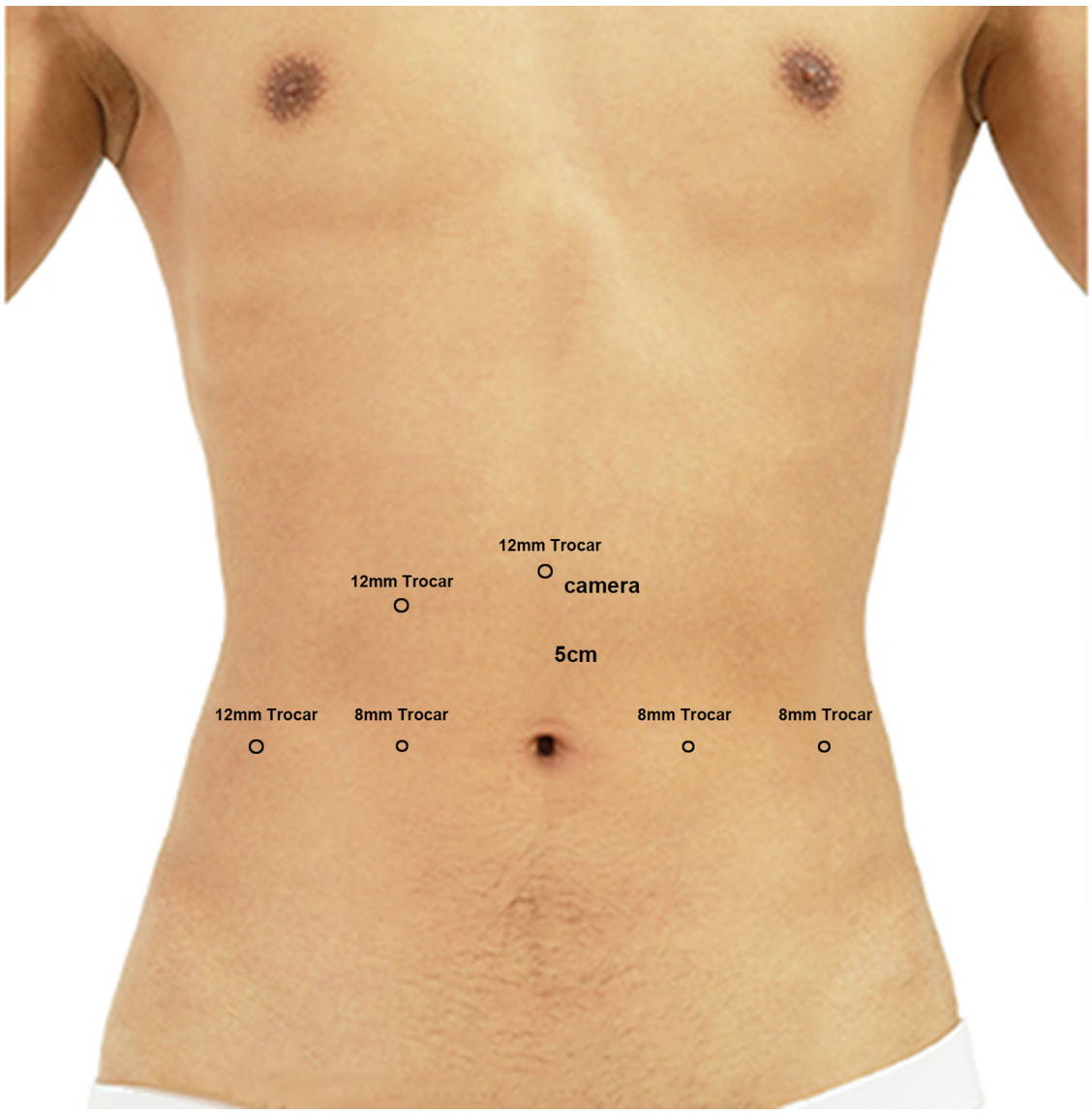

FIGURE 1 | A five-port transperitoneal approach.

midpoint of the ONB ileum was marked using absorbable sutures as the ileo-urethral anastomosis zone, the ends of the ONB ileum were marked, and a catheter was inserted through the urethra and connected to the ileo-urethral anastomosis zone and then pulled to keep the bowel in tension (**Figure 2B**). The bowel was dissected with scissors between the ileo-urethral anastomosis zone and the mesentery (**Figure 2C**), and the ureteral stent was used as a ruler to separate 15 cm of the bowel along each side of the marker (**Figure 2D**). Subsequently, the dorsal sides of the left and right intestinal canals were sutured throughout (**Figure 2E**). The intestinal canal was truncated using an ultrasonic knife at 5 cm from the end of the right intestinal canal suture and 8 cm from the end of the left intestinal canal suture. The lateral anastomosis was performed using an Endo-GIA stapler to restore the continuity of the intestine and then, the mesenteric foramen was closed (**Figure 2F**). The intestinal wall of the ileo-urethral anastomosis area was then anastomosed clockwise to the urethral stump (**Figure 2G**), and the anterior wall of the anastomotic site was suspended. A catheter and single J stents were inserted, and the ventral sides of the left and right intestinal tubes were sutured successively from the ileo-urethral anastomosis area, and the anterior wall of the reservoir was sutured (**Figure 2H**).

Ureteral Bladder Anastomosis Reconstruction

After splitting the ends of the ureters by 1 cm and anastomosing it with the Y-shaped arms with one stitch (**Figure 2I**), the single J

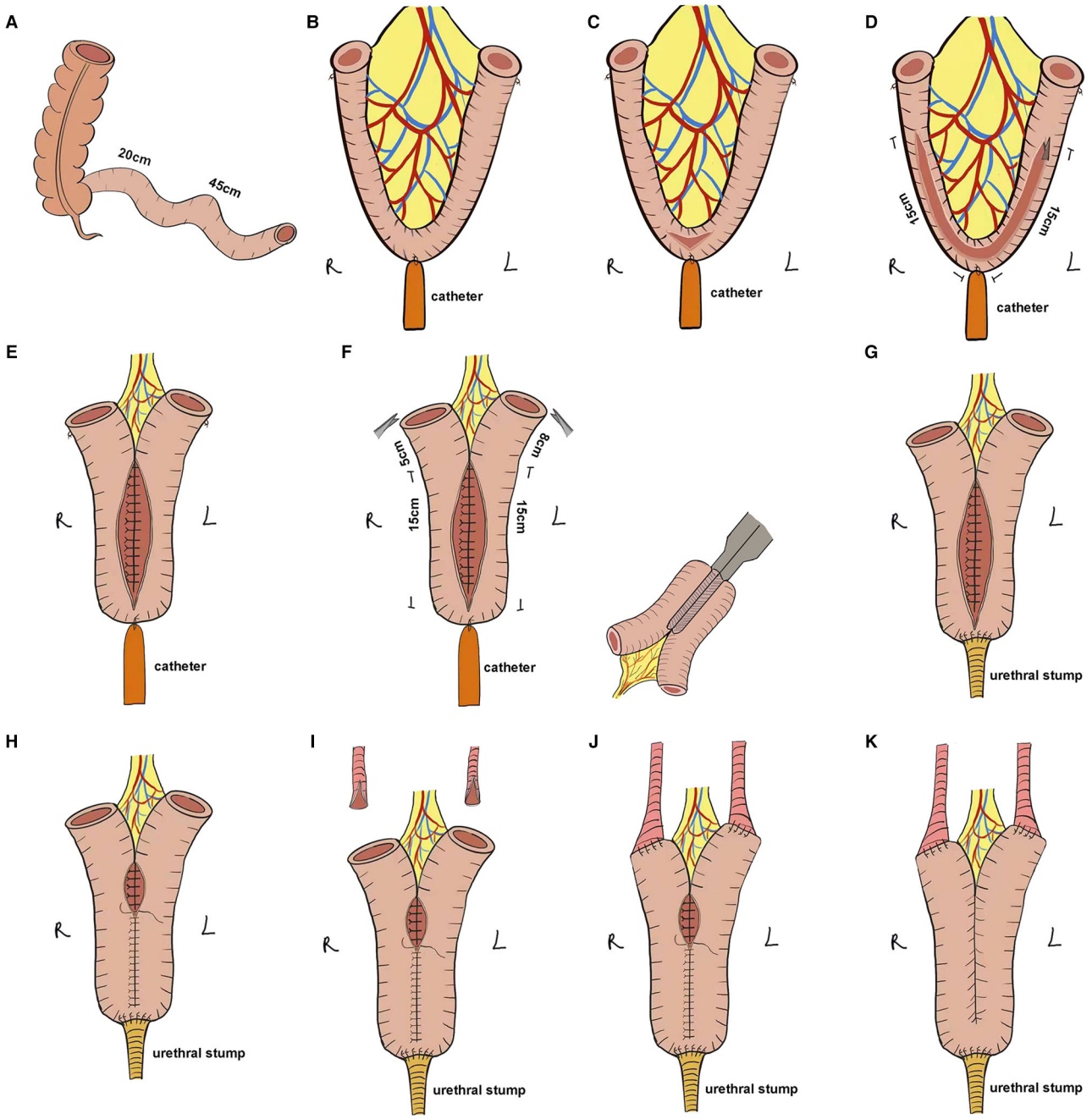

FIGURE 2 | Stepwise configuration of the complete Y-shaped ileal neobladder. (**A**) Approximately 45 cm of ileum was separated for ONB. (**B**) The ileo-urethral anastomosis zone and the ends of the ONB ileum were marked, and the catheter was connected to the ileo-urethral anastomosis area to keep the bowel in tension. (**C**) The intestine between the ileo-urethral anastomosis area and the mesentery was dissected. (**D**) Using the ureteric stent as a ruler, 15 cm of the bowel along each side of the marker was separated. (**E**) The dorsal sides of the left and right intestinal canals were sutured throughout. (**F**) The intestinal canal was truncated at 8 cm from the end of the right intestinal canal suture and 5 cm from the end of the left intestinal canal suture, and the stapler laterally anastomosed the intestine to preserve the intestinal continuity. (**G**) The intestinal wall of the ileo-urethral anastomosis area was anastomosed clockwise to the urethral stump. (**H**) The anterior wall was sutured to the reservoir. (**I**) The ureter was split 1 cm at each end. (**J**) Wallance anastomosis was performed to suture the ends of the ureter to the Y-shaped arms on either side of the reservoir in a continuous manner. (**K**) The remaining anterior wall of the reservoir was anastomosed.

stent was placed into the ureter up to the renal pelvis, followed by continuous suturing of the ends of the ureters to the Y-shaped arms on both sides of the reservoir using Wallance anastomosis (**Figure 2J**). Finally, the remaining anterior wall of the reservoir was anastomosed (**Figure 2K**), and the bilateral single J stent and catheter were exported from the ureter.

Perioperative and Postoperative Follow-Up

Perioperative and postoperative functional outcomes, postoperative complications, and postoperative voiding were evaluated in the 21 patients, and relevant imaging was performed to determine the volume of the neobladder.

Statistical Analysis

Data were analyzed using SPSS software (version 24.0). Continuous variables were expressed as mean ± standard deviation.

RESULTS

The procedure was completed in all the patients without serious complications and conversion to open surgery. The mean operative time was (321.43 ± 54.75) min including the mean time of (101.67 ± 10.88) min required to reconstruct the neobladder. The mean intraoperative blood loss was (129.09 ± 73.55) mL, and only one patient required emergency blood transfusion. The number of intraoperative lymph node dissection was 16.10 ± 6.28, one patient had positive dissected lymph nodes (2/20), and all patients had negative soft tissue surgical margins. The postoperative histopathological staging was slightly altered from that in the preoperative period, with 8 patients being diagnosed with NMIBC (1 with cTis and 7 with cT1) and 13 patients with MIBC (10 with cT2 and 3 with cT3). During the perioperative period, patients resumed fluid intake at a mean of 5.14 ± 0.79 days, and stents and catheters were removed at 13.52 ± 3.28 days. The mean total length of hospital stay for the patients was 14.71 ± 3.20 days (**Table 2**).

All patients were followed up for more than 24 months, and the mean follow-up duration was (29.76 ± 3.65) months, during which no patient died. A total of eight patients developed Clavien-Dindo grade II complications after surgery, including one patient who required blood transfusion therapy, four patients with lung infections, one patient with anemia and two patients with hypoproteinemia (**Table 3**). Patients voided freely starting two months after surgery, and at the 1-year postoperative follow-up, the mean volume of the patients' neobladder was 195.24 ± 16.07 mL and the maximum urinary flow rate was 20.64 ± 2.22 mL/s (**Figure 3** and **Supplementary Figure S1**). During the follow-up period, no patient had difficulty in urination and showed recurrence of urethral tumor, neobladder urolithiasis, ureteral anastomotic stricture, and stricture of the neobladder urethral anastomosis. However, one patient developed postoperative incomplete

TABLE 2 | Perioperative characteristics.

Variable	Result
Total operative time (min)	321.43 ± 54.75
Neobladder time (min)	101.67 ± 10.88
Estimated blood loss (mL)	129.09 ± 73.55
Blood transfusion (*n*)	1
Number of lymph nodes retrieved (*n*)	16.10 ± 6.28
Lymph node metastasis (*n*)	1 (2/20)
Positive soft tissue surgical margins (*n*)	0
Pathological stage (*n*)	
pTis	1
pT1	7
pT2	10
pT3	3
Time to liquid intake (days)	5.14 ± 0.79
Time to stent and catheter removal (days)	13.52 ± 3.28
Hospital stay (days)	14.71 ± 3.20

Data for continuous variables are presented as mean ± standard deviation.

TABLE 3 | Postoperative complications.

Variable	Result
Clavien-Dindo classification	
Grade I	0
Grade II	8
Blood transfusion	1
Lung infection	4
Anemia	1
Hypoproteinemia	2
Grade III	0
Grade IV	0

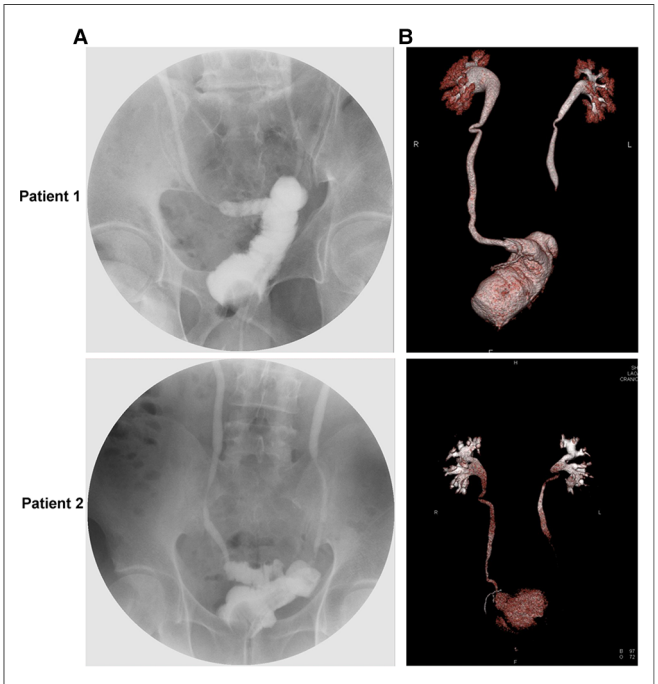

FIGURE 3 | Cystogram and three-dimensional reconstruction images of a representative postoperative Y-shaped neobladder. (**A**) Postoperative cystogram image. (**B**) Postoperative three-dimensional reconstruction image.

bowel obstruction but the symptoms improved with appropriate treatment (**Table 4**).

In addition, postoperative daytime and night-time urinary incontinence was recorded for all patients. As shown in **Table 5**, it was observed that the rates of postoperative daytime and night-time incontinences were 42.86% (9/21) and 61.90% (13/21) at 3 months, 23.81% (5/21) and 38.10% (8/21) at 6 months, and 9.52% (2/21) and 19.05% (4/21) at 1 year, respectively.

DISCUSSION

In the present study, we evaluated the clinical outcomes in 21 patients who underwent modified Y-shaped ileal ONB and found that robot-assisted modified Y-shaped ileal ONB at our center showed satisfactory perioperative and postoperative functional outcomes (**Table 6**).

There are several approaches to urinary diversion after RC, depending on the clinical characteristics and surgeon's considerations. Nevertheless, ONB has become a common choice for patients due to its similarity with the voiding mechanisms (16). Open RC was a surgical approach with a high success rate but the associated uretero-intestinal anastomosis was difficult to visualize due to high surgical difficulty and postoperative complications (17). After the report published by Gill et al. (18) laparoscopy-based RC and ONB have been further developed and matured. Robot-assisted laparoscopic radical cystectomy and neobladder reconstruction have also recently gained popularity due to the introduction of the da Vinci® SI system, and ONB reconstruction is performed at an increasing number of centers (18–20). In some medical centers, the proportion of ONB after RC has increased to 50%–90%. In 2007, Hautmann et al. (11) retrospectively summarized a total of 7,129 reports on postoperative ureteral diversion methods after RC from multiple medical centers worldwide, of which ONB accounted for 46.9%, IC accounted for 32.7%, and controlled ureteral diversion skin stoma accounted for 7.6%. However, in 2015, Hugen (21) reported that 75% of patients at the largest medical center in the United States receive ONB, with only a minority of patients (less than 15%) opting for IC.

ONB can be classified as gastric ONB, ileal ONB, ileocolonic ONB, and sigmoid ONB depending on the segment of the GI tract used (22). Due to the convenience of ileal retrieval and low pressure of the neobladder after detubularization, which is conducive to the protection of the patient's renal function, the ileum is currently most widely used to construct the neobladder (22, 23). The Camey II ileal neobladder was a modification of Camey I ileal neobladder reconstruction (24). The Camey II ileal neobladder reconstruction method separates a 65-cm long section of the ileum, arranges the bowel in a U-shape, and performs a ureter-ileal anastomosis using the Le Due method. The Camey II ileal neobladder reconstruction achieves a low-pressure reservoir that better protects the upper urinary tract function and improves daytime urinary control. Mrini et al. (25) reported that after the Camey II procedure, patients showed a postoperative ureteral reflux rate of 6.8% and ureteral anastomotic stricture rate of 8.6%, with 64.2% of patients achieving daytime urinary control immediately post-surgery and 80% daytime urinary control at 3 months post-surgery.

In 2012, Massimo and colleagues modified the Camey II procedure by decannulating a 45-cm section of the ileum and arranging it in a vertical Y-shape (12). The advantage, therein, was that the intercepted bowel was shorter and the volume of the constructed storage bladder was relatively smaller, which, together with the Y-shaped bladder, was more conducive to postoperative bladder emptying and avoidance of residual urine, thereby reducing metabolic acidosis. Massimo found that all 237 patients who received the Camey II modification were able to empty their bladders postoperatively, with daytime and night-time urinary control rates of 93.5% and 83.9%, respectively (12).

However, the incidences of ureteral neobladder stricture, neobladder urethral stenosis, and neobladder urolithiasis in Massimo's modified approach were 3.3%, 6.3%, and 16.0%, respectively. After exploring the causes of complications in Massimo's Y-shaped neobladder approach, we further improved it. Firstly, we used the da Vinci robotic operating system, which utilizes the advantages of minimally invasive robotic surgery. Secondly, we used absorbable thread in suturing the neobladder instead of staples, which, too, reduced the incidence of neobladder urolithiasis. Thirdly, we split the end of the ureter and sutured it to the intestinal break of the reservoir using the Wallance anastomosis to reduce the incidence of ureteral

TABLE 4 | 1-year postoperative characteristics.

Variable	Result
Difficulty urinating	0
Ureteral anastomotic stricture	0
Neobladder urethral anastomotic stricture	0
Urethral tumor recurrence	0
Neobladder urolithiasis	0
Incomplete intestinal obstruction	1
Neobladder volume (mL)	195.24 ± 16.07
Maximum urine flow rate (mL/s)	20.64 ± 2.22
Follow-up (months)	29.76 ± 3.65
Serum creatinine, μmol/L	69.79 ± 30.60
Overall survival, *n* (%)	21 (100)

Data for continuous variables are presented as mean ± standard deviation.

TABLE 5 | Functional outcomes.

Variable	Patients, *n* (%)		
	3 months	6 months	12 months
Daytime incontinence	9 (42.86)	5 (23.81)	2 (9.52)
Night-time incontinence	13 (61.90)	8 (38.10)	4 (19.05)

Incontinence was defined as the use of one wet pad or more.

TABLE 6 | Evaluation of the effectiveness of several robotic-assisted Y-shaped ileal orthotopic neobladder.

Study	Year	N	Neobladder and shape	Surgery Type	Operative time (min)	Neobladder time (min)	Follow up (months)	Afferent limb	Ureteroenteric anastomosis	Complications	Continence outcome
Sim (25)	2015	3	Y shape	RARC	340	NA	NA	Yes	Nesbit	NA	NA
Asimakopoulos (26)	2016	40	Modified Y shape	RARC	315	NA	26.5	No	Wallance	No stricture; 10 (25%) unilat hydronephrosis	Daytime incontinence, 0.0%; Night-time incontinence, 27.5%
Checcucci (28)	2021	45	Modified Y shape	RARC	287	165	14	Yes	Nesbit	2 (4.4%) ureteral anastomotic stricture; 7 (15.5%) acute renal failure	Daytime incontinence, 24.5%; Night-time incontinence, 28.9%
Our study	2022	21	Modified Y shape	RARC	321.43	101.67	29.76	No	Wallance	No stricture	Daytime incontinence, 9.5%; Night-time incontinence, 19.1%

neobladder stenosis. Finally, we reserved a longer urethral stump and the anterior wall of the anastomotic site was draped during the neobladder urethral anastomosis, which reduced the incidence of neobladder urethral stricture and improved urinary control in patients postoperatively.

To date, there were several different ileal neobladder procedures, including Studer ileal neobladder, Camey II ileal neobladder, M/W-shaped ileal neobladder, Kock ileal neobladder, Mainz ileal neobladder, and Le Bag ileal neobladder (10, 11, 26). The Y-shaped neobladder was first described by Fontana in 2004 (27), who demonstrated that the ileal Y-shaped neobladder showed good functional outcomes comparable to the mainly diffused ileal neobladder, and several subsequent studies have confirmed the feasibility of ileal Y-shaped neobladder surgery (13–15, 28, 29). Compared to other ileal neobladder procedures, our modified Y-shaped ileal neobladder requires only one bowel fold and simple suturing. Combined with the advantages of minimally invasive robotic surgery, the construction time of the neobladder is relatively short, which greatly reduces the surgery time and facilitates the patient's postoperative recovery. The modified Y-shaped ileal neobladder requires a shorter bowel, which is more conducive to postoperative bladder emptying and avoiding residual urine and impaired renal function, and none of the patients experienced acute kidney injury. Unlike the Y-shaped neobladder described by Fontana, we used absorbable thread instead of staples in suturing the neobladder, and none of the patients developed neobladder urolithiasis postoperatively. In addition, unlike other Y-shaped neobladder approaches, we drew bilateral single J stents from the urethra, which facilitated fixation and reduced the number of perforations in the abdominal wall, which facilitated the patient's postoperative recovery.

Although the volume of the modified Y-shaped ileal neobladder immediately after surgery was lower, after 1 year, patients achieved a volume of 200 mL and daytime and nocturnal urinary control rates of 90.5% and 81.0%, respectively. In addition, we used the Wallance anastomosis for the ureteral neobladder anastomosis, which increased the area of the ureteral ileum and greatly reduced the incidence of ureteral neobladder stenosis. Also, the sides of the Y-shaped bowel of the neobladder were connected to the bilateral ureters on both sides, the ureters did not need to be displaced again, and both sides of the intestine could play an anti-urinary reflux effect.

There were a few limitations of this study. Since this study was conducted only at our center, the number of included cases was small, and the patients were followed up for just over two years. A multicenter study with a longer follow-up period needs to be conducted. In addition, one patient in this study presented with an emergency blood transfusion. A retrospective review of the patient's clinicopathological data revealed that the patient was older and had a large tumor size and abundant blood supply, which may have caused the transfusion and required us to develop a reasonable indication. Moreover, several medical centers do not have a robotic operating system due to gaps across the regional medical centers, which may cause differential effects that need to be evaluated with further research on this technology.

CONCLUSIONS

We report the clinical efficacy of a robot-assisted modified Y-shaped ileal ONB at our center. Although the follow-up period was less, preliminary results were encouraging, with a low rate of postoperative complications and better postoperative functional outcomes. This also suggested that robot-assisted laparoscopic modified Y-shaped orthotopic ileal ONB is a scalable option for ONB.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The study was approved by the Ethics

Committee of the Southeast University Zhongda Hospital (Nanjing, China), and all patients signed written informed consent. The patients/participants provided their written informed consent to participate in this study.

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

AUTHOR CONTRIBUTIONS

MC, JW and LZ had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: MC, JW, LZ and WM. Acquisition of data: WM and SC. Analysis and interpretation of data: WM and SS. Drafting of the manuscript: WM, SC and LZ. Critical revision of the manuscript for important intellectual content: MC, JW, LZ, SC, BX and WZ. Statistical analysis: WM and SC. Obtaining funding: None. Administrative, technical, or material support: SS, BX and WZ. Supervision: MC and JW. Other (figure drawing and production): LZ and TL. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.889536/full#supplementary-material.

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EDITED BY
Nithesh Naik,
Manipal Academy of Higher Education, India

REVIEWED BY
Andrey O. Morozov,
I. M. Sechenov First Moscow State Medical University, Russia
Rustom P. Manecksha,
Tallaght University Hospital, Ireland
Daniele Castellani,
Polytechnic University of Le Marche, Italy
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National and Kapodistrian University of Athens, Greece
Andreas Bruchbacher,
Asklepios Klinik Barmbek, Germany
Panagiotis Mourmouris,
National and Kapodistrian University of Athens, Greece

*CORRESPONDENCE
Peter Sparwasser
peter.sparwasser@unimedizin-mainz.de

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Assessment of a novel smartglass-based point-of-care fusion approach for mixed reality-assisted targeted prostate biopsy: A pilot proof-of-concept study

P. Sparwasser[1]*, M. Haack[1], L. Frey[1], K. Boehm[1], C. Boedecker[2], T. Huber[2], K. Stroh[3], M. P. Brandt[1], R. Mager[1], T. Höfner[1], I. Tsaur[1], A. Haferkamp[1] and H. Borgmann[1,4]

[1]Department of Urology, University Medical Center Johannes Gutenberg University, Mainz, Germany, [2]Department of General, Visceral and Transplant Surgery, University Medical Center Johannes Gutenberg University, Mainz, Germany, [3]Department of Radiology, University Medical Center Johannes Gutenberg University, Mainz, Germany, [4]Department of Urology, Brandenburg Medical School Theodor Fontane, Neuruppin, Germany

Purpose: While several biopsy techniques and platforms for magnetic resonance imaging (MRI)-guided targeted biopsy of the prostate have been established, none of them has proven definite superiority. Augmented and virtual reality (mixed reality) smartglasses have emerged as an innovative technology to support image-guidance and optimize accuracy during medical interventions. We aimed to investigate the benefits of smartglasses for MRI-guided mixed reality-assisted cognitive targeted biopsy of the prostate.

Methods: For prospectively collected patients with suspect prostate PIRADS lesions, multiparametric MRI was uploaded to a smartglass (Microsoft® Hololens I), and smartglass-assisted targeted biopsy (SMART TB) of the prostate was executed by generation of a cognitive fusion technology at the point-of-care. Detection rates of prostate cancer (PCA) were compared between SMART TB and 12-core systematic biopsy. Assessment of SMART-TB was executed by the two performing surgeons based on 10 domains on a 10-point scale ranging from bad (1) to excellent (10).

Results: SMART TB and systematic biopsy of the prostate were performed for 10 patients with a total of 17 suspect PIRADS lesions (PIRADS 3, $n = 6$; PIRADS 4, $n = 6$; PIRADS 5, $n = 5$). PCA detection rate per core was significant ($p < 0.05$) higher for SMART TB (47%) than for systematic biopsy (19%). Likelihood for PCA according to each core of a PIRADS lesion (17%, PIRADS 3; 58%, PIRADS 4; 67%, PIRADS 5) demonstrated convenient accuracy. Feasibility scores for SMART TB were high for practicality (10), multitasking (10), execution speed (9), comfort (8), improvement of surgery (8) and image quality (8), medium for physical stress (6) and device handling (6) and low for device weight (5) and battery autonomy (4).

Conclusion: SMART TB has the potential to increase accuracy for PCA detection and might enhance cognitive MRI-guided targeted prostate biopsy in the future.

KEYWORDS

prostate biopsy, mixed reality, augmented reality, hololens, prostate cancer, smartglass

Introduction

Since the first version for PI-RADS in 2011, multiparametric magnetic resonance imaging (mpMRI) of the prostate for diagnosis of prostate cancer (PCA) has been widely adopted into daily routine. While execution for mpMRI is strictly defined, the technique for subsequent targeted prostate biopsy in case of PCA suspicion is not determined. To date several techniques for targeted prostate biopsy have been developed: in-bore MRI biopsy (MRI-TB), software fusion biopsy (FUS-TB) and cognitive fusion biopsy (COG-TB). All of them demonstrated to have approximately comparable detection rates for PCA (1). To date there is still no definite recommendation for one of these techniques (2) and therefore the discourse on how best to perform targeted biopsy continues (1–4).

Mixed reality tools proofed to facilitate the real-time integration of medical data and radiological imaging into surgical procedures (5, 6) and are thus increasingly evaluated for use in clinical practice (7). Thereby, intraoperative surgical applications for smartglasses may offer great opportunities by real-time overlay of preoperative imaging at the point-of-care (5, 7) and demonstrated to be feasible and safe (6). Most of these technical applications consist of a head-mounted display integrated to a smartglass with a see-through display for mixed reality-assisted surgery, allowing its user to execute surgery under visualization of virtual imaging while an unobstructed view to the operation field is given.

In PCA diagnosis and treatment, several virtual and augmented reality applications using smartglasses have currently been developed (7, 8). Within a pilot proof-of-concept study, we already investigated the possible benefits in using a smartglass (Vuzix Blade®, Rochester USA) for augmented reality assisted prostate biopsy (9). Here we demonstrated good feasibility and convenient detection rates but also stated the necessity of hardware enhancements especially according to image quality and the need of further prospective investigations (9). Following up on our pilot proof-of-concept study, we aimed to transfer our first experiences with SMART TB onto a lager cohort and to a more advanced mixed reality tool.

This is the first report on using cognitive point-of-care fusion technology for mixed reality smartglasses-assisted targeted biopsy (SMART TB) under usage of the smartglass Hololens (Microsoft®) for prostate cancer diagnosis.

Methods

Ten patients were included prospectively in our feasibility study after approvement by the local ethics board. Inclusion criteria were suspect for prostate cancer by moderate PSA elevation (≤20 ng/ml) and by mpMRI imaging with a maximum of three target lesions per patient while maximum size of the prostate was set at ≤120 ml. In accordance with the EAU guidelines preoperative mpMRI imaging was executed to avoid unnecessary biopsy in asymptomatic men with moderate PSA elevation (2). All patients underwent mpMRI (1.5- or 3-Tesla) of the prostate with confirmation of a minimum of one suspect prostate lesion. A genitourinary expert of local radiology department reviewed each mpMRIs and external imaging was filtered through quality checks by same genitourinary expert, while a maximum of two targets were labelled for each patient. Based on Diffusion-weighted, T2-weighted and contrast-enhanced series, MRI lesions were given in accordance to current standardization criteria a *Prostate Imaging Reporting and Data System score* (PI-RADSv2) from 1 to 5 (10). As previous described through our study group for the usage of the smartglass Vuzix® Blade we processed the mpMRI scans to produce a two-dimensional image copy including the standardised mpMRI reporting scheme with labelled index lesion, relevant axial T2-weighted images (base/mid/apex) with demonstrative landmarks and the afore labelled target lesion/lesions (9). These data were uploaded via micro-USB 2.0 now to the smartglass Microsoft® Hololens I (**Figure 1**) prior to biopsy as a JPEG file.

Targeted biopsy of the prostate was indicated in the presence of lesions with PIRADS scores between 3 and 5 in accordance to the EAU Guidelines (2). Thus, we choosed an ultrasound-guided transrectal approach using the HiVision Ascendus Ultrasound (Hitachi Medical Systems®). A preoperative application of intravenous antibiotics (ceftriaxon or ciprofloxacin) and rectal disinfection (povidone-iodine) was additionally executed. Patients' tolerance was improved by infiltration of the periprostatic plexus with local anaesthesia (mecain 2%) as it is described widely. In the meantime, while the patient still placed in lithotomy position, the uploaded mpMRI files were retrieved from the mixed reality smartglass Hololens I (**Figure 2**). Through the smartglass the biopseur was now enabled to create a mixed reality operating room at the point-of-care by attaching all previously uploaded MRI files including the prostate scheme of the prostate as holographic projection around the patient (still in lithotomy position).

Navigation of the Hololens was thereby possible hands-free through voice commands and finger tracking (**Figure 2**) under aseptic conditions. Finger tracking thereby describes the possibility of the smartglass to recognized and process user's manual interaction with the projected virtual data. Target biopsy was thereafter performed by two experienced surgeons with a transrectal software fusion biopsy case load of each more than 100 normally using the Hi-RVS Preirus-System for the HiVision Ascendus Ultrasound (Hitachi Medical Systems®). Our SMART TB was then always followed by a systematic transrectal 12-core biopsy. SMART TB was

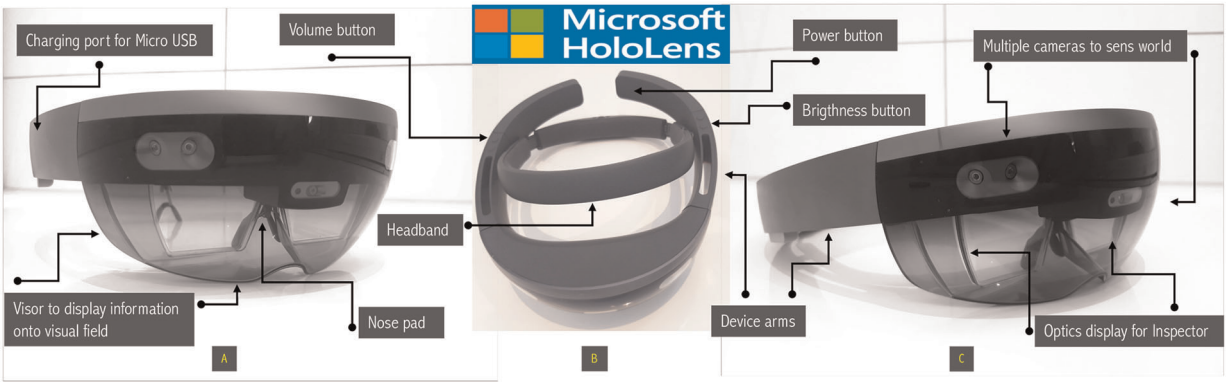

FIGURE 1
Hololens I by Microsoft® is a see-through smartglass with holographic lenses which creates 3-D models into the surrounding environment due to multiple spatial-mapping cameras and depth cameras, as well its inertial measurement unit. Navigation: eye tracking, finger tracking, voice commands. Processor: Holographic Processing Unit HPU 1.0 Intel 32-bit with Operating System Windows 10+ Windows Store; Memory: 2 GB RAM, 64 GB Flash Storage; Weight 759 g; Camera 2.4 MP photo; 1.1 MP HD video, video speed 30 FPS; Batery life 2–3 h under active use and 2 weeks standby; Connectivity to other sources through Wi-Fi 802.11ac, Bluetooth 4.1 LE and Micro-USB 2.0 (11). Figure 2 illustrates hardware components of Hololens I from (**A**) front, (**B**) side and (**C**) bird's eye view.

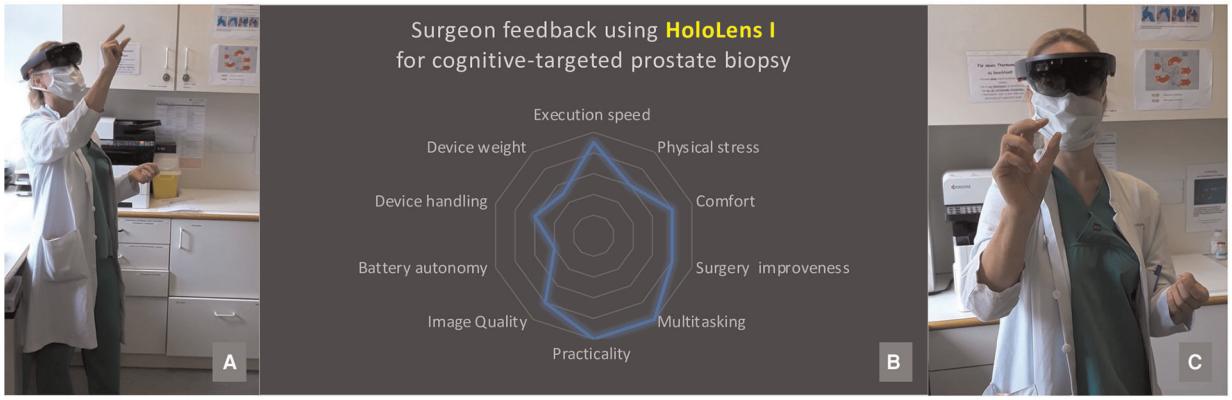

FIGURE 2
Illustration of surgeon wearing Hololens smartglass and navigation by finger tracking [picture (**A**,**C**)]. Surgeons' feedback for using Hololens I for cognitive-targeted prostate biopsy including an assessment from bad to excellent for specific domains [picture (**B**)].

compared to the concomitant executed 12-core systematic biopsy (by same biopseur) and to the abovementioned well-established MRI-based biopsy techniques. In summary, we obtained between 16 and 22 samples per patient (target biopsy, 4–10 cores; systematic biopsy, 12 cores). The number of cores taken depended on surgeon's assessment taking lesion count and size in to account. As already prescribed in our pilot-proof of concept study the surgeon cognitively matched for targeted biopsy the real-time transrectal ultrasound with the uploaded MRI images and optimization of accuracy was possible through hand-guided adjustment of the puncture line according to the specific landmarks on mpMRI images displayed in front of surgeon's eyes (9). In the meanwhile, the surgery field remained unrestricted and cognitive matching between MRI images and real-time ultrasound at the point-of-care was enabled through view-switching to display the holographic projection into the field of vision.

Examination of the separately enumerated biopsy cores was executed through a designated uropathologist expert. Assessment of SMART TB using the smartglass Hololens I by the two performing surgeons was based on following criteria (1 = bad to 10 = excellent) and ten domains adopted from Galati et al.: execution speed, physical stress, comfort, surgery improveness, multitasking, practicality, image quality, battery autonomy, device handling, and device weight (11). Descriptive statistics were used to report patient data, as well operating room times and costs for SMART TB were analyzed, while clinical data were

prospectively collected and perioperative complications and outcomes were assessed. Chi-square test was used to compare groups and those results with p values <0.05 were considered statistically as significant. Finally, we want to state that this pilot proof-of-concept study aims to assess primarily the feasibility of prostate biopsy using the smartglass Hololens I.

Results

SMART TB of the prostate was performed in 10 patients (patients A–J) with suspected PCA, while 7 patients undergoing biopsy for the first and 3 for the second time. The average age of the patients was 70.8 years, while mean PSA elevation was 8.4 ng/dl and digital rectal examination with suspicious for PCA was observed in 2 patients (Table 1).

According to the intraoperative adverse events classification (EAUiaiC) and postoperative complications classifications (Clavien Dindo), we observed no intraoperative complications and minor postoperative complications (Table 2). The average OR time was ~32 min for all cases. SMART TB is intended to expand cognitive fusion biopsy. Therefore, compared to a cognitive fusion biopsy no extra cost beside the equipment acquisition for the Hololens I are necessary. Besides general cost for MRI and biopsy equipment, the investment cost for the Microsoft® Hololens I was ~4580 USD.

TABLE 1 Patient characterization.

Patient Factors		
Parameter, unit		
Mean Age (years)	70.8	(Range 62–79)
ECOG 0	80%	
ECOG 1	20%	
iPSA (ng/ml)	8.4	(Range 4.1–8.9)
PSA ratio	0.18	(Range 0.09–0.31)
PSA density (ng/ml^2)	0.14	(Range 0.07–0.23)
Prostate volume (ml)	61.2	(Range 32–100)
Suspicious DRE, n (%)	2	20%
Previous negative biopsy, n (%)	3	30%
Total PIRADS lesions, n (%)	17	
PIRADS 3	6	35.30%
PIRADS 4	6	35.30%
PIRADS 5	5	29.40%
Localization PIRADS lesion, n (%)	17	
Apex	4	23.50%
Mid	9	52.90%
Base	4	23.50%
	17	
Peripheral zone	13	76.50%
Transitional zone	3	17.65%
Anterior fibromuscular stroma	1	5.90%

TABLE 2 Results of prostate biopsy and histological examination.

Results of Biopsy		
Overall positive Cores, n (total cores)	51	180
Positive Cores, %	28.33%	
Positive Cores systematic biopsy, n (total cores)	23	120 (12/person)
Positive Cores systematic biopsy, %	19.17%	(Range 0–41.66)
Median positive cores per person	2.3	
Positive Cores SMART TB, n (total cores)	28	60 (6/person)
Positive Cores SMART TB, %	46.67%	(Range 0–100)
Median positive cores per person	2.8	
Positive Cores per PIRADS lesion, (%)		
PIRADS 3	16.66%	(0–100)
PIRADS 4	58.33%	(0–100)
PIRADS 5	61.66%	(25–100)
Intraoperative Adverse Events (EAUiaiC)	None	0%
Postoperative complications within 7 days (Clavien Dindo >1)	None	0%
Histological Results		
Prostate cancer, Gleason grade: systematic biopsy vs. SMART TB	Systematic biopsy	SMART TB
Patient A	Gleason 6	None
Patient B	Gleason 6	Gleason 6
Patient C	Gleason 6	Gleason 6
Patient D	Gleason 6	Gleason 6
Patient E	None	None
Patient F	Gleason 7b	Gleason 8
Patient G	Gleason 7b	Gleason 7b
Patient H	None	Gleason 7a
Patient I	Gleason 7a	Gleason 7a
Patient J	PIN	PIN
PCa (Gleason $\geq 3+3=6$), n (%)	8	80%
csPCa (Gleason $\geq 4+3=7a$), n (%)	4	40%
Prostate cancer likelihood per PIRADS lesion, % (per targeted core of PIRADS lesion)		
PIRADS 3	16.67%	(16.67%)
PIRADS 4	66.67%	(58.3%)
PIRADS 5	100.0%	(61.67%)

Table 2 shows the histological results of systematic biopsy in comparison to SMART TB. Overall, 180 cores were obtained and 51 (28%) of these showed PCA of any Gleason score ($\geq 3+3=6$). 28 of 60 cores (47%) for SMART TB and 23 of 120 cores (19%) for systematic biopsy revealed PCA of any kind. The chi-square statistics revealed with a p-value of 0.000114 ($p<0.05$) a significant superiority for SMART TB. Considering the PI-RADS v2 score, PIRADS lesions ($n=17$) were distributed over the complete prostate, but they were more likely found in the mid (53%) and peripheral zone (76%). The detection rates for particular PIRADS lesions showed 17% for PIRADS 3 (1/6),

67% for PIRADS 4 (4/6) and 100% for PIRADS 5 (5/5), while detailed analysis demonstrated likelihood for prostate cancer according to each targeted core of a PIRADS lesion was 17% (PIRADS 3), 58% (PIRADS 4) and 62% (PIRADS 5).

Adenocarcinoma of the prostate was found within histological examination in eight (80%) and clinically significant prostate cancer (csPCa) in four (40%) cases regardless of biopsy technique. In addition, only due to SMART TB detection of csPCa was observed in one patient and another patient received upgrading to high risk PCA because of SMART TB, while one low risk prostate cancer (Gleason 3 + 3 = 6) was only detected by systematic biopsy.

The performing surgeon assessed SMART TB using the smartglass Hololen I towards abovementioned criteria (scale from 1 to 10): multitasking (10), practicality (10), execution speed (9), comfort (8), surgery improvement (8), image quality (8), physical stress (6), device handling (6), device weight (5), battery autonomy (4) (**Figure 2**).

Discussion

Beside the fact that technical maturity of smartglasses is yet missing (13), several studies demonstrated general feasibility, safety and usefulness of smartglasses in the field urology (6,12). Based on our findings from our initial pilot proof-of-concept study with first description of SMART TB (9) we transferred our promising experiences to a more advanced mixed-reality tool now using Microsoft's Hololens I and extrapolate our innovative approach towards a larger cohort ($n = 10$). SMART TB using the smartglass Hololens I was expectable associated with higher detection rates then the common 12-core systematic biopsy (47% vs. 19%) for PCA of any kind, while we must clarify that systematic biopsy is not the most appropriate comparator. Histological examination revealed adenocarcinoma of the prostate in 8 of 10 patients (80%), while detection of csPCa was observed in 4 out of 10 cases (40%). These findings are almost overlapping with our results from our pilot-proof-of concept study performing SMART TB using the Vuzix®Blade, were we demonstrated PCA detection rates for all SMART TB of 46%. For regular cognitive MRI-guided biopsy techniques, the literature reports here referring to larger cohorts detection rates between 27.0% and 69.7% for csPCa (9). In further comparison Wegelin et al. demonstrated respectively for the well-established but more sophisticated techniques like in-bore MRI target biopsy (MRI-TB) and MRI-TRUS fusion target biopsy (FUS-TB) detection rates for csPCa of 55% and 49% (1). However, there is some evidence that MRI-TB, neglecting its complex and expensive set-up, achieves superior detection rates compared to FUS-TB and COG-TB (14).

Rouviere et al. reported for example poorer detection rates for targeted biopsy over systematic biopsy (32.3% vs. 29.9%) in 251 men (15) than that reported for SMART TB (47% vs. 19%) in our study. Taking the findings of our pilot-proof-of concept paper into concern we also demonstrated for SMART TB using the Vuzix® Blade higher detection rates over systematic biopsy (46% vs. 27%) (9). However, due to the small cohort size ($n = 10$) in our study we have to state that a suitable comparison with these findings is currently not possible. Furthermore, according to the PI-RADSv2 score classification targeted biopsy for a total of 17 index lesions lead to detection of PCA in 17%, 67% and 100% for PIRADS 3, PIRADS 4 and PIRADS 5 lesions. Literature shows here to be highly inhomogeneous, while Barkovich et al. demonstrated satisfying overall sensitivity for suspected lesions with a PIRADS score ≥3 in their meta-analysis (including 59 studies) with observation of detection rates for csPCa after targeted prostate biopsy of 6% for PIRADS 1/2, 12% for PIRADS 3, 48% for PIRADS 4 and 72% for PIRADS 5 (16).

Summarized, we found higher detection rates using SMART TB than systematic biopsy, and although PCA was often detected by both procedures, its detection was more likely and more accurate due to upgrading when SMART TB was performed. In comparison to common cognitive MRI-guided biopsy techniques, we found no major difference concerning detection rates, even if comparison lack of evidence. In addition, SMART TB using the Hololens I was expectable performed safely for surgeons and patients, while we observed no intraoperative (EAUiaiC) and no major postoperative (Clavien Dindo) adverse events.

Some minor findings also need to be addressed. Even if to date technical maturity is yet missing (13), a rash of three-dimensional visualisation techniques using augmented or virtual reality have been investigated for surgery. These tools especially focus on education, training models, surgical planning and intraoperative guidance (17). Our findings demonstrate good overall operability for SMART TB using Microsoft® Hololens I. Assessment of SMART TB by our two surgeons according to the adopted criteria of Galati et al. (11) revealed good clinical practice in the domains of multitasking, practicality, execution speed, comfort and surgery improvement, while device handling, device weight and battery autonomy still require improvement (**Figure 2**). It is noteworthy that especially due to enhanced image quality of the Hololens I a relevant improvement of SMART TB was observed, as compared to our pilot proof-of-concept study using the Vuzix® Blade Version 1.0 (9).

However, cognitive real-time matching at point-of-care of transrectal ultrasound with the mpMRI images optimizes orientation and navigation. With future advancements in the field of mixed reality technologies, it can be assumed that optimized intraoperative guidance will lead to superior accuracy. Our results concur with the conclusion of several colleagues that technological improvements are still necessary before mixed reality devices can be used regular in operating rooms (11), as well more studies are needed to clarify their widespread use (17). With further improvements in see-

through devices optimizing image quality and the widespread use of software generating easily three-dimensional reconstruction of radiological imaging, augmented and virtual reality application for intraoperative guidance is expected to be widely implemented in clinical practice (7).

Some limitations of this study need to be addressed. First, we must state that comparing systematic biopsy and SMART TB could lead to misinterpretation of superior SMART TB detection rates, especially because both procedures were performed by same physicians. In general, SMART TB as we described above stays to date a simple cognitive target biopsy, even if next stages of technology developments will focus on generation of intraoperative matching tools for smartglasses. Our observed detection rates therefore may have been achieved with common COG-TB without using a smartglass. Additionally, even better detection rates could have been observed using MRI-TB or FUS-TB. Noteworthy, detection rates for MRI-based biopsy techniques including our SMART TB are highly dependent on the experience of the performing surgeons and their ability to understand prostate mpMRI and transrectal ultrasound (18, 19), as well our small cohort size of only ten patients represents certainly a source of bias.

Finally, we aimed to improve pure cognitive matching for target biopsy of the prostate through a mixed reality tool using a smartglass. Based on our findings we believe to have created a feasible innovative procedure that beside the need of further technical developments contains great potential to increase detection rates of csPCa in future.

Conclusion

SMART TB of the prostate might enhance MRI-guided targeted prostate biopsy and has the potential to increase detection rates of clinical significant prostate cancer in future, even if further investigation and technical developments are still highly warranted.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by Ethikkomission Rheinland-Pfalz ethic board number: 2020-15290. The patients/participants provided their written informed consent to participate in this study.

Author contributions

SP: design, execution, manuscript writing, conceptualization; HM: execution, editing; FL: data analysis; BK: data analysis; BC: technical consultant; HT: technical consultant; SK: resources, image editing; BMP: investigation; MR: critical revision; HT: critical revision, project administration; TI: supervision; HA: supervision; BH: design, manuscript writing, conceptualization, methodology. All authors contributed to the article and approved the submitted version.

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Conflict of interest

There are no conflicts of interest to declare by all authors.

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EDITED BY
Volkan Ulker,
Medicana International Izmir Hospital, Turkey

REVIEWED BY
Michael Lipkin,
School of Medicine, Duke University,
United States

*CORRESPONDENCE
Nithesh Naik
nithesh.naik@manipal.edu

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Role of three dimensional (3D) printing in endourology: An update from EAU young academic urologists (YAU) urolithiasis and endourology working group

B. M. Zeeshan Hameed[1,2,3], Amelia Pietropaolo[2,4], Nithesh Naik[3,5]*, Calvin Noronha[5], Patrick Juliebø-Jones[2,6,7], Ioannis Mykoniatis[2,8], Francesco Esperto[2,9], Milap Shah[3,10], Sufyan Ibrahim[3,11], Dasharathraj K Shetty[12], Hadis Karimi[13], Diya Sharma[14], Bhavan Prasad Rai[2,15], Piotr Chlosta[16] and Bhaskar K. Somani[2,4]

[1]Department of Urology, Father Muller Medical College, Mangalore, Karnataka, India, [2]European Association of Urology – Young Academic Urologists (EAU-YAU) Urolithiasis and Endourology Working Group, Arnhem, Netherlands, [3]iTRUE (International Training and Research in Uro-oncology and Endourology) Group, Manipal, Karnataka, India, [4]Department of Urology, University Hospital Southampton NHS Trust, Southampton, United Kingdom, [5]Department of Mechanical and Industrial Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, Karnataka, India, [6]Department of Urology, Haukeland University Hospital, Bergen, Norway, [7]Department of Clinical Medicine, University of Bergen, Bergen, Norway, [8]Urology Department, School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece, [9]Campus Bio-Medico University of Rome, Roma, Italy, [10]Robotics and Urooncology, Max Hospital and Max Institute of Cancer Care, New Delhi, India, [11]Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India, [12]Department of Humanities and Management, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, Karnataka, India, [13]Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal, Karnataka, India, [14]Department of Mechatronics Engineering, Manipal Institute of Technology, Manipal Academy of Higher Education, Manipal, Karnataka, India, [15]Department of Urology, Freeman Hospital, Newcastle upon Tyne, United Kingdom, [16]Department of Urology, Jagiellonian University in Krakow, Kraków, Poland

The management of nephrolithiasis has been complemented well by modern technological advancements like virtual reality, three-dimensional (3D) printing etc. In this review, we discuss the applications of 3D printing in treating stone disease using percutaneous nephrolithotomy (PCNL) and retrograde intrarenal surgery (RIRS). PCNL surgeries, when preceded by a training phase using a 3D printed model, aid surgeons to choose the proper course of action, which results in better procedural outcomes. The 3D printed models have also been extensively used to train junior residents and novice surgeons to improve their proficiency in the procedure. Such novel measures include different approaches employed to 3D print a model, from 3D printing the entire pelvicalyceal system with the surrounding tissues to 3D printing simple surgical guides.

KEYWORDS

urolithiasis, 3D printing, percutaneous nephrolithotomy, calyx, calculus

Introduction

Recent technological advancements have been extensively applied in medicine to improve the overall effectiveness of the care received by the patients. Technologies such as additive manufacturing and augmented reality have been broadly adopted to supplement surgeon expertise provide better overall success rates and reduce co-morbidities. 3D printing has been used to print anatomically accurate models of the human organs to be treated. These models help in viewing the 3D geometry of the organ instead of just the 2D model through different imaging like computed tomography (CT) scans. Also, the models are used for preoperative training and preparation. Complex procedures are hard to learn for junior residents because of their steep learning curve and limited case volume. These reasons render 3D models an attractive alternative to train residents and improve procedural expertise. In urology, numerous studies have highlighted its effectiveness as a medium for not only resident education but patient education as well as a part of pre-operative guidance, planning and counselling (1). Amongst published literature on applications of 3D printing in urology nearly 56% have used pre-operative surgical planning as their primary outcome. The most common being planning of procedure on kidneys such as partial nephrectomy (2–6). The second most common being prostate cancer related surgery (7–9).

Surgical management of urolithiasis involves the use of complex procedures. The three main endourological procedures are percutaneous nephrolithotomy (PCNL), retrograde intrarenal surgery (RIRS), and extracorporeal shockwave lithotripsy (ESWL). PCNL is the most efficacious option for a stone size greater than 20 mm or for stones located in the lower pole of the renal pelvis (10). For stone burdens smaller than 20 mm, any one of the three procedures can be chosen based on the surgeon's preference (11). The total stone clearance rate of PCNL is around 92%, which is a significant advantage over other endourologic procedures; nonetheless, a morbidity rate of 26% has limited PCNL's wider adoption (12). The most concerning sequelae associated with PCNL are mortality and nephrectomy, reported as 5/10,000 and 2/1000, respectively (13, 14). In general, the learning curve for PCNL is between 20 and 100 operations, with experienced urologic departments reporting 1.8% morbidity. The **Figure 1** shows the process involved in three-dimensional (3D) printing of patient-specific kidney model.

PCNL training can be done using models that fall into three broad categories: virtual reality trainers, artificial models, and models using animal organs. Virtual reality trainers are expensive (~$100,000), and animal models do not accurately replicate the human anatomy and are single-use and require stringent cleaning measures (15–17). The previous literature describes that the three-dimensional models help urologists with PCNL training. But, the necessity of this procedure for large stone sizes has created a need for exploring technological advancements that can help improve the procedure's success rate. These are especially the technologies that can simulate the patient's conditions preoperatively. Because of the incredible anatomical accuracy of the printed models and the low costs associated, 3D printing has had a significant impact in urology among the wide range of simulation technologies. It has been used successfully to enhance patient education, preoperative planning, and simulation-based training (18–21). This review explores the studies to describe the success achieved using 3D printing technology and future avenues that can be pursued to improve the usage of the technology in endourology (12). **Table 1** summarises the recent studies related to three-dimensional (3D) printing in endourology.

3D Printing for retrograde intrarenal surgery (RIRS)

Orecchia et al. (22) introduced a set of 3D printed models of the upper urinary tract and stones that were designed to improve the training process. Anonymised Digital Imaging and Communication in Medicine (DICOM) files from Computerised Tomography (CT) scan were collected from patients with renal stone cases. Six cases were selected based on the type and complexity of the pelvicalyceal system. The 3D triangulated mesh was formed using these files, which were then optimized by an expert 3D modeler and exported in stereolithographic (.stl) format. Stones were produced in two categories; soft stones with 1:1 chalk and water ratio by weight and hard stones with 1.5:1 chalk and water ratio. Six different training models, each costing between €200–400, were obtained, showing great anatomical accuracy. Five expert urologists conducted several trials using hard and soft stones. Each model was employed over 50 times without any loss of integrity due to repetitive strain or heat transfer from the laser fiber. It was proposed that this model can be used as a training tool in every surgical step of RIRS, thus helping improve surgical expertise among the trainees.

3D Printing for percutaneous nephrolithotomy (PCNL)

PCNL is considered one of the most complex procedures to treat renal calculi with a steep learning curve. With limited hands-on training, it is hard for surgeons to gain competency, and hence, several studies have investigated the role of 3D printed models in providing preoperative guidance (26). Bruyere et al. (12) treated a 65-year-old man with a 12 mm radio-opaque renal stone using a training model before the actual PCNL procedure. The model was fabricated using a

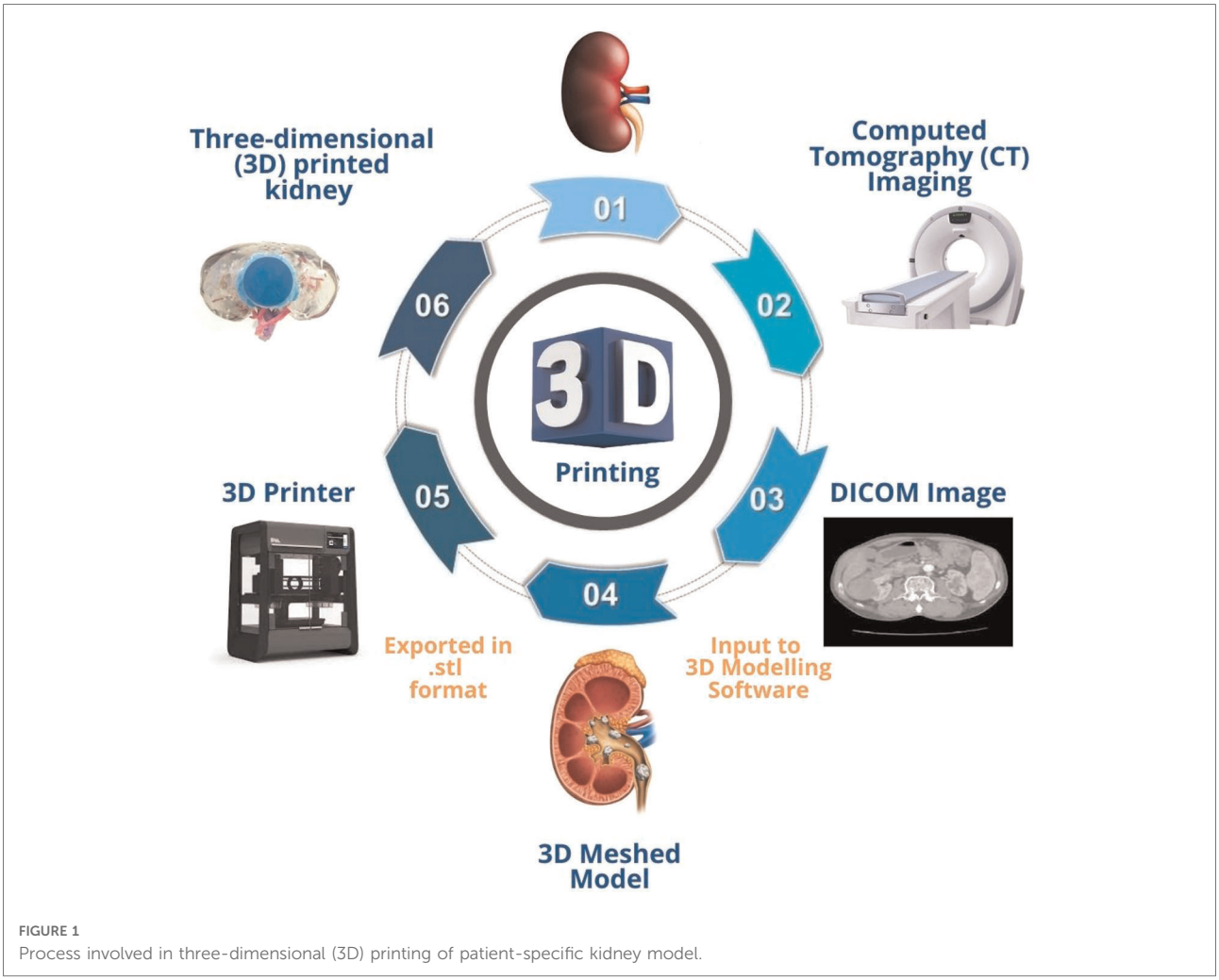

FIGURE 1
Process involved in three-dimensional (3D) printing of patient-specific kidney model.

rapid prototyping machine by Z-Corporation, which was fed with an STL file obtained by advanced three-dimensional modeling software. Rapid prototyping created an abdominal cavity, and a balloon was inserted between the kidney and the abdomen to replicate the kidney movement during respiration. Two urologists performed PCNL on the model before the patient's surgery. The procedure followed on the model was precisely replicated by the urologists on the actual patient, resulting in a successful procedure. The model was used six different times for training before the silicone was damaged.

Knezevic et al. (31) used standard CT imaging to carry out 3D printing and produce a high-fidelity physical model of the kidney and a complex renal stone. They reported multiple benefits of using 3D models over standard CT images: better treatment decision-making for the patients, supplement standard educational material, understanding the condition and need for surgery, and better preoperative preparation for the surgeons. The 3D model highly resembled the actual anatomy of the kidney and the stone. Xu et al. (23) used 3D printing to enhance the stone-free rate for the treatment of staghorn stones. This study had twelve patients with stones larger than 4 cm involving the renal pelvis and at least three major calyces. Also, all the patients were in the age group of 18–70 years with an average age of 50.6 ± 12.6 years. Each of the models' stones had an average CT Hounsfeld unit (Hu) value of 850 Hu. Full staghorn stones are challenging to treat because these are large stones that occupy all the renal pelvis and at least two major calyces (32). The 3D printed model was used for preoperative preparation and training. Patient-specific 3D models were printed, and each patient had three identical models printed, with stone models printed with gypsum and kidney models with silicone. These models were used to choose the ideal calyx to puncture, and the entire procedure was performed on the model.

Post-operative CT scans were performed on the models to check the volume of the residual stones. The stone volumes (measured in cubic millimeters) were compared between the model and the patient preoperatively, and the values were found to be close for all 12 patients. When measured post-operatively, the stone volume in patients showed a significant

TABLE 1 Summary of recent studies related to three-dimensional (3D) printing in endourology.

Author	Sample size	Materials used	Findings
Retrograde intra-renal surgery (RIRS)			
Orecchia et al. (22)	–	Water-soluble polyvinyl alcohol for scaffold; white thermoplastic polyurethane for pelvicalyceal system	Each step of the procedure was meticulously simulated to resemble real-life scenarios closely. Because of the anatomical complexities of each model and type of stone, surgeries of increasing difficulty were replicated with relative ease
Percutaneous nephrolithotomy (PCNL)			
Bruyere et al. (12)	1 (65 y.o.)	Silicone	Rapid prototyping is beneficial for resident education because it allows for creating a large number of models for research and surgical training.
Xu et al. (23)	12	Stones: Gypsum, Kidneys: Silicone	Correlation and consistency analyses revealed a high degree of consistency between patients and 3D-printed models.
Ali et al. (24)	–	Calyces and bones: Polylactide, Kidneys, and Torso: Silicone	Forty second-year residents were separated into groups A and B (A – trained using a simulator and B – trained using the 3D printed models). Residents who used the 3D-printed PCNL models performed better under all metrics.
Vernez et al. (25)	–	Thermoplastics	Twelve urology residents split into groups A and B (A – used CT scans and 3D models, B – used CT scans alone). Group A scored more in the questionnaire, implying that the 3D model is a good training resource for residents and fellows
Atalay et al. (26)	5	Acrylonitrile butadiene styrene (ABS)	Residents were 86% and 88% better at determining the number of anterior and posterior calyces, respectively, 60% were better at the understanding stone location, and 64% were better at determining the optimal entry calyx into the collecting system.
Kuroda et al. (27)	1 (46 y.o.)	-	Precise simulation of the procedure using a 3D printed model helped perform a safe and effective procedure for lithiasis in allograft kidneys and ureter.
Turney et al. (28)	–	Water-soluble polyvinyl plastic coated with silicone (PVC was then dissolved to obtain a cavity)	This silicone PCNL training model accurately replicates the anatomic architecture and orientation of the human renal collecting system. It provides a safe, clean, and effective training model for fluoroscopy-guided PCNL access.
Golab et al. (29)	1 (51 y.o.)	Polylactic Acid (PLA)	Surgical guide printing proved to be very effective during the surgery and is cheaper than printing the entire pelvicalyceal models. The quality of the 3D printout obtained using fused deposition molding was good, and hence an industrial-grade printer is not a requirement.
Ghazi et al. (30)	–	Polyvinyl alcohol	The model, tested both by experts and novices, was rated highly for its realism and educational effectiveness, with novices agreeing unanimously that the model should be used preoperatively

reduction from the preoperative values. Xu et al. (23) study findings showed that mean postoperative stone volume of $1399.9 \pm 1298.7\ mm^3$ for the models (MPoSVM) from the most precise puncture simulation. The mean patients' postoperative stone volume (MPoSVP) averaged $1{,}605.7 \pm 1{,}600.5\ mm^3$. Postoperative stone volume for the patients (PoSVP) and postoperative stone volume for the models (PoSVM) had a Pearson product-moment correlation coefficient of 0.972 ($p < 0.001$, 95% confidence interval (CI) = 0.900-0.992), and the Bland-Altman plot of PoSVP to PoSVM showed % consistency 205.8 (−725.5–1137.1) with 100% points within the limit of agreement. These findings indicate that the simulation's results can be reliably applied in realtime for the actual patient.

Ali et al. (24) used 3D printed models exclusively for training and compared the training outcomes using the 3D printed models to those of the URO Mentor™ simulator. The pelvicalyceal system was 3D printed, and the kidney model's silicone scaffold was made through polymerization by coating over the printed pelvicalyceal system. Forty second-year residents were recruited for the study, and two groups were made, with group A being the simulator group and group B being the 3D printed model group. Five different models were printed and used for the study, and the models were reassembled and repaired after each session of five residents. After the training, each resident was given a self-administered questionnaire with eight questions, each of which was to be scored between 1 and 10. Group A total average was 65.20, and for group B, it was 76.18.

The Mann-Whitney *U*-test revealed a significant difference between groups ($U = 16$, $p < 0.05$). Groups A and B did the x-ray-guided puncture during the first half of the training. The following indices received the highest scores from the participants: x-ray guided pelvicalyceal system puncture (7.30 vs. 8.10); Guidewire placement (6.60 vs. 9.00); Identification of the correct calyx for a puncture (8.70 vs. 9.60); Nephrostomy tube placement (8.00 vs. 9.88); Kidney anatomy evaluation using x-ray imaging (8.60 vs. 9.85); Tissue model feedback (8.40 vs. 9.96); Discussion of post-training errors (7.70 vs. 9.94). Following the main stage, group B performed

an extra assignment with the following marks: US-guided pelvicalyceal system puncture (8.9), Tract dilatation (9.1), Lithotripsy Skill (9.6). This ability was not examined in Group A since it was not available on the simulator utilised. The study shows that the group that used 3D printed PCNL models performed better on all metrics, and this model can be an effective tool that can facilitate preoperative training.

A pilot study by Vernez et al. (25) assessed the educational utility of the 3D printed model by separating 12 residents and fellows into two different groups where one group used the model and the CT scans (group A), and the other group relied on the CT scans alone (group B). The questionnaire gauged the members' familiarity with the stone shape, location, and orientation and their ability to locate the optimal calyx of entry to formulate a proper operative plan. The average trainee questionnaire scores for Group A and Group B were 38/50 and 29/50, respectively ($p = 0.15$). Group A demonstrated stronger familiarity with stone shape and orientation (8.2/10 vs. 6.2/10, $p = 0.097$), greater ability to select appropriate calyx of entry (8.17/10 vs. 5.2/10, $p = 0.11$), and higher overall confidence in completing PCNL (6.7/10 vs. 4.67/10, $p = 0.12$). The renal model was deemed beneficial by all trainees (6/6) who used it.

Another pilot study by Atalay et al. (26) generated anatomically accurate models of five patients, which were manufactured using fused deposition modeling (FDM), an additive manufacturing process. Acrylonitrile butadiene styrene (ABS) was used to create the models due to its toughness, high radiodensity, impact resistance, and low cost. The cost per model was roughly $100, and the print time was 2 h per model. Ten residents evaluated the five patients, initially using CT scans and intravenous urography images and then using the 3D models. After both evaluations, each resident completed a questionnaire with 40 questions to assess their ability to estimate the number of anterior and posterior calyces, find the stone location, and determine the optimal entry calyx for the surgery. An experienced urologist with over 100 PCNL surgeries had already decided on the procedure. Hence, the residents were graded based on their responses in the questionnaire, with each correct answer receiving 5 points and a wrong answer losing 1 point. Following the model presentation, recognising the number of anterior and posterior calyces increased by 52% ($p = 0.018$) and 76% ($p = 0.009$), respectively, knowing stone position improved by 28% ($p = 0.035$), and predicting the best entrance calyx into the collecting system improved by 64% ($p = 0.020$). When paired with 2D data, all residents felt that the models may help with surgical planning and could be used as teaching aids in complicated procedures.

Kuroda et al. (27) presented a case of a 46-year-old man who successfully had antegrade ureteroscopy for lithiasis in his allograft ureter. At a planned follow-up, 15 years following transplantation, computed tomography (CT) revealed a 12 mm renal stone in the transplanted kidney's renal pelvis. During follow-up, the patient had extensive hematuria as the stone had migrated to the ureter and caused hydronephrosis. Because the allograft kidney is denervated, ureteral stones do not cause considerable discomfort in kidney transplant patients. This frequently results in a delay in detecting stone disease, which can lead to renal failure and graft loss. Asymptomatic hematuria in our case allowed us to detect hydronephrosis and ureteral stone. The transplanted ureter had hydronephrosis and a 15 mm stone, as shown by ultrasound and non-contrast CT. A 3D printed model was used to assess the condition, and the puncture of the upper renal calyx was decided to be the best approach to access the stone. The surgery was carried out as planned, and a stone-free status was achieved without any complications. Antegrade URS for stone disease in the allograft ureter was successfully performed using accurate simulation and 3D imaging.

Ghazi et al. (30) created a Simulated Inanimate Model (SIM) of an idealised pelvicalyceal system and staghorn stones from DICOM images of multiple patients. This model was mainly composed of polyvinyl alcohol with different polymer concentrations and degrees of cross-linking to replicate the exact human tissue properties. Five experts (four urology, one interventional radiology) and ten novices (eight urology, two interventional radiology) participated in the study and answered two questionnaires with questions rated on a 5-point Linkert scale. The realism of the model and its educational effectiveness received scores of 4.25/5 and 4.75/5, respectively. The most significant educational impact of the model was to teach and refine technical skills (4.71) and evaluate performance (4.57). All novices agreed that training on this model should be done preoperatively. The experts performed significantly better in metrics including mean fluoroscopy time, the number of percutaneous access attempts, and the number of needle repositioning, which implies that novices benefit the most from the model in terms of improving technical skills and their expertise in the procedure.

Turney et al. (28) used 3D printing to produce an anatomically accurate human renal collecting system to train fluoroscopy-guided PCNL access. 3D models for the collecting system were printed using water-soluble polyvinyl alcohol plastic and then covered in the anatomically correct orientation in silicone. The silicone was dried, and then the printed model using water-soluble plastic was flushed out to create calyceal cavities. The model was then filled with a contrast medium, sealed with waterproof tape, and covered using a layer of dense form to replicate the tissues between the skin and the kidney. The material costs of the model are low (~$100), but the capital costs of the Mimic software used to reformat the images and extract the collecting system anatomy and the 3D printer ($3200) are high. The print time is roughly between 1 and 2 h. The advantages of this model

are that it replicates the human anatomy accurately, is clean and relatively cheaper, and aids complex and high-risk PCNL procedures for planning and forming an excellent preoperative plan. But this model is not suitable for ultrasonographic imaging due to model composition, the consistency of the foam and silicone does not precisely replicate human tissue and organs, and even though the model is recommended for multiple uses (~20), once the tract is dilated, the contrast leaks out and cannot be reused. Nevertheless, the model provides a good training platform, can supplement CT scans, and is significantly better and cheaper than most other alternatives for PCNL training.

While most 3D printed models try to resemble the kidney and stone anatomy, Golab et al. (29) explore the use of 3D printed guides to aid during the surgery. The PCNL procedure was performed with the assistance of a personalised 3D printed surgical guide used to precisely insert the needle into the renal collecting system. The procedure was performed on a 51-year-old woman with a congenital anomaly in the form of horseshoe kidneys that further complicated the PCNL procedure. The CT scan images were loaded onto the 3D Slicer software to produce 3D virtual models of structures that may interfere with the needle path. The external skin surface, kidney stone, collecting system, veins, and bowel were segmented. A safe needle insertion path was also established, and the surgical guide was created with Geomagic Design 3D. A location on the spinous processes (i.e., the L1–L4 vertebrae) was projected on the guide surface to obtain the exact placement of the surgical guide on a flat skin surface. The printed and gas-sterilized surgical guide was placed on the patient's body. After performing fluoroscopic guidance, the needle was inserted into the kidney through the external channel to a pre-calculated depth. The needle precisely reached the calculus in the renal pelvis as predicted preoperatively, and the procedure was completed. The surgical guides have the advantage of simple design and cheaper overall model production.

Conclusion

3D printing is a relatively new technology and has not been extensively used to treat nephrolithiasis. But, the studies conducted so far clearly show that this technology is helpful to visualise the patient anatomy better and aid in preoperative planning, training of residents, and improving the expertise of junior residents in procedures to treat nephrolithiasis. Due to the steep learning curve, more importance to patient care, stricter regulations, and tighter budgets, 3D printed anatomically accurate models can be very helpful in training the residents and help them overcome the initial experience barrier to a certain extent.

Author contributions

BMZ, AP, NN, and BKS contributed to the conception and design of the study. MS, SI, DRS, and PJJ organized the database. DRS, FE, IM, HK, DS and SI wrote the first draft of the manuscript. NN, DRS, BPR, CN, HK, DS and BMZ wrote sections of the manuscript. AP, PC, BPR, and BKS critically reviewed and edited the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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

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EDITED BY
Nithesh Naik,
Manipal Academy of Higher Education, India

REVIEWED BY
Pankaj N Maheshwari,
Fortis Hospital, India
Ajay Oswal,
Seth Nandlal Dhoot Hospital, India

*CORRESPONDENCE
Chen-Wei
doctorcw@126.com
Yi-Shanhong
yshh8810@sina.com

†These authors have contributed equally to this work and share corresponding authorship

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Removal of large fibrotic bladder blood clots using prostatic tissue morcellator under real-time ultrasound guidance

Ronghua Wu[1], Yonggang Shang[2†], Xing Liu[1], Wei Chen[1*†] and Shanhong Yi[1*†]

[1]Department of Urology, Xinqiao Hospital of Army Medical University, Chongqing, China, [2]Reproductive Medicine Center, the First Affiliated Hospital of Chongqing Medical University, Chongqing, China

Objective: Large fibrotic bladder blood clots are difficult to treat *via* conventional methods. Hence, we investigated the safety and reliability of real-time ultrasound guidance combined with prostate tissue morcellator in the removal of large fibrotic bladder blood clots in this study.
Methods: We chose 9 patients with large fibrotic bladder blood clots who were treated in our department from January 2019 to December 2020. Under the condition that conventional methods were ineffective in removing the bladder blood clot, real-time ultrasound guidance combined with a prostatic tissue morcellator was used to remove the large fibrotic bladder blood clot through the steps of positioning, breaking, adjusting repositioning and recrushing. After removal, the bipolar electrocautery was replaced to stop bleeding of the bladder mucosa.
Results: All patients successfully underwent the operation. After the blood clot was removed, the bladder mucosa was examined. There was no damage to the bladder mucosa or muscle layer. The urine was clear at the end of the procedure with slow irrigation, and no bleeding was found again.
Conclusion: Real-time ultrasound guidance combined with a prostate tissue morcellator was a safe, effective and quick method for the removal of large fibrotic bladder blood clots.

KEYWORDS
ultrasound guidance, prostatic tissue morcellator, bladder blood clot, removal, application

Introduction

As a result of trauma, surgery and other factors leading to blood accumulation in the bladder, hematuria leading to clot retention is a common urological emergency. Once the bladder distends and catheter gets blocked, patient has abdominal distension, severe pain with bladder spasms and is in severe discomfort (1). If neglected, can cause bladder overdistension or bladder rupture and would be a serious threat to the patient's life and health (2).

Reasonable and effective removal of blood clots in the bladder is the primary task to solve this part of urological emergency (3). Fresh bleeding can be resolved by

replacing the urinary catheter and washing under a cystoscope (4). However, for the slow accumulation of blood or rapid haemorrhage in the bladder, the urinary catheter is repeatedly blocked and forms a large organized bladder blood clot. The conventional treatment methods, such as using a catheter or ellik evacuator for removal, are characterized by poor efficacy, difficult suction, unclear field of vision, long operation time and vulnerability to accidental damage (5, 6). Therefore, it is necessary to perform a new method of surgical treatment to deal with this urological emergency.

In recent years, based on the development of holmium laser enucleation of prostate, a prostate tissue morcellator has been developed, which can quickly break and suck out the large lobe prostate tissue, shorten the operation time and it is safe and reliable (7). However, in patients with large prostate especially with diffuse bleeding, the vision may be unclear leading to increased risk of bladder mucosal injury during morcellation (8). For such situations, a recent study has demonstrated the improved safety and efficiency of ultrasound-guided morcellation (9).

According to the above principles and experiences, under the real-time guidance of ultrasound, we used a prostatic tissue morcellator to evacuate the blood clot, and improve vision so that hemostasis could be achieved. Nine patients were successfully treated, which is reported in this study.

Methods

Clinical data

Nine patients presented with neglected blood clot retention in bladder because of a variety of reasons. All patients had lower abdominal distension, dysuria, urinary catheter blockage and repeated suction failure. A blood clot was confirmed by ultrasonography and CT scan. The imaging manifestations of large blood clot in bladder under CT scanning and ultrasound were presented in **Figure 1**. Their average age was 70.66 ± 19.65 years. The maximum diameter of the blood clot in the bladder was 9.5 cm, and the minimum was 6.5 cm. The average volume of the bladder blood clot was 205.94 ± 107.49 ml. The average onset time of urinary catheter obstruction was 42.44 ± 15.06 h. The basic characteristics of the included subjects are presented in **Table 1**.

Equipment setup

In this study, we uesed a prostate tissue morcellator (China-made Great White Shark Tissue Shredder) to remove blood clots from the bladder. A photograph of the morcellator was presented in **Figure 2**.

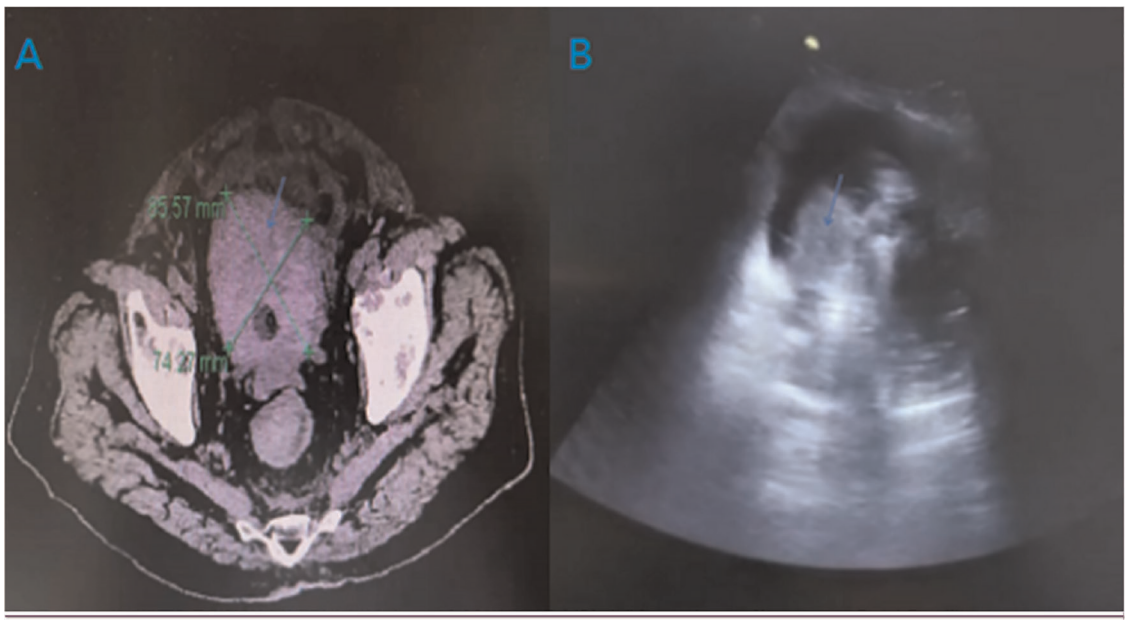

FIGURE 1
Imaging manifestations of large blood clot in bladder under CT scanning and ultrasound [(A): CT, (B) ultrasound; blue arrow: blood clot].

TABLE 1 The basic characteristics of the included subjects.

Case	Age (Years)	Primary disease	Detection method	Clot size (cm)	Clot volume (cm^3)	Duration of disease (Hours)	Operating Time (Mmins)	Conservative methods
1	37	Dangerous Placenta Previa	Ultrasound	7.9*8.0*8.0	262.91	18	35	Catheter aspiration
2	87	Prostate cancer	CT	8.5*7.5*7.0	232.05	23	42	Eillk
3	91	Bladder cancer	CT	5.7*3.4*5.0	50.39	45	51	Eillk
4	79	TURP	Ultrasound	11.5*9.6*7.0	401.86	65	40	Eillk and catheter aspiration
5	93	TURP	Ultrasound	6.9*7.8*6.0	167.91	45	53	Catheter aspiration
6	65	TURP	Ultrasound	5.8*5.7*6.3	108.30	56	36	Catheter aspiration
7	45	Hemorrhagic cystitis	CT	9.6*7.0*8.2	286.54	48	52	Catheter aspiration
8	72	Cystolithotripsy	CT	7.8*7.0*8.0	227.1	34	45	Eillk
9	67	Renal tumor	CT	8*0.4.0*7.0	116.48	48	48	Eillk and catheter aspiration

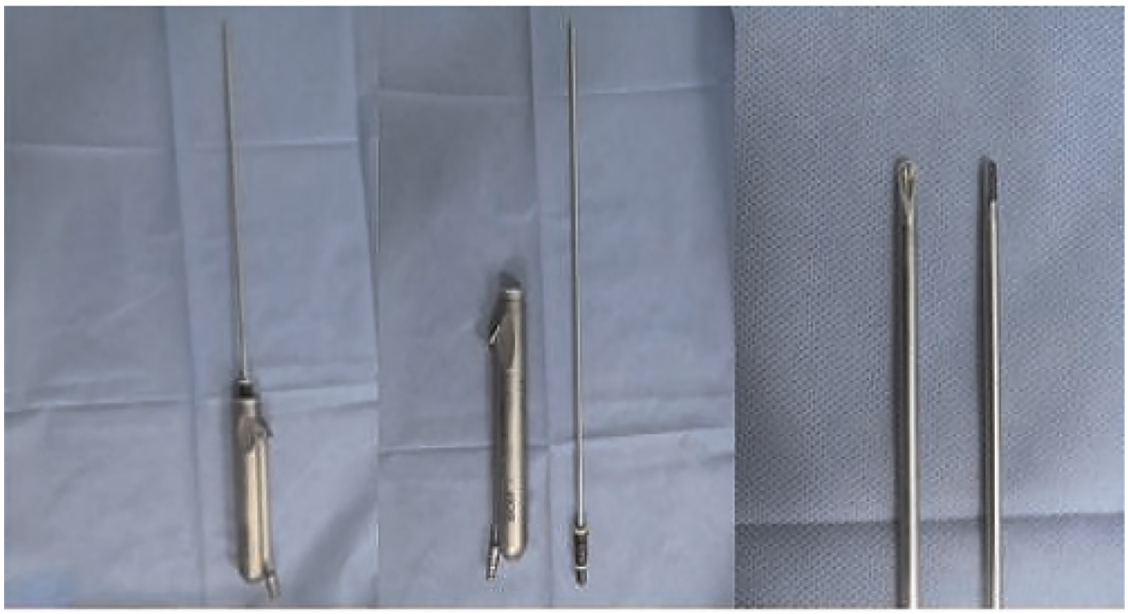

FIGURE 2
A photograph of the morcellator.

Operation methods and techniques used

Under general anasthesia, in lithotomy position after sterile draping, ultrasonographic evaluation of the bladder was done to confirm the clot and to rule out bladder perforation. The prostate tissue morcellator was placed in the bladder and under real-time ultrasound and cystoscopic guidance clot evacuation by morcellator was started. The photograph of fibrotic bladder blood clot under cystoscope was presented in **Figure 3**.

Under real-time ultrasound guidance, the knife head was first placed in the centre of the blood clot. We adjusted the ultrasonic scanning section, and it was repeatedly confirmed that the knife head of the prostate tissue crusher was located in the centre of the blood clot. The cutter head was upwards, the method of point stepping was adopted, each step 3 times, stop 1 time, and adjust the suction gear at the same time to ensure the consistency of real-time water inlet and outlet speed. After removing the central part of the blood clot, the front end of the cutter head was gradually moved in the direction of the remaining clot taking precaution that the

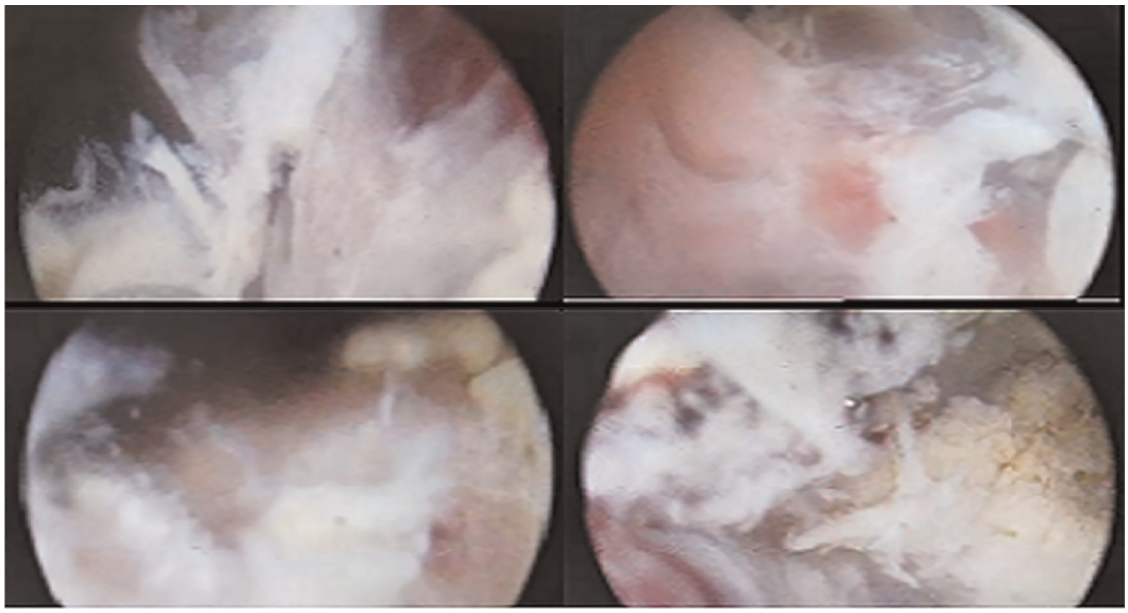

FIGURE 3
The fibrotic bladder blood clots under cystoscope.

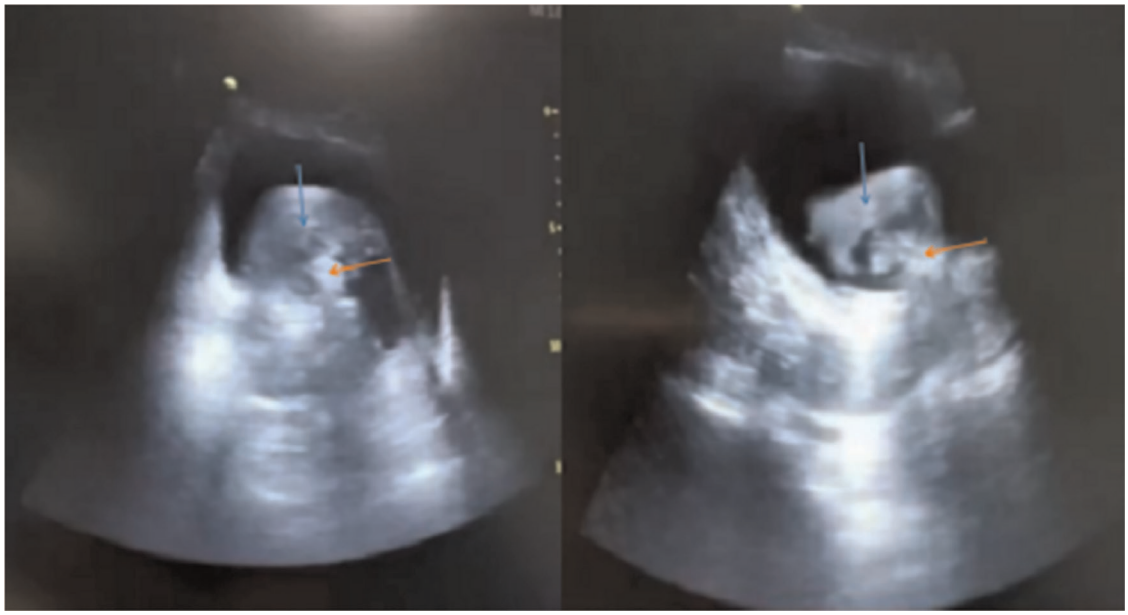

FIGURE 4
The morcellator in the centre of the blood clots under ultrasound guidance (blue arrow: blood clot; Red arrow: morcellator).

cutter head is away from the bladder mucosa. With the gradual removal of blood clots, the visual field became clear, once the vision became clear the terminal small free floating clots were removed under cystoscopic vision. Finally hemostasis was achieved using bipolar cautery. The photograph of morcellator in the centre of the blood clots under ultrasound guidance was presented in Figure 4. For the parts that were easy to bleed, we used the bipolar electrocautery and gradually removed the blood clots. After haemostasis, we closed the water inlet, observed the visual field and water colour, and

checked the whole bladder mucosa, bilateral ureteral openings and bladder triangle. When there was no obvious active bleeding and all bladder mucosa was visible, the operation was ended.

Results

The operation was successfully completed in all cases, all bladder blood clots were removed, and there was no bladder mucosal injury caused by the prostatic tissue morcellator. The washing colour of all patients was clear after the operation. The average operation time is 44.6 min.

Discussion

Bladder bleeding is a common emergency in the department of urology. For bladder blockage caused by acute bleeding, there are many methods to remove bladder blood clots, including replacing urinary catheters and increasing the speed of flushing fluid (10). However, for chronic bleeding, blood clots gradually increase, blood clot organization occurs in the later stage; conventional removal methods have poor efficacy, and patients who undergo such conventional treatments continue to have symptoms such as lower abdominal pain, which is more difficult to treat.

At present, the most commonly used method to remove bladder blood clots is endoscopic blood clot removal and manual bladder irrigation (4, 11), however, there were some disadvantages, such as low suction efficiency and unclear vision. This method might cause bladder mucosal damage and bladder perforation, prolong the operation time and increase the risk of infection (12, 13). One study reported that a tissue pulverizer could be used to remove bladder blood clots. However, when cleaning the large fibrotic clot filling the whole bladder cavity, the inlet and outlet water could not maintain a balance, the treatment effect was poor, and there was a certain risk when the blood clot was broken in a turbid field of vision (14).

Our treatment method has a distinct advantage in difficult situation of neglected large clot retention. As we perform clot evacuation by prostate tissue morcellator under ultrasound control, the crusher is always kept in the center of the blood clot and there is no over distension of the bladder. This avoids the risk of bladder mucosal injury and bladder perforation. We found this procedure safe and rapid reducing the stress on the treating surgeon. Our study was similar to a research suggested that ultrasound guidance combined with tissue morcellator could be an additional tool to utilize during difficult cases when cystoscopic visualization during prostate morcellation was limited (9).

The disadvantage of this method is that it requires the cooperation of both a radiologist and urologist. Radiologist need to track the cutter head orientation of the prostate tissue crusher in real time. In addition, in the early stage of operation, when the field of vision is unclear, it is necessary to manually control the water inflow to prevent bladder rupture and other injuries caused by excessive pressure. It requires the cooperation of many people to complete the whole operation. Additionally, our study is a single arm observational study with a small sample size. A larger multi-institutional randomized controlled trial is important.

Conclusion

Under real-time guidance ultrasound, we changed the direction and depth of the cutter head of the prostatic tissue morcellator and controlled the breaking rhythm, which is a safe, effective and quick method to address the large fibrotic bladder blood clot.

Data availability statement

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

Ethics statement

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

Author contributions

RW, YS, SY are the main implementation of surgery, XL contribution the primary nursing care, WC contribution to the design and funding. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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

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