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Journal Policies

Insight Urology is the official journal of the Thai Urological Association under Royal Patronage. We accept submissions on interesting urological topics from physicians and all medical providers. The topics must not have been previously published.

Objectives

1. To enhance medical research in urology
2. To instigate academic discussions in urology
3. To distribute dedicated works and research in urology

Our experts and native English speakers will review all chosen topics. All of the content and opinions in this journal belong solely to the authors, and do not express the opinions of the editors or the Thai Urological Association under the Royal Patronage.

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Date of Issue Semi-annually (June and December)

Editorial

The seventh issue of Insight Urology (ISU) was published online in December 2023. It comprises four original articles, two review articles, and one case report. It covers several fields of urology, such as general urology, oncologic urology, endourology, and kidney transplantation.

Two review articles were submitted by renowned international authors, namely **"Bibliometric analysis of the relationship between metabolic study and urolithiasis. A key tool in patient management"** and **"Urological malignancies in kidney transplant recipient patients".** We are confident that you will enjoy reading and applying the knowledge in these articles to your present urological work, especially when treating stones in adult patients and cancers in kidney transplantation.

The front cover of this issue features four photographs of new tools and items in the modern Thai urology. The first photograph is of **Robotic Assisted Laparoscopic Surgery** in Rajavithi Hospital. The second is of **Morcellator Instrument** in Phra Pinklao Hospital, while the third photograph is of **High-Intensity Focus Electro Magnetic Chair** in Ramathibodi Hospital. The fourth is of **Video-Urodynamic Study** in Maharaj Nakorn Chiang Mai Hospital.

The back cover of this issue features four additional pictures of current buildings and training facilities. The first picture is of the **Thammasat Medical Skill and Education Center** in Thammasat University Hospital. The second is of the **Bhumisiri Mangkhalanusorn Building and HRH Princess Maha Chakri Sirindhorn Proton Center** where the robotic surgery system and proton therapy take place in King Chulalongkorn Memorial Hospital, while the third is of the **Organ Transplant Ward** in Sunpasittiprasong Hospital. The fourth is of **Soft Skills Training** in Songklanakarind Hospital.

The Editorial Board of ISU hopes that the cover of this issue represents the present stage of modernizations in Thai urology. Just as a quote from the well-known Zen master Thich Nhat Hanh states **"The best way to take care of the future is to take care of the present moment,"** we sincerely believe that Thai urology can improve in the future if good work is done in the present. Concentrating on this moment will create a beautiful future.

No reserve. No retreat. No regret.

Assoc. Prof. Phitsanu Mahawong, M.D.
Editor in Chief of Insight Urology

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Original Article

Risk factors of Fournier's gangrene associated with mortality in Sunpasittiprasong Hospital

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Keywords:
Fournier's gangrene, prognosis, risk factors, index, mortality, necrotizing fasciitis

Abstract

Objective: To determine the mortality rate in patients with Fournier's gangrene (FG) in Sunpasittiprasong Hospital and to identify potential risk factors associated with mortality among patients of FG.

Materials and Methods: This retrospective cohort study investigated patients diagnosed with FG in Sunpasittiprasong Hospital from 2016 to 2021. Data related to clinical presentation, demographics, comorbidities, etiology, laboratory investigation, and therapeutic intervention of the patients were recorded. Prognostic severity indexes were calculated. All factors were statistically analyzed using univariate and then multivariate analysis.

Results: Of 62 patients, the mortality rate was 29% (18 of 62). The significant risk factors for death included patients with kidney disease, septic shock, respiratory failure, acute kidney injury, low mean arterial blood pressure (MAP), admission to ICU and prolonged ventilator used. Risk factors from the laboratory data included abnormal coagulogram, high serum creatinine, lactate, and low bicarbonate. Some prognostic scoring systems were able to predict prognosis and mortality. Multivariate analysis revealed that patients with kidney disease ($p = 0.007$) or respiratory failure at presentation ($p = 0.020$) were significantly associated with mortality.

Conclusions: The significant risk factors associated with mortality among patients with FG were kidney disease or respiratory failure. Some prognostic scoring systems may be applied to Thai patients with FG to predict prognosis.

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Introduction

Fournier's gangrene (FG) is severe necrotizing fasciitis (NF) at the perineum and genitalia resulting from synergistic polymicrobial infection. It usually happens in males aged 30-60 years old.[1] FG is a life-threatening disease because of its rapidly progressive and severe nature. The mortality rate in FG ranged from 16 to 40%[2] even though aggressive debridement and appropriate antibiotics were given. Many studies have shown that factors that affect the outcome of patients with FG can be classified into 3 groups[3]: host-related factors, disease-related factors, and treatment-related factors. Host-related factors included age1,[4-9], gender[4], underlying hypertension[7], diabetes mellitus (DM)[3,10], cardiac disease[5,8], kidney disease[1,6,7,9-11], lung disease[8,9], and cancer.[8] Disease-related factors were clinical signs and symptoms, source of infection[4,12], extent of the disease[1,6], presence of septic shock[8,9], respiratory failure, abnormal laboratory test results, electrolyte imbalance[3,5], coagulopathy[5,7,10], and liver failure.[11] Treatment-related factors included time-to-surgery[8], duration of ventilator-use[8], estimated blood loss (EBL)[8], colostomy[8], and dialysis.[8] Several studies have described the effective use of scoring systems to predict the mortality of patients with FG including Fournier's gangrene severity index (FGSI)[11], Uludag Fournier gangrene's severity index (UFGSI)[13], and the Age-adjusted Charlson Comorbidity Index (ACCI).[14] These can facilitate the design of the most appropriate and feasible management strategies.

In Thailand, currently, there have been no studies on either mortality in FG or the risk factors contributing to the mortality. One study which was related to the issue was a retrospective study from Yasothorn Hospital that found a mortality rate associated with necrotizing fasciitis (NF) for 19%[15], Therefore, we conducted this study with the aim of clarifying the risk factors that affect the mortality in FG to predict the prognosis and assist in early intervention to prevent the progression of the disease.

Materials and Methods

The data was retrospectively reviewed from medical records. Patients diagnosed with FG, who were admitted to Sunpasittiprasong Hospital from January 2016 to June 2021 were included in this study. Diagnosis was confirmed using a combination of clinical, gross anatomic and microbiologic findings. Exclusion criteria were patients for whom the mortality data could not be tracked and when previous debridement had been carried out before visiting Sunpasittiprasong Hospital. Patients who died within 30 days from the date of hospital admission were classed as the nonsurvival group and those who survived within 30 days from the date of hospital admission as the survival group. The data from the two groups were compared to identify the factors associated with death. The study protocol was approved by the Ethical Committee of Sunpasittiprasong Hospital (Protocol number: 052/64 R).

All patient records were analyzed to determine host-related factors, including age, preexisting illnesses, bedridden status, smoking, alcohol use, herb or steroid use and length of hospital stay (LOS). Clinical-related factors included symptoms on admission, physical findings on admission, laboratory results, site of origin of the necrotizing infection, extent and depth of spread, and microbiology of tissue cultures. Treatment related factors included debridement status, number of debridements, time to surgery, operative time, estimated blood loss (EBL), colostomy or suprapubic cystostomy (SPC) performed, and post-operative factors such as duration in ICU or ventilator use. We used 3 prognostic score systems, FGSI, UFGSI, and ACCI, to determine any clinical significance of the factors and their application in Thai patients.

Demographic data and descriptive statistics are presented as mean ± standard deviation (SD.), or median and interquartile range (IQR). To assess possible risk factors for mortality, univariate analyses were completed initially to aid in determining the variables that should be included in a stepwise logistic regression model. Chi-square test or Fisher exact test were used to compare categorical data between the survival and nonsurvival group. For measured variables, the student T-test or Mann-Whitney U test were used to compare the mean or median values between the two groups. The factors with p-values of <0.05 from the univariate analysis were selected for inclusion in the initial step of the multivariable analysis. The level of statistical significance was set at a value of $p < 0.05$. The statistical analyses were performed using Statistical Package for Social Sciences (SPSS®) Statistics version 22.0.

Results

Eighty-three patients with Fournier's gangrene were admitted to Sunpasittiprasong Hospital from January 2016 to June 2021. There were 62 patients who met the inclusion criteria. The mean age was 55 years, the mean period from onset of symptoms to hospital admission was 3 days, and LOS was 14 days. Patients who survived had a significantly longer length of stay in hospital (17 vs 5 days, p-value 0.001). Eighteen patients (29%) died within 30 days after admission. More than a half of these had at least 1 co-morbid disease (63%). Twenty-two patients (35.5%) had DM and, 15 (24.2%) had hypertension. The other demographic characteristics and medical history or comorbidities are shown as in Table 1. There was no significant correlation between demographic characteristics and the underlying disease and mortality in the nonsurvival and survival group, including age, HIV infection, DM, hypertension, heart disease, liver disease, lung disease, stroke, or cancer. Similarly, behavioral factors such as alcohol consumption, smoking, bedridden status, herbal or steroid use were not found to be significantly associated with mortality either. Only patients with pre-existing renal impairment showed a significant association with mortality in both univariate and multivariate analysis (p-value 0.006).

In terms of clinical presentation factors, there was a significant association between patients with respiratory failure within 48 hours (p-value 0.001), septic shock (p-value 0.003), acute kidney injury (AKI) (p-value 0.030) or low mean arterial pressure (MAP) (p-value 0.010) and mortality in univariate analysis. There was no association between mortality and other vital sign parameters. The majority of patients had urogenital area involvement (61.3%), followed by pelvic area (30.6%) and beyond pelvic area (8.1%) at first presentation. The primary source of infection was urogenital (53.2%), followed by anorectal (30.6%) and skin infection was 16.1%. We did not find the relationship between area of disease involvement and mortality nor in the site of infection. The neither urogenital, anorectal or skin disease had

Table 1. Demographic data between the two groups

Demographic data	N	All patients	n	Nonsurvival	n	Survival	P-value
Age (years)	62	54.9 (±16.7)	18	58.2 (±18.0)	44	53.5 (±16.2)	0.312
LOS (days)*	62	14 (7-28)	18	5 (1-12)	44	17 (9-32)	0.001
Co-morbid disease n (%)							
HIV	62	1 (1.6)	18	0 (0)	44	1 (2.3)	1.000
DM	62	22 (35.5)	18	8 (44.5)	44	14 (31.9)	0.346
HT	62	15 (24.2)	18	5 (27.8)	44	10 (22.8)	0.748
Cardiac disease	62	4 (6.5)	18	1 (5.6)	44	3 (6.9)	1.000
Liver disease	62	7 (11.3)	18	4 (22.3)	44	3 (6.9)	0.179
Lung disease	62	3 (4.8)	18	0 (0)	44	3 (6.9)	0.550
Stroke	62	3 (4.8)	18	1 (5.6)	44	2 (4.6)	1.000
Renal impairment*	62	6 (9.7)	18	5 (27.8)	44	1 (2.3)	0.006
Malignancy	62	5 (8.1)	18	0 (0)	44	5 (11.4)	0.309
Comorbidities n (%)							
0	62	23 (37.1)	18	5 (27.8)	44	18 (40.9)	0.331
1	62	20 (32.3)	18	6 (33.3)	44	14 (31.8)	0.908
> 1	62	19 (30.6)	18	7 (38.9)	44	12 (27.3)	0.186
Past history n (%)							
Smoker	62	22 (35.5)	18	9 (50)	44	21 (47.8)	0.871
Alcohol use	62	30 (48.4)	18	7 (38.9)	44	15 (34.1)	0.720
Bedridden	62	15 (24.2)	18	5 (27.8)	44	10 (22.8)	0.748
Herb use	62	5 (8.1)	18	2 (11.2)	44	3 (6.9)	0.622
Steroid use	62	2 (3.2)	18	0 (0)	44	2 (4.6)	1.000

*Significant at $p < 0.05$

LOS = Length of stay, DM = Diabetes mellitus, HT = Hypertension, HIV = Human immunodeficiency virus.

a significant relationship with mortality as shown in Table 2.

Laboratory parameters at the time of admission are summarized in Table 3. We found that most of laboratory parameters did not reflect survivability such as complete blood count (CBC), some electrolytes, blood urea nitrogen (BUN) and liver function test (LFT). However, patients in the nonsurvival group had significantly higher serum creatinine (p-value 0.032), and serum lactate (p-value 0.002) and lower bicarbonate (p-value 0.001) and albumin (p-value 0.016) than those in the survival group. A coagulogram tended to be more prolonged in the nonsurvival patients in the univariate analysis. But none of these factors were significantly associated with mortality in the multivariate analysis.

Table 4 lists the treatment factors. Debridement was carried out in 57 patients, representing 91.9% of the total sample. Of these, the median time to surgery was within 19.5 hours after admission to the hospital and the median number of times undergoing debridement during admission was 3 times (1-3). Most patients were assessed preoperatively using the American Society of Anesthesiologists (ASA) classification III (37%), median duration of surgery was 45 minutes, Median EBL was 50 mL and the majority of procedures were carried out under general anesthesia (GA) (87.7%). Significantly more of the patients who underwent debridement survived in comparison to those who did not undergo debridement. Considering time to debridement, we found that the time to operation in survivors was slightly longer than in the nonsurvivors (19.5 vs 17.5 hours) but did not achieve statistical significance. Operative time, EBL or number of instances of debridement were not found to be related to mortality. A diverting colostomy was performed in 32.3% of patients in our series, but this was not significantly associated with mortality. Unlike patients who had not undergone suprapubic cystostomy, there was significant association with mortality in the univariate analysis (p-value 0.045). Out of the 62 patients, 30 required admission to the intensive care unit (ICU) (48.4%). The median length of ICU stay was 7 days (2-9). All admitted to ICU required mechanical ventilator support which had median time of 3 days (1-7). We also found that patients who survived had a

Table 2. Clinical and etiology parameters between the two groups

Clinical and etiology	N	All patients	n	Nonsurvival	n	Survival	P-value
Symptom duration (days)	62	3 (2-7)	18	3 (2-7)	44	3 (2-7)	0.826
Clinical condition at admission n (%)							
Metabolic acidosis	18	12 (66.7)	8	7 (87.5)	10	5 (50.0)	0.152
Respiratory failure*	62	19 (30.6)	18	11 (61.2)	44	8 (18.2)	0.001
AKI*	62	28 (45.2)	18	12 (66.7)	44	16 (35.4)	0.030
Septic shock*	62	30 (48.4)	18	14 (77.8)	44	16 (36.4)	0.003
Physical examination n (SD)							
Temperature (°C)	62	37.7 (±1.2)	18	37.4 (±0.9)	44	37.8 (±1.2)	0.134
HR (bpm)	62	99 (±18)	18	104 (±20)	44	100 (±18)	0.423
RR (bpm)	62	20 (20-20)	18	20 (18-24)	44	20 (20-20)	0.993
SBP (mmHg)	62	109 (±21)	18	102 (±23)	44	112 (±20)	0.075
DBP (mmHg)*	62	66 (±12)	18	59 (±14)	44	69 (±10)	0.021
MAP (mmHg)*	62	80 (±13)	18	73 (±15)	44	83 (±12)	0.010
Area involvement n (%)							
Urogenital	62	38 (61.3)	18	13 (72.3)	44	25 (56.9)	0.258
Pelvic	62	19 (30.6)	18	5 (27.8)	44	14 (31.9)	0.754
Beyond pelvic	62	5 (8.1)	18	0 (0)	44	5 (11.4)	0.309
Source of infection							
Skin	62	10 (16.1)	18	4 (22.3)	44	6 (13.7)	0.457
Anorectal	62	19 (30.6)	18	5 (27.8)	44	14 (31.9)	0.754
Urogenital	62	33 (53.2)	18	9 (50)	44	24 (54.6)	0.745

*Significant at $p < 0.05$

HR = Heart rate, RR = Respiratory rate, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, MAP = Mean arterial blood pressure, AKI = Acute kidney injury, MDR = Multiple drug resistance, SD = Standard deviation.

Table 3. Laboratory parameters between the two groups

Laboratory	n	Nonsurvival	n	Survival	P-value
Hematocrit (%)	18	27.3 (±7.1)	44	31.1 (±7.7)	0.077
Hemoglobin (g/dl)	18	9.0 (±2.5)	44	10.4 (±2.6)	0.055
White blood cell (x10^3/mm^3)	18	9.97 (1.31-12.22)	44	13.65 (4.94-19.02)	0.092
Platelet count (x10^3/mm^3)	18	171.5 (12.0-415.5)	44	203.0 (20.5-298.8)	0.389
Sodium (mmol/l)	18	133 (±7)	44	133 (±6)	0.722
Potassium (mmol/l)	18	3.9 (±0.7)	44	3.6 (±0.7)	0.181
Chloride (mmol/l)	18	97 (±8)	44	99 (±7)	0.424
Bicarbonate (mmol/l)*	18	16 (±5)	44	21 (±5)	0.001
Blood urea nitrogen (mg/dl)	18	30 (18-39)	44	22 (20-44)	0.180
Creatinine (mg/dl)*	18	2.37 (1.13-6.80)	44	1.00 (0.95-2.68)	0.032
aPTT (s)*	16	45.2 (32.8-96.1)	33	34.6 (26.6-56.3)	0.006
PT (s)*	16	19.4 (17.7-46.5)	33	16.1 (15.9-22.0)	0.000
INR*	16	1.61 (1.48-4.29)	33	1.35 (1.34-1.86)	0.001
AST (U/l)*	10	145 (17-2275)	19	30 (82-239)	0.044
ALT (U/l)	10	55 (12-220)	19	25 (9-102)	0.085
Alkaline phosphatase (U/l)	10	156 (52-170)	19	105 (51-83)	0.353
Total Bilirubin (mg/dl)	10	1.5 (0.2-3.5)	19	0.7 (0.4-7.1)	0.362
Direct Bilirubin (mg/dl)	10	1.1 (0.1-2.9)	19	0.4 (0.3-5.1)	0.390
Albumin (g/dl)*	10	1.9 (±0.7)	19	2.5 (±0.7)	0.016
Lactate (mmol/l)*	6	20.9 (4.7-23.1)	7	2.9 (1.5-6.5)	0.002

*Significant at $p < 0.05$
aPTT = Activated partial thromboplastin time, PT = Prothrombin time, INR = International ratio, AST = Aspartate transaminase, ALT = Alanine amiotransferase.

Table 4. Treatment factors between the two groups of patients

Laboratory	n	All patients	n	Nonsurvival	n	Survival	P-value
Debridement* n (%)	62	57 (91.9)	18	13 (72.3)	44	44 (100)	0.001
Time to Surgery (hour)	57	19.5 (8.8-23.8)	13	17.5 (5.0-22.0)	44	19.8 (9.1-24.0)	0.387
Op time 1st DB (minutes)	57	45 (33-63)	13	50 (33-88)	44	45 (31-60)	0.789
Number of DB (time)	57	3 (1-3)	13	2 (1-3)	44	3 (1-4)	0.289
EBL (ml)	57	50 (40-100)	13	50 (40-125)	44	100 (35-100)	0.690
Diverting Colostomy n (%)	57	20 (32.3)	13	5 (38.5)	44	15 (34.1)	0.754
SPC* n (%)	57	11 (17.7)	13	0 (0)	44	11 (25)	0.045
Post op care							
ICU stay (days) n (SD)*	30	7 (2-9)	16	4 (1-8)	14	8 (5-10)	0.120
On Ventilator (days) n (SD)	30	3 (1-7)	16	4 (1-12)	14	3 (2-5)	0.448

*Significant at $p < 0.05$
Op = operative, DB = debridement, EBL = Estimate blood loss, SPC = Suprapubic cystostomy, ICU = Intensive care unit, SD = Standard deviation.

significantly statistic longer length of ICU stay.

The FG prognostic score systems are shown in Table 5. In our study, the average FGSI, UFGSI and ACCI scores were all higher in the nonsurvival group. Mean FGSI and UFGSI score was more than 9 in the nonsurvival group. Using a FGSI and UFGSI threshold value of 9, there was a 94% probability of death with a score greater than 9, and below 9 was associated with an 81% probability of survival).[3,11] The prognostic scores that

Table 5. Prognostic score

Prognostic score n (SD)	Prognostic score n (SD) Nonsurvival group n = 18	Survival group n = 44	P-value
FGSI*	12.0 (7.5-21.3)	6.5 (8.0-15.3)	0.001
UFGSI*	13.5 (8.5-22.3)	9.0 (10.0-17.8)	0.005
ACCI	3.5 (0.3-2.0)	2.0 (1.8-3.3)	0.215

*Significant at $p < 0.05$
SD = Standard division, FGSI = Fournier's gangrene severity index score, UFGSI = Uludag Fournier's gangrene severity index score, ACCI = Age-adjusted Charlson comorbidity index.

Table 6. Multivariable analysis

	Adjusted OR	95% C.I.	P-value
Renal impairment*	39.19	(2.73-561.67)	0.007
Respiratory failure*	9.99	(1.43-69.84)	0.020
AKI	1.33	(0.23-7.63)	0.748
Septic shock	1.62	(0.24-11.11)	0.626
INR	0.99	(0.81-1.22)	0.955

*Significant at $p < 0.05$
SD = Standard division, FGSI = Fournier's gangrene severity index score, UFGSI = Uludag Fournier's gangrene severity index score, ACCI = Age-adjusted Charlson comorbidity index, OR = Odd ratio, C.I. = Confidential interval, AKI = Acute kidney injury, INR = International ratio.

were significantly associated to mortality were FGSI and UFGSI scores (p-value 0.001, 0.005).

In the multivariate analysis, shown in Table 6, we found that only patients with pre-existing renal impairment or respiratory failure within 48 hours after admission were significantly associated with mortality associated with FG (p-value 0.007, 0.020).

Discussion

Fournier's gangrene is a life-threatening clinical condition, first described by a French dermatologist and venereologist, Jean Alfred Fournier in 1883.[16] FG is an infection caused by aerobic and anaerobic bacteria, spreading along the subcutaneous and fascial plane across the perineum, genital area and sometimes beyond the pelvic area to the lower abdomen or inner thigh. This progressive necrotizing fasciitis of the genitourinary tract has a clinical symptom of an abrupt onset of painful scrotal swelling with rapid progression to gangrene. Systemic signs, including sepsis and septic shock consequently cause respiratory failure or AKI which can occur in10-40%.[12,16] In our series it was evident in 48.4% of cases. FG is still reported as a potentially fatal disease with a high mortality rate of 16-40%.[2,5,9,16-18] In our study the mortality rate was 29%.

Patients with FG included in this study as well as those described in other reports, had advanced age and higher levels of comorbidity which may be related to the mortality due to FG, especially in the case of DM, and HT. However, our study did not find any association between age or underlying disease and mortality, with the exception of patients who had renal impairment. Several reports have suggested that chronic kidney disease (CKD) was a risk factor for mortality in FG.[1,6,7,11,18] One report had a hypothesis that sepsis may exacerbate preexisting renal dysfunction especially in CKD patients.18 This was consistent with our multivariate analysis results, which showed that patients with previous renal insufficiency were significantly associated with mortality.

DM is a factor commonly acknowledged as increasing susceptibility to infection. Some studies have reported that 20-70% of patients with FG had DM.[16,18-20] Hahn et al.[18] believed that the effect of DM on the progression of the disease was due to a decrease in phagocytic and intracellular

bactericidal activity and neutrophil dysfunction. Many studies, however, have reported that DM was not found to associated with FG mortality[8,11,12,16] as was the case in our study.

As mentioned before, FG presents as sudden pain, genital swelling, and rapid progression. Palmer et al.[21] reported that area affected by FG was associated with the treatment outcome. Logically, an increase in the body surface area (BSA) involved would cause greater severity and result in an increased risk for poor prognosis. Several studies confirmed these findings.[3,18] Also, Corcoran et al.[17] found that although total BSA involved was suggestive of poor prognosis, only involvement of the lower extremities and abdominal wall was associated with inpatient mortality. However, a few studies did not find a relationship between extended disease and FG mortality as was the case in our study. This may be due to the difficulty of defining and measuring the exact boundaries of an affected area of disease, which can affect the results.

The common causes of FG are urogenital (periurethral abscess, urethral stricture, indwelling catheter, traumatic catheterization, perineal trauma), anorectal (perianal abscess, fistula in ano, rectal biopsy, rectosigmoid malignancy), or cutaneous infection or local trauma.[2,16] In this current study, the most common etiology was urogenital infection followed by anorectal and skin infection. As was reported in in other series, in ours there was no correlation between etiology and mortality.[16,22] In severe case, sepsis and septic shock may occur, followed by multiple organ failure and finally death. Our univariate analysis found that septic shock, MAP < 65 mmHg, AKI, coagulopathy, high serum lactate and respiratory failure within 48 hours of the time of admission were significantly associated with death, but only patients with respiratory failure within 48 hours were a significant predicting factor for mortality in the multivariate analysis. Metabolic acidosis did not appear to be significantly associated with mortality. Arterial blood gas measurements were not frequently performed at the time of admission which may cause a bias in our results.

From the multivariable analysis the risk factors significantly affecting the mortality in FG in our study were patients who had a previous history of renal disease or those presenting with respiratory failure within 48 hours of admission. However, we still recommend that early recognition, hemodynamic support, aggressive resuscitation, urgent and aggressive surgical debridement, and prompt treatment with empirical broad-spectrum antibiotics are important cornerstones for a successful outcome as described in many other series.[4,16,23,24] The time interval between the onset of symptoms and initial debridement has been reported as being a major factor of predicting mortality[25,26], but not all studies have corroborated that.[27,28] The results are still controversial, and the exact time to carry out the operation needed to be clarified. A large retrospective study, including 379 FG patients, has suggested that early surgical debridement within 2 days of admission reduces FG mortality.[29] Moreover, the data pertaining to the recommended number of instances of surgical debridement performed in each patient is still controversial as some studies found it to be a significant parameter of mortality, while others not.[28,30,31] Faucher et al.[32] stated that initial surgery should be the most important time to debridement, with the aim of resecting all necrotic and infected tissue, regardless of the wound that is created and the potential problems of complete closure. Therefore, a greater number of debridement procedures might not affect the mortality as was the case in our series. A diverting colostomy is sometimes needed to decrease the possibility of contamination, especially in the presence of anorectal involvement or sphincter destruction.4 Some studies have shown significantly lower mortality in patients without colostomy[31,33,34] as well as suprapubic cystostomy, used to adequately diverted urine if a Foley catheter cannot be accomplished.[35,36] However, neither procedure led to a significant difference in survival in our multivariate analysis.

To predict mortality in Thai patients with FG, different scoring systems were used. Our study chose FGSI, UFGSI and ACCI as validated indexes to find whether they were equally applicable in Thai patients. The FGSI score, created in 1995 by Laor et al.[11] included 9 clinical and laboratory parameters. The newer and novel UFGSI, which was created by Yilmazar et al. in 2010 3, also added age and extent of the disease with a maximum of 43 points. Both scoring systems had a cutoff point of 9 which provides a good discriminatory capacity regarding mortality. ACCI, created by Charlson et al.[13], is used to classify the comorbid

conditions which might alter the risk of mortality has a cut-off point of 4. In our studies, the prognostic scores that were statistically significantly associated with mortality were FGSI and UFGSI. We can assume, from the results of the study, that both systems could be applied in Thai patients to help in predicting the prognosis of the FG patient. However, we thought that these scores may take time to calculate in real-life clinical practice. We therefore believe that both tools should be studied further and improved to make their application easier and more effective in general practice for physicians in Thailand.

Our retrospective study is associated with inherent limitations. We focused on mortality and perioperative outcomes only in the patients that visited or were admitted to Sunpasittiprasong Hospital during the study period. Therefore, the patients that had been partially treated or debrided in other hospitals before being referred to our tertiary care unit might affect the outcome of the study. In addition, general care techniques and wound management strategies have evolved significantly over the period covered by our patient registry, which may have impacted on our results.

Conclusions

Fournier's gangrene remains a surgical and urological emergency with high morbidity and mortality. Pre-existing renal impairment and patients presenting with respiratory failure are associated with higher mortality. Early recognition, resuscitation and treatment with aggressive debridement with antibiotics remain the best approach to prevent subsequent septic shock and respiratory failure. Early diagnosis and prompt time to surgery are crucial for a successful outcome. FGSI and UFGSI might be appropriate in Thai patients with FG.

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Conflict of interest

The authors declare no conflicts of interest.

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Original Article

Efficacy of inhalation of a nitrous oxide and oxygen mixture for pain management during rigid cystoscopy: a randomized controlled trial

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Keywords:
Entonox, nitrous oxide, cystoscopy, pain

Abstract

Objective: To evaluate the efficacy of pain management using inhalation of a nitrous oxide and oxygen mixture during rigid cystoscopy.

Materials and Methods: A total of 55 patients were prospectively selected and randomized to receive oxygen (27) or Entonox (28). Both groups were given the respective gas for 3 minutes via breath-activated facemask before cystoscopy and continued to breathe the gas until the end of the procedure. The oxygen and Entonox groups received 20 ml 2% lidocaine gel intraurethral 15 minutes before the procedure. Heart rate, and numeric pain rating scales were recorded before, during, and after the cystoscopy.

Results: Fifty-five patients were randomized into two groups, 27 were given oxygen and 28 Entonox. There were no statistically significant differences between the groups in terms of baseline patient characteristics. Intraoperative rigid cystoscopy pain scores were significantly lower in the Entonox group than in the oxygen group (2.4 vs 4.2, p = 0.009). There were no significant differences between the two groups as regards postoperative pain, intraoperative and post-operative heart rates, and side effects.

Conclusion: Entonox significantly reduces intraoperative cystoscopy-related pain, without significant complications.

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Introduction

Cystoscopy is the most commonly used urologic procedure for both diagnostic and therapeutic purposes such as bladder cancer detection or surveillance, bladder biopsy or ureteral catheterization. Even though many procedures can be performed with a flexible cystoscope to reduce intraoperative pain and discomfort, several procedures still require rigid cystoscopy, which is more painful than flexible cystoscopy.

Studies have demonstrated that insertion of intraurethral lidocaine gel before cystoscopy can reduce pain, but the efficacy of pain management is still subject to debate.[1,2] Current best practice is intraurethral instillation of 20 ml of 2% lidocaine gel 15 minutes before cystoscopy.[3] The most painful part of any urethral procedure occurs when the instrument passes through the external urethral sphincter, which is controlled by the pudendal nerve.[4]

Nitrous oxide, or laughing gas, is a colorless and odorless gas that has analgesic, sedative, anxiolytic, euphoric, and amnesiac effects. It is extremely soluble in blood and eliminated quickly via the lungs. The analgesic effect starts within 20 seconds of inhalation and reaches the maximum effect within 3-5 minutes. These features make nitrous oxide an attractive analgesic option for day-case procedures, including urological interventions.[5]

Entonox® (Linde (Thailand) Public company limited) is a commercial gas product that is composed of 50% nitrous oxide and 50% oxygen. It is a safe and rapidly effective agent used for anesthesia, analgesia and anxiolysis. Entonox is used for pain management in urologic situations in the emergency department such as renal colic pain[6], and also for flexible cystoscopy[7], transrectal ultrasound-guided biopsy for prostate cancer[8,9], or extracorporeal shock wave lithotripsy.[10] Rigid cystoscopy causes more pain than flexible cystoscopy, but it is widely used, and to date no previous studies into the efficacy of Entonox in rigid cystoscopy procedures have been published.

Therefore, we conducted a randomized controlled trail (RCT) to compare the levels of efficacy between Entonox® and a placebo (oxygen) inhalation for pain management during rigid cystoscopy. A secondary outcome was change of heart rate because heart rate normally increases with pain severity.

Materials and Methods

This RCT was conducted from November 2021 to November 2022. The study was approved by the Ethics committee of Thammasat university (Protocol Number: MTU-EC-SU-1-044/64) and the Thai Clinical Trail Registry (TCTR) Committee on November 6, 2021. The TCTR identification number is TCTR20211106001.

Participants

Inclusion criteria were all patients at least 18 years old who needed to undergo rigid cystoscopy with 22 Fr diameter sheath instruments, and who were willing to give their informed consent to participate in the study.

Exclusion criteria were patients who had history of lidocaine or nitrous oxide and oxygen mixture inhalation allergy, neurological disease impairing pain perception, could not communicate in the Thai language, had a history of pneumothorax, had facial injury or maxillofacial bone fracture, or who had a contraindication for use of Entonox.

Randomization

Randomization was performed using permuted blocks of 4 to 6 with assignment by an independent statistician using STATA version 12.0. Gas tank and valve mask appearance were similar for both Entonox and oxygen. Only the nurse in-charge knew which gas tanks were oxygen or Entonox. The in-charge nurse was the same person throughout the study and was the person who prepared the gas tanks for procedures however, never participated in procedures or recorded information. After patients were informed and had given their consent to join this research, they were randomly allocated gas assignment labels in sealed opaque envelopes, which were opened by the in-charge nurse before cystoscopy as shown in Figure 1.

Blinding

Patients and attending physicians, including the endoscopist, scrub nurse, and practical nurse, were blinded to the type of gas.

Pain scores and subjective outcomes, including adverse events, were assessed by the scrub nurse using a numeric rating scale. Heart rates were monitored by practical nurses who were also blinded to the type of gas.

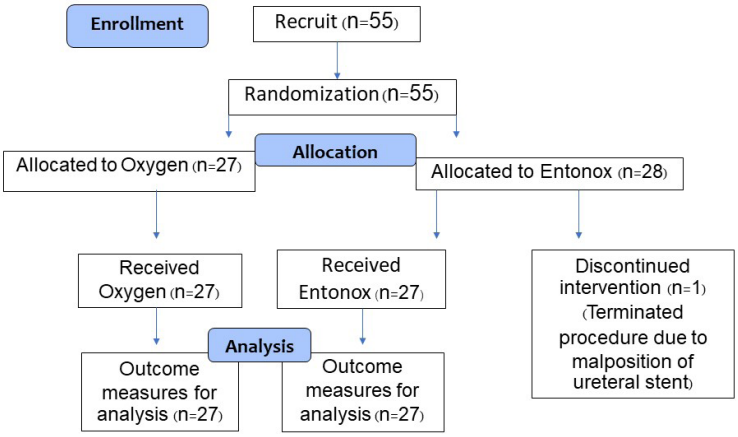

Figure 1. Flow diagram of the RCT.

Interventions

All patients, in both the Entonox® group and the placebo group, received 20 ml 2% lidocaine gel (AstraZeneca®) intraurethrally 15 minutes before cystoscopy. Then, via a breath activated demand valve mask, patients in the Entonox group inhaled Entonox and patients in the placebo group inhaled oxygen, from 3 minutes before cystoscopy until the procedure was completed.

Heart rate and pain score were evaluated before starting the procedure, 15 minutes after starting the procedure, every 15 minutes during the procedure, and immediately after completion of the cystoscopy. Pain perception was recorded using a numeric rating scale.

Statistical analysis was performed using STATA version 12.0. Significance was assumed at a p-value of less than 0.05.

Sample size

Based on a pilot study of 10 cases at Thammasat University Hospital, we compared pain scores between patients who used Entonox and patients who used oxygen during rigid cystoscopy. We found that patients who used oxygen had a numeric pain rating scale of 4.5±2.5 SD but patients who used Entonox had a numeric pain rating scale of 2.5±2.5 SD.

Our sample size was estimated and tested using a two-sided test based on type 1 error 5% and power 80%, suggesting a total of 52 patients (26 per group) were needed. Taking into account a potential loss of data and incomplete procedure of 5%, 54 patients were set as the target (27 per group).

Results

A total of 55 patients were recruited in this study. Twenty-eight patients out of the 55 were randomized to the Entonox group and 27 patients to the oxygen group. One patient from the Entonox group was later withdrawn from the study. (The endoscopist changed that patient's operation to ureterorenoscopy (URS) because a double J stent was malpositioned.) Therefore, 27 patients in each group were analyzed in this study. There were no statistically significantly differences between the groups in terms of sex, age, previous cystoscopy, indication for cystoscopy, additional procedures and timing of the operation as shown in Table 1.

Pain scores during intraoperative cystoscopy in the Entonox group were statistically significantly lower than in the oxygen group (2.4 vs 4.2, p = 0.009) but there were no significant differences in the pre-operative period (0.3 vs 0.4, p = 0.765) or the immediate post-operative period (0.6 vs 1.1, p = 0.177) (Table 2).

There were also no significant differences in heart rate including preoperative cystoscopy (80.9 vs 78.1, p = 0.451), intraoperative cystoscopy (80.9 vs 76.3, p = 0.195) and post-operative cystoscopy (80.9 vs 78.1, p = 0.451) as shown in Table 3.

The main side effects noted by patients were nausea (1 patient (3.7%)), dizziness (4 patients (14.8%)) and euphoria (1 patient (3.7%)). All of these were transient without serious adverse events and were resolved before discharge. There were no significant differences in side effects between the Entonox group and the oxygen group (p = 0.5) (Table 4).

Table 1. Demographic data of the two groups (N=55)

Patient characteristic	Group placebo (n=27)	Group intervention (n=27)
Sex, n (%)		
Male	13 (48.15)	17 (62.96)
Female	14 (51.85)	10 (37.04)
Age (year), mean (SD)	58.7 (11.8)	59.5 (13.1)
Previous cystoscopy, n (%)	12 (44.44)	16 (59.26)
Indication for cystoscopy, n (%)		
Hematuria	4 (14.81)	6 (22.22)
Bladder cancer	3 (11.11)	8 (29.63)
LUTS	3 (11.11)	2 (7.41)
Ureteric calculi	10 (37.04)	3 (11.11)
Vesical calculi	7 (25.93)	6 (22.22)
UTI	0	2 (7.41)
Additional procedures, n (%)		
Biopsy	1 (3.70)	1 (3.70)
Ureteric catheter insertion	13 (48.15)	9 (33.33)
Timing of operation, mean (SD)	23.1 (11.1)	20.7 (9.9)

SD = standard deviation, n = number, LUTS = lower urinary tract symptoms, UTI = urinary tract infection.

Table 2. Comparing of pain scores using the pain rating scale at pre-cystoscopy, during cystoscopy and post-cystoscopy in both groups.

Pain score	Group placebo (n=27)	Group intervention (n=27)	P-value
0 min, (SD)	0.4 (1.6)	0.3 (1.1)	0.765
15 mins, (SD)	4.2 (2.7)	2.4 (2.2)	0.009
Post-op 0 min, (SD)	1.1 (1.7)	0.6 (1.0)	0.177

SD = standard deviation, n = number, min = minute, mins = minutes.

Table 3. Demonstrated comparing the changing of the heart rate at pre-cystoscopy, during cystoscopy and post-cystoscopy of both groups.

Heart rate	Group placebo (n=27)	Group intervention (n=27)	P-value
Baseline bpm, (SD)	78.1 (13.0)	80.9 (13.2)	0.451
HR at 15 min bpm, (SD)	76.3 (12.9)	80.9 (12.7)	0.195
Post op HR bpm, (SD)	78.1 (13.0)	80.9 (13.2)	0.451

SD = standard deviation, n = number, bpm = beats per minute, HR = heart rate, min = minute.

Table 4. Comparison of adverse events between the groups.

Adverse event, n (%)	Group placebo (n=27)	Group intervention (n=27)	P-value
Nausea	0	1 (3.7)	0.5
Dizziness	3 (11.11)	4 (14.81)	0.5
Euphoria	0	1 (3.70)	0.5

Discussion

Nitrous oxide is an interesting inhalation agent because of its analgesic, anxiolytic and amnesic properties. It can be used as a pain medication. Both the anxiolysis and analgesic effect are probably responsible for the lower pain levels seen in the Entonox group in this study. Nitrous oxide effects are dependent on the concentration

inhaled, and at 50% concentration, N_2O will cause mainly analgesia and anxiolysis, A 50% concentration inhaled for 3 minutes can cause complete or partial relief of pain in 75% to 80% of patients, without affecting the cardiovascular system.[7] The effect dissipates within 4 minutes as the gas is excreted from the lungs.[11]

Entonox is used to control pain in a wide range of medical situations, especially during labor. Many randomized controlled trials (RCT) have found Entonox more satisfactory than pethidine or oxygen. It can reduce the use of pethidine during labor pain without significant increase in maternal and neonatal complications.[12-15] Another study found that colonoscopy patients using Entonox felt no more discomfort than those sedated intravenously. Entonox was not associated with a reduction in colonoscopy quality, and patients who received Entonox recovered more rapidly than patients who received intravenous sedation.[16,17]

Interest in the use of Entonox for diverse urological procedures has been increasing recently. In one study, Entonox plus fentanyl was found to decrease pain severity in renal colic patients to a greater extent than oxygen plus fentanyl, and it became effective significantly faster (1.23 vs 1.71 min, $p < 0.0001$).[6] Another RCT demonstrated that Entonox was more rapid and more potent in reducing pain in renal colic patients than morphine sulfate.[18] Several studies have investigated using Entonox to reduce pain during transrectal ultrasound-guided prostate biopsy. Patients who receive Entonox during the operation had significantly less intraoperative pain than patients who received placebo, with only mild side effects such as drowsiness.[8,9,19]

A study comparing Entonox, pethidine and air in extracorporeal shockwave lithotripsy (ESWL) found no significant difference between Entonox and pethidine in reducing pain; therefore, Entonox is another potential analgesic option for ESWL.[10] Another study compared the efficacy of pain management in male patients less than 55 years old who underwent flexible cystoscopy. Patients in the Entonox inhalation group had significantly lower pain score and pulse rate than the patients in the air group, with only minor side effects, , including light-headedness, and tingling sensation. None of patients had serious complications.[7]

This study is the first RCT to compare the efficacy of Entonox and oxygen inhalation for pain control management during rigid cystoscopy. Our primary results show that pain during intraoperative cystoscopy was significantly lower in the Entonox group, with no significant differences observed in postoperative pain, heart rate, and side effects. Our results confirmed the findings of previous studies, which demonstrated similarly lower pain in Entonox group than in oxygen groups during various urological procedures.

The mechanism of action of nitrous oxide which produces analgesic and antinociceptive effect has been clearly identified. It induces opioid peptide release in the periaqueductal gray, which activates descending inhibitory pathways, resulting in modulation of nociceptive processes in the spinal cord.[20]

A limitation of our study is that in this instance no record of the number of bladder tissue biopsies or the number of attempts at ureteric catheterization. Nor did it record any long-term side effects of Entonox. Nitrous oxide can cause cardiac depression. Therefore, it should be used with caution in patients who have cardiac failure.[7] Contraindications of Entonox are the presence of head injury or elevated intracranial pressure, drug intoxication, hemodynamic instability, pneumothorax, bowel obstruction, or any other condition with a pathological, air filled body cavity.[5]

One particular concern is exposure of staff to Entonox as they work with patients frequently and for extended periods. The effect is dependent on the dose and exposure time. Excessive dose or duration of exposure to Entonox could result in reduction in fertility, development of cancer, or hematopoietic changes.[7] Information from this study can improve the quality of healthcare. It is useful for physicians and urologists who perform rigid cystoscopy under local anesthesia as an office-based procedure or in day cases. It can reduce the discomfort of patients undergoing a range of procedures or surgical interventions without intravenous sedation, which may cause adverse events and increase cost of treatment.

In summary, Entonox has both anxiolytic and analgesic effects, which significantly reduce pain in many urological procedures, including rigid cystoscopy, without significant complications. Entonox is a potential option for pain management for rigid cystoscopy.

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Conflict of Interest

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Original Article

Postoperative infection after ureterorenoscopic lithotripsy in Songkhla Hospital

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Keywords:
URSL, postoperative infection, urinary tract infection, risk factors

Abstract

Objective: Ureterorenoscopic lithotripsy (URSL) is the procedure of choice for treatment of ureteral stones. Postoperative acute pyelonephritis (APN) is a serious complication after URSL which may potentially progress to urosepsis and death. In this study we aimed to explore and record potential predictive factors associated with postoperative APN after URSL.

Materials and Methods: Ninety patients (2016-2022) with ureteral stone managed with URSL were identified. Postoperative APN was defined in patients with a body temperature > 38 °C which persisted for at least 48 hours after URSL with clinical symptoms and/or urine culture was positive for organism growth. Multivariable analysis with logistic regression was used to identify predictive factors for postoperative APN.

Results: Seven patients (7.8%) experienced postoperative APN and six patients (85.7%) developed systemic inflammatory response syndrome. All patients were managed conservatively with selective antibiotics, specifically treated with meropenem (n = 3), piperacillin/tazobactam (n = 3), and imipenem/cilastatin (n = 1). Most patients with postoperative APN were women (5/7 patients, 71.4%). The median age of the seven postoperative APN patients was 57.6 vs 54 years ($p = 0.48$) and the hospital stay was longer 5 vs 2 days, ($p < 0.01$). Preoperative APN was found in 12 patients (13.3%) and six patients (50%) developed perioperative APN. The multivariable analysis, showed that the only independent factor of postoperative APN was a history of preoperative APN

Conclusion: Postoperative infection is a serious condition after URSL that can increase the risk of morbidity and mortality. A single significant risk factor for postoperative infection was a history of preoperative APN. These patients should receive rigorous postoperative care to avoid serious complications.

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Introduction

Presence of urinary stones is one of the most common benign conditions in urology. The incidence of this condition varies by region and ethnicity. The lifetime incidence is approximately 10-15% and is increasing gradually year on year.[1] In Thailand the incidence of urinary stones was 94 cases per 100,000 population per year and 20% of these patients suffered from ureteric calculus.[2] Patients with ureteric stones frequently present with symptoms early in the course of the disease and can lead to serious conditions. The symptoms include pain, urinary tract infection (UTI), hematuria, and deterioration of kidney function.[3,4] The management of ureteric stones has dramatically changed from open surgery to minimally invasive surgery over the past 20 years. The treatments of choice include expectant management, medical expulsive therapy, shockwave lithotripsy, laparoscopic ureterolithotomy, and ureterorenoscopic lithotripsy (URSL).[5,6] Recently URSL has been accepted as the reference treatment and first-line treatment for ureteric stones. This procedure provides higher stone free rates, relatively fewer complications, and the reduced need for additional procedures.[7] However, postoperative complications based on several series ranged from 2.5% to 6.7%.[8,9] The most common postoperative complications were up-migration, perioperative infection, and damage to the ureter. The risk of postoperative infection is a particularly potentially serious complication because it may progress to severe sepsis and lead to death.[8-11]

Recent studies revealed prolong operation times,[5,12-14] female,[12,15,16] asymptomatic bacteriuria,[12,14,15,17] history of pyelonephritis,[13,16] and lower body mass index (BMI)[18] as the potential risk factors for postoperative infection after URSL. Our objective was to investigate and report on postoperative infection after URSL and identify the potential risk factors for this condition.

Materials and Methods

After institutional review board approval (SKH IRB 2022-MD-IN3-1043) was received, we retrospectively reviewed the data of 90 patients with upper urinary tract stones who underwent URSL at Songkhla Hospital from January 2016 to December 2022. Patient characteristics including age, sex, BMI, mobility status, preoperative ureteral stent placement, stone diameter, number of stones, stone location, preoperative pyuria, preoperative urine culture status, history of preoperative pyelonephritis, comorbidity, and operative time were collected. Patients all received prophylactic ceftriaxone 2 grams. In patients who had a history of allergy to penicillin, ciprofloxacin 400 mg was given. Acute pyelonephritis is defined as fever (> 38 °C), chills, flank pain, nausea, vomiting, or costovertebral angle tenderness with or without positive urinalysis and urine culture. A diagnosis of systemic inflammatory response syndrome (SIRS) was made based on presence of two or more of the following four criteria: white blood cell count > 12,000/mm^3 or < 4,000/mm^3; body temperature < 36 °C or > 38 °C; heart rate > 90/min; respiratory rate > 12/min; or $PaCO_2$ < 32 mmHg.

Procedure

For patients with preoperative ureteral stent placement, the stent placement was performed four weeks before surgery, and the ureteral stent was removed at the start of the URSL procedure. We used a 6/7.5 Fr rigid ureterorenoscope (Richard Wolf Medical Instruments Cooperation, Knittlingen, Germany). Stones were fragmented using a holmium: YAG laser (JenaSurgical MultiPulse Ho 35W, Jena, Germany) and a 400 μm laser fiber with an energy level of 0.5-1.5 J at a rate of 5-20 Hz. We picked out fragments using a nitinol stone retrieval basket (Zero Tip, Boston Scientific, Natick, MA, USA). A 16 Fr urethral catheter was inserted at the end of the procedure in all cases. A 6 Fr ureteral stent was placed if indicated and removed 2-4 weeks after the URSL.

Statistical analysis

Continuous variables are reported as mean ± SD or median with interquartile range (IQR). Categorical variables are presented as number (percentage). Continuous variables were compared using T-test and Wilcoxon test as appropriate. Categorical variables were compared using Chi-square or Fisher exact tests. The risk factors for postoperative infection were determined using logistic regression to estimate the odds ratios with 95% confidence intervals. P-values < 0.05 were considered statistically significant. The analyses were performed using the R program version 4.1.1.

Results

The baseline characteristics of 90 patients managed with URSL are shown in Table 1. The median age was 54 years and 55 patients (61%) were male. Sixteen patients (18%) had hypertension and 36% were diabetic. The median hospital stay and BMI were 2 days and 25.3 kg/m^2, respectively. The mean operation time was 53 minutes and 28 patients (31%) underwent preoperative internal stenting. Twelve patients (13%) had a history of APN before the operation and preoperative pyuria was observed in 37 patients (41%). Only15 patients (17%) had asymptomatic bacteriuria. The median size of ureteric stone was 0.5 cm and 75 patients (83%) had one ureteric calculus. All patients received antibiotic prophylaxis. Eighty-eight patients (98%) received ceftriaxone, and patients with a history of allergy to penicillin received ciprofloxacin.

Table 1. Patient characteristics and preoperative findings

		Total (N=90)	Perioperative APN (n=7)	No perioperative APN (n=83)	P-value[a]
Patient related	Sex				0.105
	Male, n (%)	55 (61.1)	2 (28.6)	53 (63.9)	
	Female, n (%)	35 (38.9)	5 (71.4)	30 (36.1)	
	Age (years), mean (SD)	54.3 (12.8)	57.6 (13.7)	54 (12.7)	0.477
	Hospital stays (days), median (IQR)	2 (1.2,8)	5 (5,6)	2 (1,2)	< 0.001
	Weight (kg), median (IQR)	68 (61.2,78)	58 (46.5,79)	68 (62,78)	0.197
	BMI (kg/m^2), median (IQR)	25.3 (23.4,28.6)	22.7 (18.9,27.1)	25.3 (23.9,28.9)	0.185
	< 23, n (%)	18 (20)	4 (57.1)	14 (16.9)	0.025
	≥ 23, n (%)	72 (80)	3 (42.9)	69 (83.1)	
	Diabetes mellitus, n (%)	16 (17.8)	1 (14.3)	15 (18.1)	1
	Hypertension, n (%)	32 (35.6)	4 (57.1)	28 (33.7)	0.241
Surgical related	Operative time (min), mean (SD)	53.1 (21)	59.3 (31.9)	52.5 (20)	0.417
	Preoperative internal stent, n (%)	28 (31.1)	4 (57.1)	24 (28.9)	0.198
	Mobility status, n (%)	89 (98.9)	7 (100)	82 (98.8)	1
	Preoperative pyuria, n (%)	37 (41.1)	6 (85.7)	31 (37.3)	0.018
	Preoperative APN, n (%)	12 (13.3)	6 (85.7)	6 (7.2)	< 0.001
	Preoperative asymptomatic bacteriuria, n (%)	15 (16.7)	6 (85.7)	9 (10.8)	< 0.001
	Escherichia coli	8 (53.3)	4 (66.7)	4 (44.4)	
	Escherichia coli ESBL	1 (6.7)	1 (16.7)	0 (0)	
	Group B *Streptococcus* spp.	1 (6.7)	0 (0)	1 (16.7)	
	Klebsiella pneumoniae	3 (20)	1 (16.7)	2 (22.2)	
	Pseudomonas aeruginosa	1 (6.7)	0 (0)	1 (11.1)	
	Number of stone, median (IQR)	1 (1,1)	1 (1,1)	1 (1,1)	0.798
	Size of stone				
	Width (cm), median (IQR)	0.5 (0.5,0.8)	0.7 (0.6,0.8)	0.5 (0.5,0.8)	0.612
	Length (cm), median (IQR)	0.9 (0.7,1)	1 (1,1)	0.9 (0.7,1)	0.248
	ATB prophylaxis n(%)				1
	Ceftriaxone	88 (97.8)	7 (100)	81 (97.6)	
	Ciprofloxacin	2 (2.2)	0 (0)	2 (2.4)	

[a]p-values were calculated using Chi-square test for categorical variables and T-test and Wilcoxon test for continuous variables. Fisher's exact test was used for comparison of categorical variables with low incidence. All comparisons assess the distribution of parameters across the type of postoperative events.

APN = acute pyelonephritis, SD = standard deviation, IQR = interquartile range, BMI = body mass index, ESBL = extended-spectrum beta-lactamase, ATB = antibiotic.

Seven patients (7.8%) experienced postoperative APN and six patients (85.7%) developed SIRS. The seven APN patients were treated with meropenem (n = 3), piperacillin/tazobactam (n = 3), and imipenem/cilastatin (n = 1) (Table 2). Most patients with postoperative APN were women (5/7 patients, 71.4%). The seven patients with postoperative APN had a higher median age compared to the overall age of the 90 patients but the results were not statistically significant (57.6 vs 54.3 years, p = 0.48). Hospital stay, however, was significantly longer (5 vs 2 days, p < 0.01). The average onset of clinical APN was 12.1 hours after the procedure. Twelve patients (13.3%) had a history of preoperative APN, and 6 (50%) of these patients developed postoperative APN. The size and number of ureteral stones were similar in both the preoperative and postoperative APN groups. Figure 1 illustrates the incidence of postoperative APN, which was observed in approximately 10% of each year. The multivariable analysis indicated that an independent factor for postoperative APN was a history of preoperative APN (Table 3).

Table 2. Patients with perioperative acute pyelonephritis

n = 7 patients	Data
Signs and symptoms	
Onset of fever, mean (SD)	12.1 hours post-op (8.4)
SIRS, n (%)	
No	1 patient (14.3)
Yes	6 patients (85.7)
Body temperature, mean (SD)	38.8 degree Celsius (0.5)
Heart rate, mean (SD)	104.3/min (22.1)
Respiratory rate, mean (SD)	20/min (1.2)
Laboratory results	
WBC count, mean (SD)	12425/mm^3 (4089)
WBC count in UA, n (%)	
0-1	2 patients (28.6)
5-10	2 patients (28.6)
50-100	2 patients (28.6)
> 100	1 patient (14.3)
Postoperative positive U/C, n (%)	2 patients (28.6)
Postoperative pathogen from U/C, n (%)	1 patient (50)
Escherichia coli	1 patient (50)
Escherichia coli ESBL	
Postoperative positive H/C, n (%)	0 patients (0)
Treatment	
ATB for APN, n (%)	
Meropenem	3 patients (42.9)
Piperacillin/tazobactam	3 patients (42.9)
Imipenem/cilastatin	1 patient (14.3)

SD = standard deviation, SIRS = systemic inflammatory response syndrome, WBC = white blood cells, U/A = urinalysis, U/C = urine culture, ESBL = extended-spectrum beta-lactamase, H/C = hemoculture, ATB = antibiotics, APN = acute pyelonephritis, min = minute.

Discussion

The majority of cases in urology are patients with presence of a urinary stone, which is a clinical challenge because most patients usually present with acute symptoms such as flank pain, hematuria, UTI, and a deterioration in kidney function.1,3,4 The management of ureteric stones varies depending on the clinical presentation and patient conditions.[5,6] Acute management includes pain killer medication and/or insertion of an

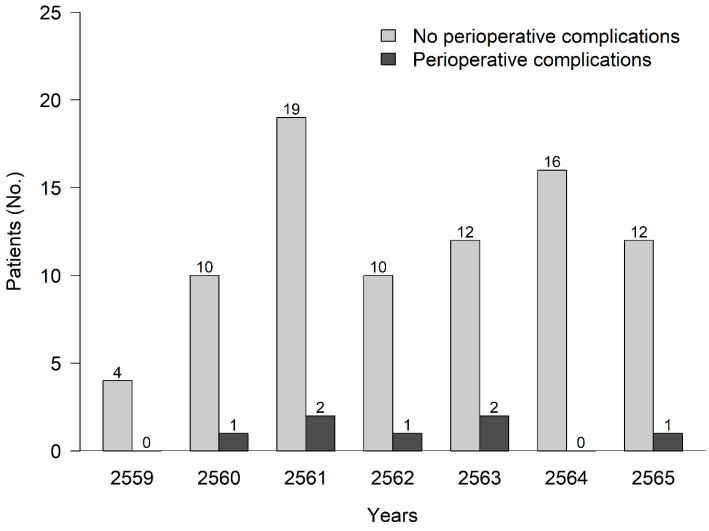

Figure 1. Distribution of ureterorenoscopic lithotripsy operations performed in Songkhla Hospital from 2016 to 2022. The incidence of perioperative acute pyelonephritis was between 5 and 10% each year.

Table 3. Analysis of risk factors of perioperative acute pyelonephritis after URSL[a]

Factors	Univariate			Multivariable[b]		
	OR	95% CI	P-value	OR	95% CI	P-value
BMI < 23 kg/m^2	6.57	1.31-36.59	0.02	4.19	0.43-51.07	0.22
Preoperative pyuria	10.06	1.62-194.82	0.04	6.80	0.59-13.93	0.16
Female	4.42	0.89-32.18	0.09	1.17	0.95-13.94	0.89
History of APN	77.0	10.9-1589.29	< 0.001	33.31	3.66-803.45	0.006
Diabetes mellitus	0.75	0.04-4.89	0.80			
Hypertension	2.62	0.54-14.07	0.23			
Number of stone (s)	0.66	0.05-1.71	0.60			

[a]Asymptomatic bacteriuria variable was removed from analysis; [b]Factors with p < 0.10 were moved forward for multivariable analysis.
URSL = ureterorenoscopy with lithotripsy, OR = odds ratio, CI = confidence interval, BMI = body mass index, APN = acute pyelonephritis.

internal urinary stent.[17] URSL is the reference treatment for ureteric stones when the patient's condition is stable and/or the patient is free of infection.[7] However, postoperative complications are relatively high (range 2.5-6.7%) in relation to other equivalent procedures.[8,9] One of the most serious postoperative complications is infection. This complication can cause acute kidney injury and can progress to severe sepsis that may lead to death.[8-11] Recently published reports revealed that prolonged operative time[5,12-14] and a history of preoperative pyelonephritis[13,16] were potential predictive factors for perioperative infection. Our analysis focused on postoperative APN after URSL and management and outcomes after treatment for this condition. The primary endpoint was to provide the independent risk factors for postoperative APN.

Postoperative infection occurred in 8% of patients in our study. Six out of the seven patients (85.7%) with postoperative infection developed SIRS. No patient had clinical progression to severe sepsis and/or organ failure. Only two patients (29%) had postoperative positive urine cultures for organisms. Therefore, the clinical symptoms and/or initial laboratory outcomes may be more important than the results of urine cultures for physicians to initially manage these conditions. All patients with postoperative infection were managed conservatively with selective antibiotics. The incidence of postoperative infection was approximately 10% each year. The incidence of postoperative complications in this study seemed to be higher in comparison to recent similar studies. For patients with postoperative APN, 6 out of 12 patients (50%) had a history of preoperative APN before intervention. A history of preoperative APN was the only independent factor associated with postoperative APN. The mean time to develop postoperative infection was 12 hours after the procedure. High risk patients, especially patients with a history of preoperative APN, should be closely observed for at least 12 hours after the procedure.

Our study showed a substantial association between preoperative and postoperative APN. The findings revealed that 6 out of 12 patients, 50%, with a history of preoperative infection experienced a postoperative infection. Our data were consistent with reports in the recent literature regarding the association between a history of preoperative APN and postoperative infection. Shreya et al. reported that a positive preoperative UTI or a prior history of UTI were the predisposing factors that increased the risk of postoperative infection.[18] In our study, 7.8% of patients developed postoperative APN and 86% of these patients developed SIRS. Our data were consistent with recent studies. A urine culture is the most important tool for a diagnosis in such patients. Unfortunately, 29% of the patients in this current study had a positive postoperative urine culture and five patients (71%) had a significant number of WBCs in the postoperative urine. Mariappan et al. reported urine culture results that neither represented nor predicted infected stones or renal pelvic urine infection.[19] The clinical symptoms and basic laboratory results are important tools for initial treatment and stone culture. However, a renal pelvic urine culture may be needed

to confirm a diagnosis and enable adjustment of the antibiotics.

Even though the American Urological Association and European Association of Urology guidelines recommend performing a urine culture and treat asymptomatic bacteria before the procedure, the guidelines were not followed due to health policies or patient limitations.[20,21] Cole et al. reported that 20.9% of patients who developed postoperative infection did not have a preoperative urine culture[22] but in our study urine samples were taken from all patients for preoperative urine culture and all patients received antibiotic prophylaxis before the procedure.

Antibiotic prophylaxis tends to reduce perioperative infection and septicemia and identification of organisms from preoperative urine culture is crucial information for choosing the prophylactic antibiotic and also to inform later treatment However, intraoperative pathogens may differ from organisms identified preoperatively.[21] In patients with a history of preoperative APN in particular, a preoperative urine culture provides essential evidence for selection of the prophylactic antibiotic.[17] Recent studies reported that a ureteral access sheath and preoperative ureteral stent potentially offered reduced risk of postoperative complications and infection.[17,20-23] A ureteral access sheath reduces collecting system pressure and decreases the rate of ureteral injury; therefore, the incidence of post-URS infections declined.[17] Although preoperative stent placement facilitates the endoscopic procedure and improves stone free rate, the presence of preoperative ureteral stents for more than one month was associated with a higher risk of sepsis and was associated with occult bacterial colonization. In these reports, all patients with preoperative stent underwent URSL within four weeks and a preoperative stent was not an independent factor for postoperative APN.[17,21-23]

Patients with urosepsis after URSL should be managed intensively and closely monitored. Appropriate antibiotics and supportive care are necessary in these patients. Urosepsis-related mortality was found to be 2.5 times higher in patients with urinary obstruction. If the clinical condition does not improve after treatment with broad-spectrum antibiotics, further investigations are required. Cross-sectional imaging and urgent decompression need to be considered. There is no consensus on the optimal waiting time to observe the effects of antibiotics but if the clinical condition does not show improvement within 48 hours, drainage should be performed.[18] In our report, all patients with postoperative infection were managed conservatively with selective antibiotics. None of the patients in this study required drainage or admission to the intensive care unit.

Our study has some limitations. The population was relatively small and was carried out at a single institute. An addition, since the nature of this study was retrospective, selection bias was potentially present along with missing data. However, our study has identified a potential risk factors for developing urosepsis after URSL. We believe this information can help urologists provide apposite postoperative care for urinary stone patients.

Conclusions

Postoperative infection is a common and serious complication after URSL. It may progress to urosepsis leading to death. All patients with this condition in this study were successfully treated with conservative management with antibiotics. The history of preoperative infection was the only predictive factor for postoperative infection.

Conflict of Interest

The authors declare no conflicts of interest.

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Original Article

Clinical outcomes of Holmium Laser Enucleation of the Prostate (HoLEP) in benign prostatic hyperplasia patients in Rajavithi Hospital

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Keywords:
HoLEP, holmium laser, enucleation, benign prostatic hyperplasia

Abstract

Objective: To evaluate the outcomes and safety of the surgical technique holmium laser enucleation of the prostate (HoLEP) in patients with benign prostatic hyperplasia (BPH) for whom surgeryis indicated.

Materials and Methods: The demographic characteristics, duration of surgery, blood transfusion rate, weight of tissue removed, catheterization time and complications were recorded in 25 patients who underwent HoLEP surgery between January 2021 and May 2022 in Rajavithi Hospital. The International Prostate Symptom Score (IPSS), quality of life score (QoL), peak flow rate (Q-max), post-void residual urine volume (PVR), hematocrit (Hct) and prostate-specific antigen (PSA) levels were comparedbefore and after surgery.

Results: The mean age of the patients was 71.28±7.54 years. There were statistically significant differences between mean preoperative and postoperative Hct (%) (40.5± 5.9 and 38.4±5.1), $p = 0.001$. Only 1 in 25 patients had 1 unit of blood transfusion. One month postoperatively the mean PSA had decreased from 4.55 to 1.2 ng/ml ($p < 0.001$); mean IPSS had improved from 21.0 to 7.0 ($p < 0.001$); mean QoL score had improved from 4.47 to 1.10 ($p < 0.001$); mean PVR had decreased from 98.0 to 39.7 ml ($p = 0.002$) and the mean Q-max had increased from 8.0 to 17.8 ml/sec ($p = 0.015$). The mean catheterization time was 2.40±0.57 days. There were no serious complications or incidence of TUR syndrome in this study.

Conclusion: HoLEP is a safe alternative to the current gold standard transurethral resection of the prostate for BPH patients as there are fewer complications with similar functional outcomes

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Introduction

Benign prostate hyperplasia (BPH) is the most common cause of the pathologies that affect bladder outlet obstruction in men. The incidence of BPH is up to 50% in the sixth decade.[1] Transurethral resection of the prostate (TURP) has been the gold standard for the endoscopic surgical treatment of BPH for many years.[2] Holmium laser enucleation of the prostate (HoLEP) has been used as an alternative treatment for BPH since 1995 by Gilling et al.[3] Now a days, according to the recent European Association of Urology (EAU) guidelines, HoLEP is an alternative to TURP or open prostatectomy due to similar mid to long term efficacy.[4] Also, the American Urology Association (AUA) guidelines recommend HoLEP as the surgical treatment for all sizes of BPH especially in the patients being treated with anticoagulant and / or antiplatelet therapy.[5,6] In this study, we report the surgical techniques and outcomes of HoLEP in our hospital.

Materials and Methods

A total of 25 patients underwent HoLEP by a single surgeon between January 2021 and May 2022 in Rajavithi Hospital for treatment of BPH. This study was approved by the Research Ethics Committee of Rajavithi Hospital in May 2021 with the protocol number 64090.

We performed cystoscopy every patients before HoLEP procedure to evaluate the prostate anatomy and exclude other causes of lower urinary tract symptoms.

The following parameters were recorded underlying disease, mean age, operative time, weight of tissue removed, catheterization time, length of hospital stay, pathologic result and complications. The pre-operative IPSS, QoL, PSA, Q-max, and PVR were compared with the same parameters 1 month postoperatively. Pre-post operative Hct was also compared with post-operative readings. A paired Student t-test was used to compare the data with $p < 0.05$ considered as significant.

In this study,the three-lobe HoLEP technique was carried out in all patients by the same surgeon who used a 26 Fr laser resectoscope with a 30 degree lens Wolf brand. The laser device was a Holmium-YAG laser 120-watt Lumenis with 550 microns of laser fiber. The laser power setting was 2J and 50Hz for cutting, and 1J and 20Hz for coagulation. The morcellator used was a PIRANHA Wolf model connected with a 0 degree nephroscope for removal of prostatic adenoma. The irrigating fluid was normal saline.

The operation was begun with the patient in the lithotomy position after general or spinal anesthesia, the 26 Fr laser resectoscope and sheath were inserted and the bladder was evaluated, and the ureteric orifices, bladder neck and verumontanum were identified. We inserted the resectoscope with an obturator lens (Wolf brand) without dilating the urethra but in narrow urethral lumen cases we used a metal dilator before inserting the resectoscope. First, the author made the inverted-U shaped incision by laser around the verumontanum to identifythe surgical capsule of the median lobe (Figure 1). Then the incision was made at 5 and 7 o'clock depth to the surgical capsule (Figure 2). Then the median lobe was enucleated to the bladder in a retrograde fashion. The left lateral lobe enucleation was started by mucosal incision from the 5 to 12 o' clock position at the

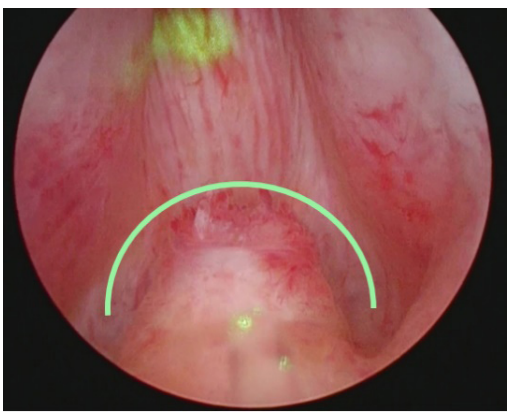

Figure 1. Inverted-U shape incision was made around the verumontanum.

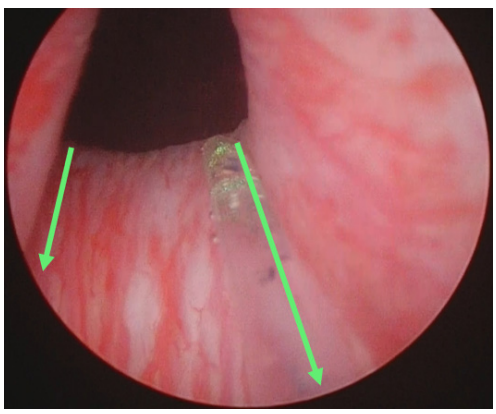

Figure 2. The incision was made in the 5 and 7 o'clock positions at the bladder neck deep into the surgical capsule to connect to the inverted-U shape incision.

apex of the prostate to release the adenoma tissue from the urethral sphincter (Figure 3). The incision was then made at the anterior commissure of the prostate. The left lateral lobe was enucleated by retrograde fashion towards the bladder (Figure 4). The right lateral lobe enucleation was begun by mucosal incision from the 7 to the 12 o'clock position at the apex of the prostate then the right lateral lobe was enucleated by retrograde fashion to the bladder same in a similar way to the left lobe. After completing the enucleation of three lobes of the prostate, the author used the laser to stop any bleeding of the prostatic fossa before morcellation. Then ephroscope was changed to the same sheath and the morcellator was used to remove the floating adenoma from the bladder. At the end of operation, the author inserted a 22 Fr three-way urethral catheter with 30 mL of balloon with continuous bladder irrigation by normal saline. Urethral traction was made in some cases if the urine became red.

Results

The demographic data of patients who underwent HoLEP are shown in Table 1. Mean age was 71.28±7.54 years. Twenty four percent of patients had diabetes mellitus, 40% had hypertension, and 12% had heart disease. All of patients who took antiplatelet or anticoagulant drug stopped the medication before surgery. Seven out of the 25 patients had an indwelling urethral catheter before surgery due to urinary retention. The mean operative time was 185.4±77.1 minutes. The mean resected tissue volume was 44 g. Estimated blood loss was 225.60±77.13 ml as estimated by the anesthesiologist. Catheterization time was 2.40±0.57 days and length of stay was 2.6±0.7 days. Pathological result of H0LEP tissue were mostly BPH except one patient who was diagnosed with prostate cancer adenocarcinoma Gleason 3+4.

Preoperative and postoperative data are compared in Table 2. There were statistically significant differences between mean preoperative and postoperative Hct (%) (40.5±5.9 and 38.4±5.1), p = 0.001. Only 1 out of 25 patients had 1 unit of blood transfusion. At 1 month postoperatively, mean PSA had decreased from 4.55 to 1.2ng/ml ($p < 0.001$). Mean IPSS improved from 21.0 to 7.0 ($p < 0.001$). Mean QoL score improved from 4.47 to 1.10 ($p < 0.001$). Mean PVR had decreased from 98.0 to 39.7 ml (p = 0.002). Mean Q-max had increased from 8.0 to 17.8 ml/sec (p = 0.015).

No serious complications or TUR syndrome developed in any patient in our study. The total rate of complications was 20% (5 of 25 patients), 1 patient (4%) required one unit of blood trans-

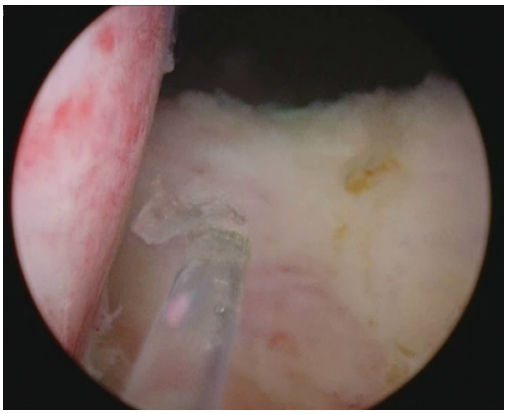

Figure 4. Median and left lobes of the prostate were enucleated to the bladder.

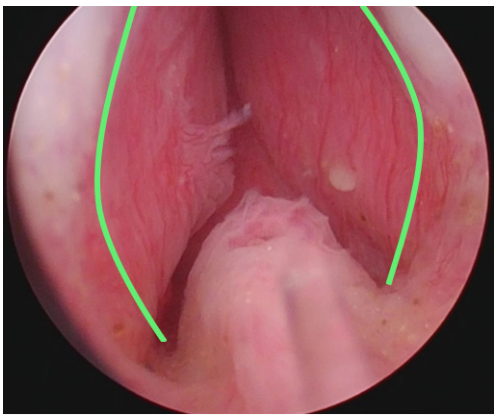

Figure 3. The green lines showed the mucosal incision at the apex of the prostate (urethral sphincter release left and right lobe).

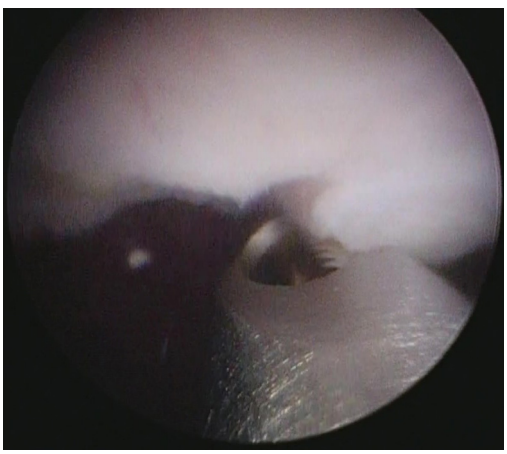

Figure 5. Morcellator (facing up) was used to remove the floating adenoma from the bladder.

Table 1. Demographic and clinical characteristics of the patients.

Data	Total (n=25)
Age (years), mean (min-max)	71.3 (51-86)
Operative time (minutes), mean (min-max)	185.4 (60-360)
Resected tissue volume (g) (min-max)	44.0 (5.0-82.0)
Blood loss (ml) mean ±SD	225.60±77.13
Catheterization (days) mean±SD	2.40±0.57
Length of stay (days), mean (min-max)	2.6 (2-5)
Pathology n (%)	
BPH	19 (76.0)
BPH with prostatitis	5 (20)
Adenocarcinoma Gleason 3+4	1 (4.0)

SD = standard deviation, BPH = benign prostatic hyperplasia.

Table 2. Comparison between preoperative and postoperative parameters.

Data	Preoperative	Postoperative	P-value
Hct (%), mean±SD	40.5±5.9	38.4±5.1	0.001*A
QoL, mean±SD	4.47±1.21	1.10±1.37	< 0.001*A
PSA (ng/ml), median (min-max)	4.55 (0.6-86.0)	1.2 (0.1-37.8)	< 0.001*B
IPSS, median (min-max)	21.0 (6.0-32.0)	7.0 (1.0-17.0)	< 0.001*B
Q-max (ml/sec), median (min-max)	8.0 (0.0-20.4)	17.8 (8.5-38.5)	0.015*B
PVR (ml), median (min-max)	98.0 (0.0-500.0)	39.7 (0.0-183.0)	0.002*B

Values were represented as n (%), The p-value from paired t-testA and Wilcoxon signed Rank testB, *significant at $p < 0.05$.
Hct = hematocrit, SD = standard deviation, QoL = quality of life, PSA = prostate specific antigen, IPSS = International Prostate Symptom Score, Q-max = maximum flow rate, PVR = post-voided residual.

fusion, 1 patient (4%) had capsular perforation needing prolonged urethral catheterization, 1 patient (4%) had overflow incontinence from a prior neurogenic bladder, and 2 patients (8%) had contracture of the bladder neck at 3 months of follow up and a transurethral incision of bladder neck was required.

Discussion

TURP has been established as the gold standard for conventional surgical procedures for many decades[7] but complication rates increase in cases involving more enlarged prostate glands (> 80 g) such as TUR syndrome and bleeding.[8] In treatment of a large prostate gland, open prostatectomy (OP) is one of the most effective surgical treatments but it is the most invasive surgical method and is now used less in this endoscopic era.[9] HoLEP is one of the endoscopic surgical methods which uses a Holmium laser to enucleate the prostate gland as in an open prostatectomy, pushing the prostate tissue into the bladder and then removing the tissue by morcellator.

Jhanwar et al.[10] reported the outcome of prospective randomized study which included 164 patients in whom TURP was performed in comparison with HoLEP. The prostate volumes of TURP and HoLEP patients were 74.5±12.56 and 75.6±12.84 g, respectively ($p = 0.60$). The resected prostatic volumes in TURP and HoLEP were 44.80±9.87 and 48.49±10.87, respectively ($p = 0.03$). The hemoglobin loss (g/dl) in TURP and HoLEP was 0.63±0.6 and 0.47±0.46 g/dl, respectively ($p = 0.08$). No patients in either group required a blood transfusion or involved complications such as TUR syndrome. Postoperative bladder irrigation time, catheterization time, and postoperative length of stay in the hospital were significantly higher in the TURP group. There were no significant differences in the IPSS, Q-max and PVR between groups. The disadvantage of HoLEP found in this study is the longer operative time than the TURP procedure.

Zhang et al.[11] carried out a meta-analysis of efficacy and safety of HoLEP versus TURP in 26 randomized controlled trials (3,283 patients). The outcomes between HoLEP and TURP in IPSS, Q-max, and QoL at 1, 3, and 6 months postoperative were not significantly different. At 12 months postoperatively, IPSS and Q-max in the HoLEP group were significantly better than in the TURP group. The benefits of the HoLEP group over the TURP group are shorter hospital stay, lower hemoglobin loss, and a decrease in serum sodium and transfusion rate. However, there was a shorter operative time in the TURP than in the HoLEP group.

Li et al.[12] carried out a meta-analysis of efficacy and safety of endoscopic enucleation (HoLEP, bipolar plasma vaporization enucleation, plasmakinetic enucleation) versus open prostatectomy for large BPH (> 80 g) in 7 randomized controlled trials (735 patients). There were no significant differences in IPSS, Q-max, QoL and PVR at 3, 6 and 12 months postoperatively between the two groups. The catheterization time and hospital stay were shorter in the endoscopic enucleation group. The decrease in hemoglobin was less in the endoscopic enucleation group and fewer blood transfusions were required. There were no significant differences in complication rates between two groups. The operative time was longer in endoscopic enucleation in comparison with OP.

Higazy et al.[13] reported a randomized controlled trial of the outcome of H0LEP versus bipolar transurethral enucleation of the prostate (120 patients). The prostate volume was 135.2±34.8 ml and 125±26.9 ml for HoLEP and bipolar enucleation of the prostate (BPEP), respectively. The HoLEP group had a shorter operative time of 83.43±6.92 minutes in comparison with 94.7±12.2 minutes in the BPEP group. HoLEP was associated with an earlier catheter removal time (days) (1±0.23 vs 1.79±1.6, p = 0.02) and shorter hospital stay (days) (1±0.24 vs 1.49±0.6, p = 0.01) in comparison with BPEP. Postoperative IPSS, QoL, Q-max, PVR, PSA, prostate volume reduction and perioperative complications were comparable between the two groups. Regarding the cost analysis, HoLEP was more cost-effective than BPEP.

The disadvantage of HoLEP is related to the long learning curve, the literature showing that a satisfactory level of competence is reached after between 25 and 50 operations.[14] A structured mentoring program seems to enable faster progress.[15] Also the higher cost of HoLEP instruments such as the laser fiber and morcellator may be limiting factors of this surgical method in developing countries.

In this study, there were significant improvements in IPSS, QoL, Q-max and PVR postoperatively without serious complications or incidence of TUR syndrome. The carrying out of conventional TURP requires additional bladder traction on postop day 0, continued bladder irrigation on day 1, stopping bladder irrigation on day 2 and removal of the urethral catheter on day 3. Thus, the mean catheterization time of HoLEP may be shorter than the conventional use of the TURP procedure.

The main limitation of this study is that the surgeon is in the early stage of experience of this technique. However, the small number of patients and the lack of directly comparative data such as is needed for a randomized controlled trial are also limitations.

Conclusion

HoLEP is a safe alternative to the current gold standard practice of transurethral resection of the prostate for BPH patients as there are fewer complications with similar functional outcomes. This team believe that HoLEP might be positioned in the guidelines as the recommended gold standard surgical treatment for any size of the prostate in the future.

Conflict of Interest

The author declares no conflict of interest.

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Invited Review Article

Bibliometric analysis of the relationship between metabolic study and urolithiasis. A key tool in patient management

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Keywords:
Urolithiasis, prevention, metabolic evaluation, hypercalciuria

Abstract

Objective: Our objective was doing an analysis of available bibliography to understand tendencies in publications regarding the role of metabolic evaluation in the management of urolithiasis.

Materials and Methods: A retrospective bibliometric analysis of the available medical literature ranging from the year 2001 to 2022 was performed on the Web of Science platform. The graph analysis was done using Microsoft Excel and the bibliographic mapping analysis was done on the VOSviewer software.

Results: A total of 120 references were found in 63 journals, with a decrease in the rate of publications in the last 5 years. The country, journal, and institution with the largest number of manuscripts were the United States, Journal of Urology, and the University of Bonn, respectively. The author with the largest number of publications was Sarica Kemal. The mapping and analysis of the keyword evolution with respect to the timeline centered on the terms: "prevention", "metabolic risk factors", "obesity", "primary hyperoxaluria", and "medical management".

Conclusion: Metabolic evaluation is a fundamental tool in the overall approach of these patients. Despite the decrease in the rate of research on the association between metabolic evaluation and urolithiasis in recent years, the importance of a complete assessment of these patients from the first symptomatic episode has been demonstrated, as it helps to determine the risk of recurrence of the disease, and to establish a treatment plan focused on prevention. This first bibliometric analysis on metabolic evaluation and urolithiasis depicts the importance of giving continuity to research on the risk factors of urolithiasis that may be modified and treated.

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Introduction

The incidence of urolithiasis has mainly increased in industrialized countries.[1] The ascending tendency in the number of cases is associated with a higher rate of diagnosis (due to the current available technology), but also with geographic and environmental factors, as well as an increase in diseases like obesity and metabolic syndrome.[1-3]

Despite its relatively low mortality rate, urolithiasis poses significant challenges due to the exponential risk of recurrence, long-term complications such as progressive renal function deterioration[3-5], and the socioeconomic impact it imposes.[6] Therefore, it is imperative to conduct a comprehensive evaluation of each patient and strive to develop individualized treatment plans with a primary focus on preventive measures. To achieve this, it is crucial to have a thorough understanding of the physiological underpinnings of urolithiasis and the various factors involved in lithogenesis.[2,3,7] Recent studies have revealed that a considerable number of urolithiasis patients also suffer from concurrent treatable metabolic conditions[3,5], further emphasizing the need for a holistic approach to their management.

The metabolic evaluation assesses most metabolic abnormalities through urinary and blood biochemical tests. Depending on the risk of recurrence, either a basic or specific metabolic evaluation is performed. These studies provide enough information to elaborate specific treatment plans for urolithiasis and make it possible to diagnose up to 90% of patients, as well as to reduce the rate of recurrence to less than 25% in the long-term.[3]

Hence, this study consists of the formulation of a bibliometric analysis that evaluates the contributions, tendencies, and research hot spots associated with the metabolic evaluation and urolithiasis.

Materials and Methods

Database

Initially, we searched for MeSH terms on the PubMed website to ensure a wholesome approach to the topic. "Metabolic evaluation" and "urolithiasis" comprised the subcategories necessary to conduct a literature search. Furthermore, we utilized Clarivate Analytics' Web of Science Core Collection (WoSCC) in its high impact reviews section to search for articles and citations associated with metabolic evaluation and urolithiasis.

Search Strategy

A single literature search of publications on metabolic evaluation and urolithiasis was performed to anticipate database updates. The chain search was described as follows: Topic=(metabolic evaluation and urolithiasis) AND Abstract=(metabolic evaluation and urolithiasis). There were no language limitations. The articles included were those with titles and abstracts associated with the topic. Two articles were excluded as the subjects of their studies were animals and another four were excluded as their titles and abstracts did not coincide with the search. The articles' information concerning titles, keywords, abstracts, authors, institutions, and reference registries was downloaded and stored in Microsoft Excel format for its subsequent analysis and in text format (.txt) to be used in the VOSviewer (version 1.6.16) software.

Data Analysis

The data was downloaded and analyzed by two researchers (G.P., C.S.). Microsoft Excel was used to create the bar graphs and the tables concerning the year of publication, authors, countries, institutions, most productive journals, and most cited publications. Subsequently, the selected files were analyzed. Also, using the platforms Scimago and Journal Citation Reports, a search of measurements such as: H index, impact factor 2021 (IF 2021) and the Journal Citation Reports 2021 (JRC 2021) was performed. These measurements, respectively, made it possible to: analyze the academic productivity level of researchers, countries, and journals; the scientific quality of journals; and to identify the journals' classification. Lastly, through the VOSviewer software, we obtained the total link strength (TLS), which indicates the strength of association between co-authorship and co-citation and co-occurrence.

Data Visualization

In this study, we used Microsoft Excel 2019 to create bar graphs and tables that summarize the main information included, as well as the VOSviewer (version 1.6.16) software to assess the relationship between: co-authorship of authors, countries, and institutions; of co-citation of

authors and references; and of co-occurrences of keywords. Bibliometric maps were elaborated to illustrate: the collaboration between countries, institutions, and authors; the strength of association between authors according to the number of times that they were cited; and the strength of association between the articles depending on whether they appear together.

Results

A total of 126 documents were found in the search and 120 were included (97 articles, 26 reviews, 8 review reports, 1 editorial material) in accordance with the selection criteria. We excluded animal studies and articles with title and abstract that did not correspond to the subject (Annex 1).

Research on this topic has been conducted globally over the past two decades. Starting from 2010, there has been a notable increase in publications, with an average of more than five articles per year. The peak of research activity in this area was observed in 2017, followed by a gradual decline in publication output since then. It is noteworthy that the top 10 most cited articles on this subject were published prior to 2015, indicating their enduring significance and impact on the field (Figure 1).

Most Productive Countries Analysis

A total of 34 countries have published articles related to this topic. As shown on table 1, the countries with more than 15 publications are the United States (28%), Turkey (20%) and Germany (14%). Even though 60% of the countries in the top 10 are European, the first two most productive countries are the United States with 34 articles and Turkey with 24 articles. Also, in terms of the H index (307) and total citations (3,702 times), the United States also placed first in comparison to Turkey, which came in second but had significantly lower total citations (436 times). As for the analysis of cooperation between countries, Germany had the largest international

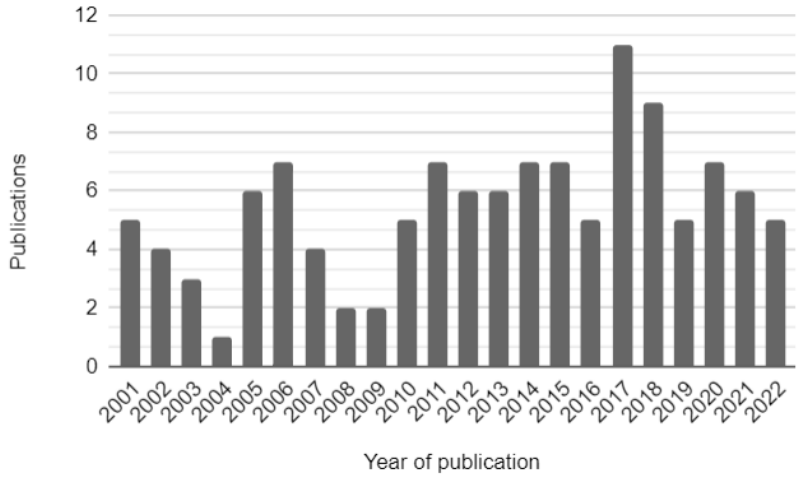

Figure 1. Annual number of publications on metabolic study and urolithiasis research.

Table 1. The 10 most productive countries in relation to metabolic studies and urolithiasis.

Rank	Country	Publication	Percentage (%)	H-index*	Total citations	Average citations per paper
1	United States	34	28	307	3,702	0.78
2	Turkey	24	20	99	436	0.67
3	Germany	17	14	205	1,697	1.42
4	Iran	8	7	59	234	0.6
5	Canada	6	5	170	898	1.07
6	Italy	6	5	190	1,938	1.57
7	France	5	4	174	1,263	1.81
8	England	4	3	202	1,650	1.52
9	Netherlands	4	3	181	1,096	210
10	Poland	4	3	61	83	0.64

* Filtered by area: Medicine, subject: Urology and year 2021

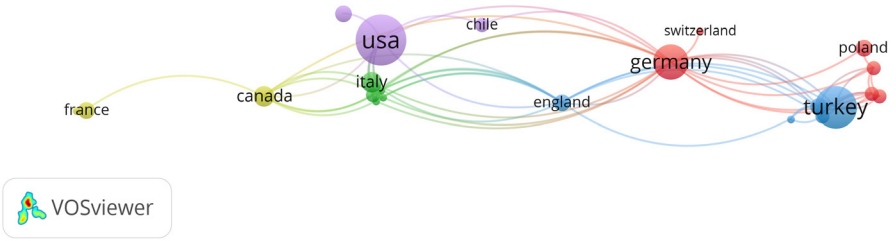

Figure 2. Co-authorship visualization network of countries generated using VOSviewer. The node size is proportional to the number of publications, and the thickness of the connection line indicates the cooperation frequency map.

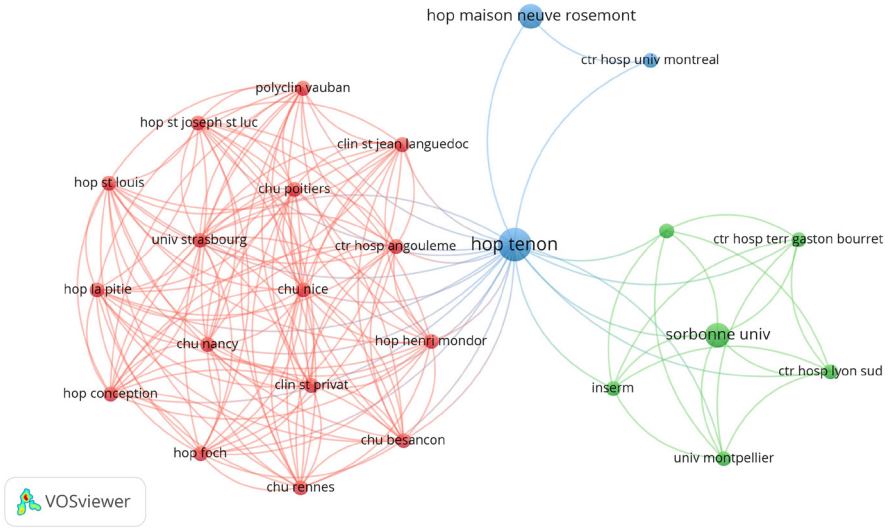

Figure 3. Institution co-authorship visualization network generated using VOSviewer.

cooperation, which included the United States, Turkey, Canada, and Italy (Figure 2). The lines between knots indicate the co-authorship between countries and the thicker the line, the greater the cooperation, referred to as total link strength (TLS). The co-authorship visualization map showed that the top 5 TLS corresponded to Germany (TLS:24), the United States (TLS:14), England (TLS:13), Turkey (12) and Austria. The only Latin American countries that cooperated with the most productive countries were Brazil and Chile, which were co-authors with the United States and Germany.

Main Institutions' Contributions

A total of 24 institutions have participated in the research on metabolic study and urolithiasis. The first three institutions, with the largest contributions, were the University of Bonn in Germany, Public Assistance Hospitals of Paris in France, and the Cincinnati Children's Hospital Medical Center in the United States, with a total of 8, 5, and 5 published articles respectively. The number of French institutions (N=4) that are part of the top 10 is notable despite France placing seventh in contributions, which suggests cooperation among them (Annex 2).

Figure 3 shows cooperation between institutions. A total of 220 institutions with more than 1 published article were found, of which the first 3 in terms of TLS were the Tenon Hospital in France (TLS=24), Besancon University Hospital in France (TLS=98) and Nancy Regional University Hospital in France (TLS=16). However, most institutions were scattered and those that cooperate limit such efforts to national institutions.

Author Analysis

A total of 497 authors were included. Table 2 shows the top 10 most productive authors. Sarica Kernel, Hoppe Bernd, Laube Nobert took the first three places, with 9, 6, and 5 published articles respectively. A co-authorship web visualization map was created using VOSviewer software and the threshold for the minimum number of documents was set at 3. Finally, 10 authors that reached the threshold were identified and it was demonstrated that Minevich Eugene, Defoor

Table 2. Top 10 most productive authors with the most citations

Rank	Author	Country	Publications
1	Sarica Kemal	Turkey	9
2	Hoppe Bernd	Germany	6
3	Laube Norbert	Germany	5
4	Minevich Eugene	United States	5
5	Straub Michael	Germany	5
6	DeFoor William	United States	4
7	Jackson Elizabeth	United States	4
8	Asplin John R	United States	3
9	Hesse Amber	United States	3
10	Preminger Glenn	United States	3

William, Jackson Elizabeth, Asplin John, Sheldon Curtis and Reddy Pamond have cooperated closely (Annex 3). Also, the international cooperation present between them is notable.

Moreover, a co-citation visualization map was generated using VOSviewer software and the threshold for the minimum number of author citations was set at 20. Lastly, 15 authors that met the threshold were found and it was possible to observe that Hoppe B had made significant contributions in the research field of metabolic evaluation and urolithiasis (Annex 4).

Main Journals' Contributions

The articles included were published in a total of 63 journals, including 41 journals with 1 article. According to the results shown on table 3, the three most productive journals were the Journal of Urology with 11 publications (9,2%), the Journal of Pediatric Urology with 7 (5,8%), and Pediatric Nephrology with 7 (5,8%). Additionally, the total number of citations from Kidney International was 57,360, a much larger number than other journals. In keeping with the Journal Citation Report (JCR) of 2021, among the 10 most cited journals, 4 were found in the Q1 category. Two journals: Urological Research and The Scientific World Journal did not have an updated JCR.

Most Cited Reference Analysis

This study included a total of 120 publications of which 30 articles had been cited at least 30 times. Table 3 numbers the 10 most cited documents, of which Skolarikos et al. placed first with 186 citations, followed by Gambaro et al. and Hoppe et al. with 119 and 108 citations respectively. 80% of the most cited articles belong to American Journals, however, a Dutch article placed first. As for the areas of research: Urology-Nephrology, Pediatrics and Internal Medicine were the first. Nonetheless, the most cited articles were found belonging only in the first few fields (Annex 5).

In total, our study cited a total of 2862 references. Ali Tekin (52) had the largest total citation number, with 20 citations and VanDervoot, K et al. (54) placed second with 19 citations (Annex 6).

Table 3. Top 20 journals related to metabolic study and urolithiasis research

Rank	Journals	Country	Publicaciones	IF (2021)	JCR (2021)	H-index*	Total citations
1	Journal Of Urology	United States	11	7,641	Q1	265	51,677
2	Journal Of Pediatric Urology	England	7	1,921	Q3	49	4,446
3	Pediatric Nephrology	United States	7	3,652	Q1	113	12,251
4	Urology	United States	6	2,633	Q2	182	24,074
5	Journal Of Endourology	United States	5	2,619	Q2	95	8,166
6	Iranian Journal Of Kidney Diseases	Iran	4	1,468	Q4	34	1,027
7	Urological Research	United States	4	1,476	Q3*	-	-
8	World Journal Of Urology	Germany	4	3,661	Q1	88	9,909
9	Current Opinion In Urology	United States	3	2,808	Q3	61	2,310
10	Frontiers In Pediatrics	Switzerland	3	3,569	Q1	48	9,940
11	Urolithiasis	United States	3	2,861	Q2	65	1,600
12	Archivos Espanoles De Urologia	Spain	2	0,43	Q4	25	642
13	BJU International	England	2	5,969	Q1	154	23,142
14	BMC Urology	England	2	2,09	Q3	46	2,421
15	CUAJ - Canadian Urological Association JournaL	Canada	2	2,052	Q3	20	2,796
16	Iranian Journal Of Pediatrics	Iran	2	0,62	Q4	28	2,761
17	Kidney International	United States	2	18,998	Q1	288	57,360
18	Pediatric Clinics Of North America	United States	2	3,58	Q1	90	5,332
19	Progres En Urologie	France	2	1,090	Q4	34	1,175
20	The Scientific World Journal	United States	2	1,524	Q1**	103	1,453

**In the year 2014. **In the year 2010*

Table 4. The 20 keywords with the highest frequency related to the metabolic study research in urolithiasis

Rank	Keyword	Frequency	TLS	Rank	Keyword	Frequency	TLS
1	Urolithiasis	77	389	11	Epidemiology	13	81
2	Nephrolithiasis	42	241	12	Nephrocalcinosis	13	76
3	Renal Calculus	32	204	13	Excretion	12	75
4	Child	36	200	14	Medical management	10	75
5	Hypercalciuria	20	135	15	Risk Factor	13	75
6	Risk factor	20	126	16	Prevention	11	74
7	Calcium	17	106	17	Metabolic evaluation	16	71
8	Pediatric Urolithiasis	18	102	18	Oxalate	11	68
9	Risk	18	91	19	Shock wave lithotripsy	16	68
10	Prevalence	15	88	20	Stone	14	61

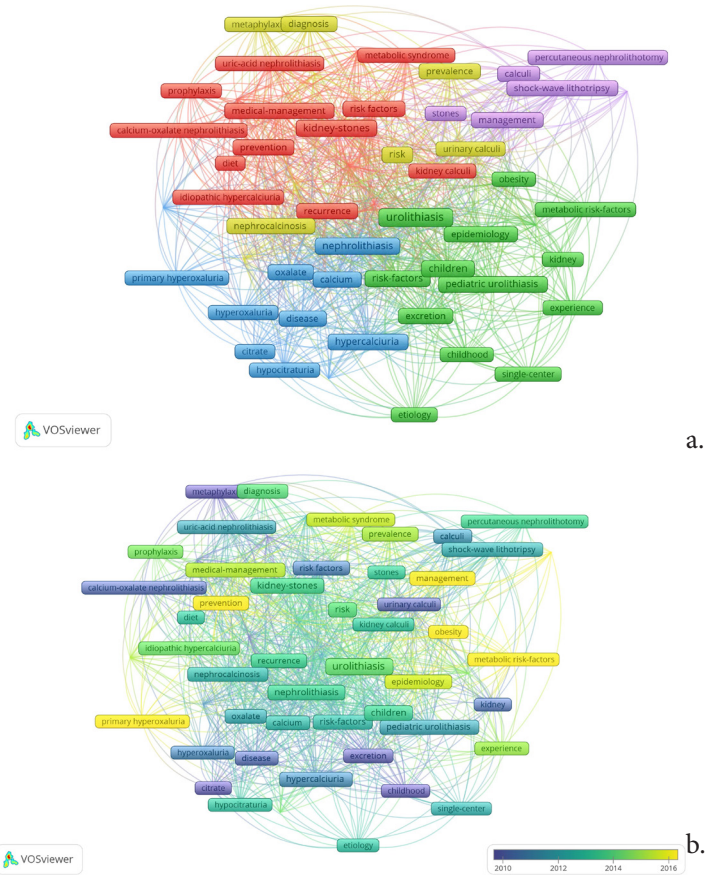

Figure 4. a. Keyword co-occurrence visualization map between metabolic study and urolithiasis, b. Overlay visualization map of keywords over time.

Keyword Co-Occurrence Analysis

Our study included a total of 518 author keywords and 56 keywords had a minimum frequency of at least 5 times. Table 4 showed the 20 keywords with the highest frequency. Among them, urolithiasis placed first (73 times), followed by nephrolithiasis (40 times) and child (36 times).

VOSviewer was used to create a keyword web visualization map and a superposition visualization map that made it possible to analyze and understand the tendencies of the research topics, as well as to comprehend the changes that they undergo through time. As shown on figure 4a, there are 5 clusters, each one illustrated with a specific color. The red group is composed of words such as: “Medical treatment”, “metabolic evaluation” and “potassium citrate”, which is why it is labeled as #Cluster 1: Medical treatment measures and risk factors. The green group, with its main keywords being “urolithiasis”, “children”, “pediatric urolithiasis”, and “risk factors”, is classified as #Cluster 2: Risk in the pediatric population. The

blue group comprised the key words: "nephrolithiasis", "hypercalciuria", "calcium" and "oxalate", with a particular focus on deposit anomalies that must be studied in the metabolic evaluation, and it is depicted as #Cluster 3: Lithiasic metabolic evaluation abnormalities. The yellow group centered mainly on risk, diagnosis, and prevalence, which is why it can be understood as Cluster #4: Epidemiological and Diagnostic Studies. Lastly, the purple group, with the main keywords "by shock wave lithotripsy" and "percutaneous nephrolithotomy" and "ureteroscope", focuses on the surgical treatment of urolithiasis, which is why it can be referred to as #Cluster #5: studies associated with surgical interventions.

Figure 4b is the keyword superposition visualization map that shows the change in keywords through time. The yellow codes represent the most recent keywords that could potentially become crucial topics for current research. It is shown that "prevention", "metabolic risk factors", "obesity", "primary hyperoxaluria" and "management" are keywords that have frequently appeared in the last 7 years, which suggests that future research will focus on the identification of risk factors such as obesity and in developing strategies to elaborate a treatment plan focused on prevention.

Discussion

Conducting a comprehensive metabolic evaluation of urolithiasis patients, starting from the initial episode, enables the identification and treatment of underlying conditions, as well as the implementation of tailored lifestyle modifications to address individual patient needs. This approach plays a crucial role in reducing the recurrence rate and, consequently, minimizing the complications associated with recurrent episodes.[8-10] Recognizing the significance of this subject matter, it is pertinent to explore the impact, trends, and future directions of research in this field. Understanding these aspects will contribute to advancing knowledge and improving patient outcomes in the management of urolithiasis.

The present study reveals a progressive decline in the number of publications within the past five years. Although no clear trend in the focus of recent research has emerged, there is a consensus on the importance of conducting metabolic evaluations to guide appropriate medical, surgical, and dietary interventions.[11] This tendency may be attributed to information saturation, prompting researchers to explore new fields that complement existing knowledge.[9]

Urolithiasis is a multifactorial disease influenced by environmental factors, regional variations, lifestyle choices, diet, and comorbidities. Industrialized countries exhibit the highest incidence rates1, which aligns with the findings of this study. Despite publications originating from 82 countries, the top ten most productive countries, except for Iran, predominantly consist of developed nations. Notably, Chile, Brazil, and Argentina, countries with high human development indices in Latin America, also contributed to the research output.

Analyzing productivity, quality, and academic standing, the United States demonstrated a higher H index and total citation count compared to other countries. Turkey ranked second but exhibited a lower index than countries with lesser contributions, indicating a need for improved quality publications despite the increase in article output.

Regarding journals with the highest percentage of publications on the topic, it is worth mentioning that the journal with the highest impact factor in the specialty, Kidney International, does not rank among the top ten. Notably, two of the three leading journals in terms of publications are pediatric journals: The Journal of Pediatric Urology (5.8%; 7) and Pediatric Nephrology (5.8%; 7). This signifies a research interest in pediatric patients, a population group experiencing a rise in urolithiasis cases. Diagnosing pediatric cases can be challenging, often with underlying genetic and metabolic abnormalities.[1,7] Moreover, the analysis of research areas revealed that 80% of articles were categorized under Urology/ Nephrology and Pediatrics.

Sarika Kemal, based in Turkey, emerged as the author with the most publications, considering Turkey an endemic zone for urolithiasis in both pediatric and adult populations.[5] His 2015 literature review, ranking first among the most cited studies, focused on study approaches and treatment algorithms for low and high-risk urolithiasis recurrence.[4] In his subsequent publications in 2019 and 2020, he conducted prospective studies to identify new risk and protective factors in urolithiasis, such as obesity[12] and breastfeeding.[13]

On the other hand, the most cited author, Hoppe B, concentrated on research within the pediatric population, driven by the underdiagnosis and potential long-term complications associated with untreated cases.[7]

Through co-occurrence analysis using VOSViewer, five distinct clusters encompassing diagnosis, medical and surgical interventions, and prophylactic treatment in urolithiasis were identified. A specific cluster centered around metabolic evaluation included the most frequently diagnosed metabolic diseases. Furthermore, the visual map highlighted recent studies focused on identifying metabolic risk factors to facilitate appropriate treatment and prevent future urolithiasis episodes. Emerging topics like obesity are just beginning to be incorporated and are expected to be prominent areas of research in the future.

Limitations

There are no other bibliometric studies on this topic to date, which is why it is not possible to compare the obtained results. Additionally, only one database was used for the literature search, which suggests that certain publications on this topic may have been excluded. Moreover, the article selection was done according to title followed by abstract, which may have resulted in publications being included whose main topic may not have been the relationship between urolithiasis and metabolic evaluation.

Conclusions

Metabolic evaluation plays a pivotal role in the management of patients diagnosed with urolithiasis. By employing this approach, healthcare professionals can effectively identify concurrent diseases that significantly impact the patient's risk of recurrence and potential complications. Notably, research in this field is primarily led by developed countries, given the higher prevalence of urolithiasis in these regions. However, it is imperative to foster collaboration and knowledge exchange with developing countries to enhance the global understanding of this condition.

An analysis of research focus reveals an encouraging trend wherein new investigations are exploring additional comorbidities, such as obesity, as potential risk factors for urolithiasis. This development underscores the importance of further studies aimed at adopting a comprehensive approach and delivering individualized treatment strategies. By continuing to delve into these areas, the medical community can achieve a more holistic understanding of the disease and improve patient care accordingly.

Conflict of Interest

The authors have no conflict of interest to declare.

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Invited Review Article

Urological malignancies in kidney transplant recipient patients

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Keywords:
Renal transplant, renal cell carcinoma, urothelial carcinoma, urological malignancy

Abstract

Kidney transplantation is now established as the ideal treatment option for end-stage renal disease (ESRD) and renal cell carcinoma (RCC) patients. Since the first kidney transplant in the 1970s, research has allowed us to understand the long term sequelae of kidney transplant patients (TXPs) including the risks of increased malignancy from immunosuppression.

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Introduction

Renal transplantation started in the 1970s.[1,2] In the initial days, only 20 deceased donor kidney transplants were performed between 1970 and 1976. In comparison, data from 2021 Singapore's Renal Registry reflected 555 kidney transplants performed from 2016 to 2021.[3] The advances made to immunosuppressive therapy, legal regulations implemented to improve kidney donation rates, as well as the development of minimally invasive surgical techniques for donor nephrectomy,[4] helped to build the success of kidney transplantation. Compared to kidney dialysis, kidney transplantation is associated with better clinical outcomes in terms of better quality of life and mortality rates, even in the long term.[5] It is the current gold standard of treatment for end-stage renal disease (ESRD). Compared with remaining waitlisted in dialysis, kidney transplantation is associated with improved survival, quality of life for the patients and entails a lower cost for the society.[6]

While kidney transplantation remains the mainstay of treatment for ESRD and RCC patients, the downside of having a kidney transplant is an increased malignancy risk post-transplant. Cancer is one of the leading causes of mortality and morbidity in kidney transplant recipients (TXPs), accounting for 56% of deaths in recipients with a functioning renal graft.[7] A 2017 study done by The American Society of Transplantation and the American Society of Transplant Surgeons revealed that TXPs have a 7-fold risk of renal cell carcinoma (RCC) and 3-fold risk of urothelial carcinoma (UC) compared to the general population.[5] This has been postulated to result from the use of immunosuppressive agents post-transplant, which can cause DNA damage, as well as viral-induced cancers like PTLD (EBV), Kaposi Sarcoma (HHV 8), and HCC (Chronic Hep B, Hep C Viruses) due to the suppression of T-cell functions.

In view of the increased awareness of the importance of malignancies after kidney transplantation, this urological focused article aims to

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discuss the most common and important urological malignancies post-transplant: RCC and UC.

Renal Cell Carcinoma

Introduction

RCC accounts for most malignant urological cancers, with a number of subtypes – clear cell (most common), papillary, chromophobe, and medullary. Over the past years, with the increased use of cross-sectional imaging including computed tomography (CT), the detection rates of RCC have increased in both the general population and kidney transplant population. This has led to an improved understanding of the epidemiology, presentation and management of these cancers post transplantation.

Epidemiology

The risk of RCC in kidney transplant patients is reported to be about 5-10 times higher compared to the general population. It is predominantly (90%) encountered in the native kidneys; and rarely in the kidney allograft.[8] Table 1 summarizes the epidemiological data review of RCC in kidney transplant patients compared with ESRD and the general population.[9] Compared to the general population, it reports the increased lifetime risk of RCC in both ESRD (x3) and kidney TXPs (x5-7), as well as that of the standardised incidence ratio (SIR). Malignancy risk is usually expressed as the SIR, which compares the respective incidence of a malignancy with the rate found in the general population.[10] RCC SIR is approximately 2.6/100,000 in the general population; in comparison to an increased mean rate of 4.87/100,000 in that of ESRD patients, and further increased rate of 9.7/100,000 in kidney TXPs.[9]

Furthermore, in terms of recurrence risk, it has been studied that the risk of RCC recurrence was similar between transplant and dialysis.[11] This is further supported by data from the Frankfurt Transplant Center, where a large number of kidney recipients featured renal cell and urothelial carcinoma among the highest of urological cancers. In this group, 44% actually succumbed to their disease.[12]

Clear cell remains the most common histological RCC subtype, however ESRD patients and TXPs reports increased risks of papillary subtype RCC with incidence of papillary RCC after renal transplantation of up to 30%.[13]

Risk Factors

Risk factors for RCC specific to each population are listed above (Table 1). Postulated risk factors for the increase in malignancy in a transplanted population are immunosuppression-mediated DNA damage, activation of proto-oncogenes and overexpression of growth factors, interference with DNA repair mechanisms and the loss of immune surveillance and activation of viruses.[9]

Table 1. Epidemiological data review of renal cell carcinoma in kidney transplant patients compared with end-stage renal disease and the general population.

	General population	End-stage renal disease	Kidney transplantation
Lifetime risk	1.62 %	3X	5-7X
Standardised incidence rate (/100,000)	2.6-9.2	4.87 (95% CI 4.1-5.7) Younger population	9.7 (95% CI 5.7-16.5) Biphasic peaks 1st, 4-15 (6) years even younger age
Risk factors	Male, age, smoking	+ Acquired cystic disease tuberous sclerosis + Dialysis duration (3 years)	+Lifelong immunosuppression +Retransplants +Viral infections
Histology / location	Clear cell 75% Papillary 12 %	Clear cell Papillary 35-45%	Native kidneys > 90% Allograft < 10%
Prognosis	T1-T2 - 90% 5-year Advanced - 20% -60% Recurrence -10-30% Metastasis - 13 months survival	Lower stage and grade Acquired cystic disease associated RCC – WHO 2016 classified indolent	73% early stage Worse survival for late stage

RCC in Native Kidneys

Despite the increased risk of RCC development in TXPs, it has been reported that most RCCs in TXPs happen to be incidental, low-stage, low-grade tumours with good prognosis.[14] These tumours are generally small and asymptotic and their diagnosis is usually incidental.[15] If the cancers are diagnosed pre-transplant, patients with ESRD should still be eligible to be placed on the transplant waitlist with minimal delay after treatment and confirmation of localised low-grade cancers.

Laparoscopic radical nephrectomy is currently the main approach to RCC in native kidneys, and can be done via both the Laparoendoscopic Single Site (LESS) or Retroperitoneoscopic 3 scope approach. Locally, the Retroperitoneoscopic 3 port approach is preferred because it does not involve the transperitoneal space. The retroperitoneal approach is a safe and effective technique which allows for the preservation of peritoneal integrity for pretransplant peritoneal dialysis. Further advantages include ease of kidney access by developing the existing potential retroperitoneal space and avoidance of the transperitoneal approach with the resultant reduced risk of injury to and interference from intra-abdominal organs.[16]

Pre-transplant screening for cancer in the native kidney is controversial. However, it has been advocated as RCC has been reported to be bilateral in 20% of ESRD patients.[17] Current pre-transplant screening recommendations for transplant candidates were typically not well validated. According to the European Renal Best Practice Transplantation Guidelines[18], screening in ESRD patients is usually performed following the same protocols suggested for the general population. This topic currently depends on the opinions of expert clinicians, oncologists and screening specialists. The reasons for screening for early cancers in pre transplant ESRD patients are firstly, if RCC, at discovery of presentation, is of a large size or symptomatically picked up, a 25-30% recurrence rate and subsequent 80% mortality was noted. Secondly, according to the European Association of Urology (EAU)[19] and European Renal Best Practice (ERBP) guidelines, such patients, with more locally advanced cancers, would need to wait for an interval of 2-5 years before being able to be listed for transplant, compared to an immediate waitlist admission for small, low-grade RCC cases as mentioned previously.

National country-wide data has been collected in terms of 3 studies from 2 main transplant centers in Singapore – National University Hospital (NUH) and Singapore General Hospital (SGH). A study was done regarding native kidney RCC, stating the outcomes of TXPs who subsequently developed RCC (Table 2). The first study in NUH involving TXP patients with RCC and ESRD from 2010-2013 showed 10 incidental cases of RCC with 3 symptomatic discoveries. Although outcomes were good for the majority and a 100% survival rate was reported, 2 patients at 3 years progressed to distant metastases – likely those with a higher stage of RCC at diagnosis.[20]

The second study from SGH published in the AJT journal, depicted 10 cases of RCC, all patients of whom initially had native renal cysts.[9] Due to regular follow-up and early detection of the cancers, outcomes and survival were both stellar.

Lastly, the third study, also based in SGH, mainly of ESRD patients, depicted only half of the RCC cases with an incidental discovery. This led to poorer outcomes in terms of staging at the time of surgery, as well as survival rates (90%).[21]

Hence, in accordance with the data in Table 2, NUH Singapore recommends RCC screening of the native kidneys beginning 1 month post-transplant. For patients with native renal cysts, the surveillance interval would be 2 years; for those without, 5 years.

This differs from the EAU 2018 Guidelines, whereby ultrasound was performed annually for advanced chronic kidney disease (ACKD), previous RCC, as well as Von Hippel-Lindau (VHL) patients.[19] However, the cost effectiveness and overtreatment impact of such screening measures is still unknown.

RCC in Allograft Kidneys

Found to be much rarer and only occurring in 10% of TXPs with RCC, the prevalence rate of allograft kidney RCC is only 0.2-0.5% amongst all kidney transplant patients.[22] Most occur de-novo, and Singapore locally reports no occult malignancy donor transmission when last studied at the ministry level.

Management of such cancers requires an individualised approach for each patient. Options include nephron sparing approaches including

Table 2. Outcomes of kidney transplant patients with subsequent development of native kidney renal cell carcinoma.

Studies	NUH (2010-2013) Lu J, et al. BJU Int 2014;113:1-37.	SGH (1995-2007) Goh A, et al. Am J Transplant 2011;11:86-92.	SGH (2000-2010) Chen K, et al. Scand J of Urol 2015;49:200-4.
N	13 (7 Transplantations)	10 (Transplantations)	73 (End-stage renal disease)
Incidence	10	10 (All native renal cysts)	41 (56%)
Mean age	54.7±13.7	52 (36-65)	53.6±11.8
Mean years post transplantation	-	4.6	-
Surgery	4 Transperitoneum/7 Retroperitoneum/2 Open	6 Minimally invasive surgery/ 4 Open	73% Minimally invasive surgery
Clavien Dindo classification >2	0	-	-
Tumour size	2.6±2.2	2.5 (1.6-5.5)	-
Clear cell carcinoma	6/13 (46%)	6/10	45 (61%)
Cancer grade <3	6/13 (46%)	-	-
Stage 1	11 (84.6%)	9 (90%)	64 (87.6%)
3 Year follow up	100% Survival 2 Distant metastasis	100% Survival 5 Year overall survival 100%	90% Survival 5 Year overall survival 68.5%

partial graft nephrectomy, percutaneous radiofrequency ablation or cryoablation vs. radical graft nephrectomy.[23] In all patients, an attempt to preserve kidneys is warranted with nephro-sparing approaches, with the choice of the surgery being done either open or with minimally invasive surgical techniques.

The gold standard would be akin to that of a non-transplanted kidney – a partial nephrectomy for localised RCCs where technically feasible.[24] Specific to allograft kidney RCCs in TXPs, the most commonly attempted approach is open allograft partial nephrectomy, both extra-capsular and extraperitoneal via the previous incision. Careful pre-operative planning is required with the aid of CT scans and other forms of imaging to maintain hilar control. Certain surgical techniques include that of clamping the iliac artery above and below the anastomosis during warm ischemia with the venous outflow unclamped or mass clamping the hilum for dissection. The common goal is to minimise warm ischemic time, or perhaps even establish zero ischemia. This is because clinical evidence has demonstrated that transplanted kidneys with prolonged ischemic time are more susceptible to long-term deterioration.[25]

Figure 1 shows a 46 year old male patient presenting in 2017 with an incidentally 4 cm renal mass in the kidney transplant. A partial nephrectomy was done successfully (Figure 2) with careful planning, and final histology showing high grade pT3a, ISUP G3 RCC resulting from sinus, renal and segmental vein involvement and clear resection margins. In February 2021, almost 4 years post-surgery, the patient was reported to be recurrence free with a functioning graft.

This approach has been reported by a mini-review published in the American Journal of Transplantation done in 2017, analysing 56 studies covering 163 patients and 174 masses. Of these patients, about 131 out of 174 masses were treated with nephron-sparing methods like partial nephrectomies or ablation. In terms of recurrence rates post-partial nephrectomy, the study reported a low rate of 3.6%[23], rather comparable to non-transplanted native kidneys which had partial nephrectomies done.

Implication on Medical Management

Post-transplant, to reduce the risk of RCC development, immunosuppression dose reduction and the use of Mammalian target of rapamycin (mTOR) inhibitors (Sirolimus/Everolimus) can

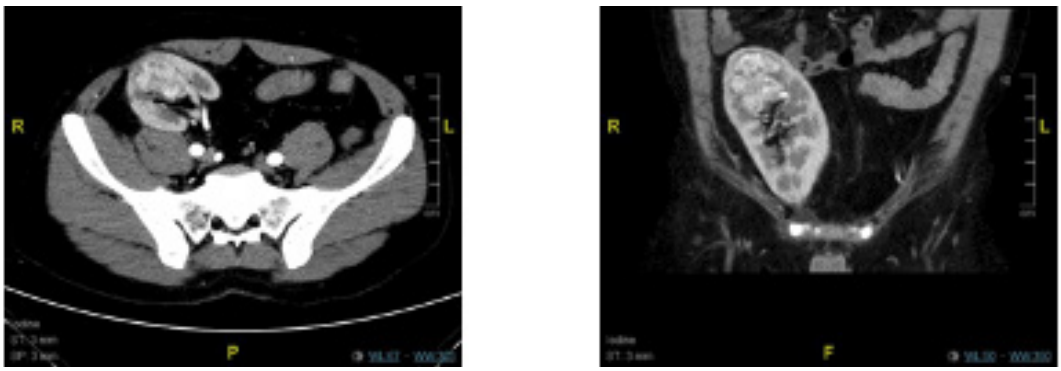

Figure 1. 46-year-old male with high grade pT3a, ISUP G3 RCC resulting from sinus, renal and segmental vein involvement and clear resection margins.

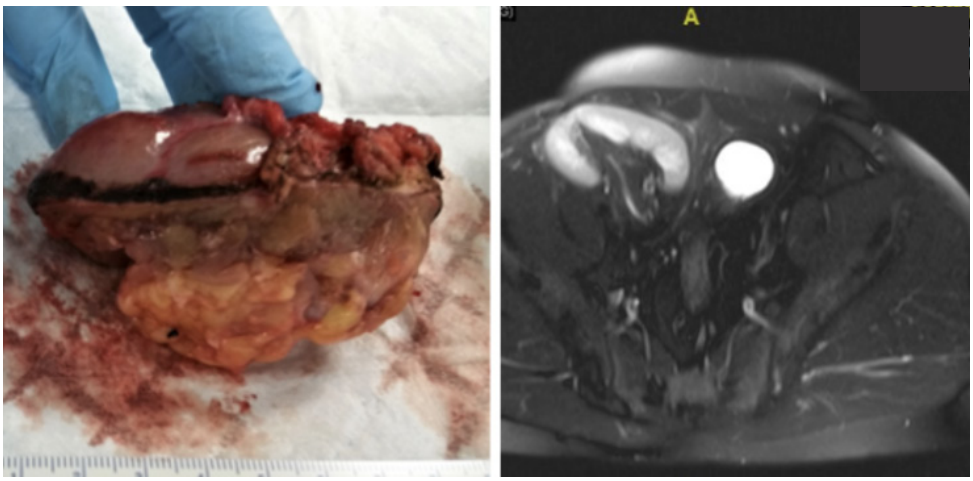

Figure 2. Excision of 4 cm renal mass (left); CT scan of the same patient at 4 year work follow-up, depicting a functional graft (right).

be considered.[26] mTOR inhibitors are advocated instead of other anti-proliferatives including mycophenolic acid due to the following reported advantages: less incidence of viral infections (especially, Cytomegalovirus and BK / Human Polyomavirus 1), less neutropenia and low blood platelets, and a possible reduction in long-term incidence of solid neoplasia. Moreover, in low immunological risk patients, mTORi is advocated by some to allow safe minimization of calcineurin inhibitors (CNI), which in the long term could theoretically prolong graft survival.[27]

In the case of metastatic disease, research currently has no consensus for the use of TKI or immune checkpoint inhibitors (ICI). Several studies have revealed that ICI can produce several immune-mediated toxicities involving different organs, such as the skin, the gastrointestinal tract, the liver, and, of course, the kidney. The most frequent lesion of immunotoxicity in the kidney is acute interstitial nephritis (AIN), although other nephropathies have also been described as a consequence of the use of ICI, such as glomerulonephritis and acute thrombotic microangiopathy, among others.[28] Further research is awaited for the use of these agents in TXPs.

Urothelial Carcinoma

Epidemiology

UC accounts for about 0.02% incidence rate in the general population. Currently, data on risk recurrence of urothelial carcinoma is scarce.[12] UC incidence among kidney TXPs compared to the general population ranges from 1.6 to 3.3.[29,30] This incidence rate is increased by 3.15x in ESRD patients, and apparently even more in our local Asian population by a further 14x.[31,32] At initial staging, Asian populations were found to have the worst tumour characteristics (muscle invasion, higher grade) at presentation.[33,34] Most TXP patients with urothelial cancers present with bladder cancer (92%), while upper tract urothelial

cancer (UTUC) accounts for the remaining 8%. Median time of presentation from TXP was reported to be 4.5 years from time of transplantation. At presentation, kidney TXPs present with worse tumour characteristics (37% with muscle invasive bladder cancer and 34% with late stage cancer).[35]

The risk factors of UC are well known and include male gender, age, smoking, and use of aristolochic acid.[36] In TXPs, lifelong immunosuppression increases the risk of BKV infection; that has been implicated in the development of urothelial cancer. Evidence from a multivariate study reports an increased risk of 11.6 times of developing UC in TXP patients with BKV infection when compared to general population.[37] There were also higher rates of BK viremia in transplant patients with UC, with a systematic review finding viruria in 29% and viremia in 11% of renal TXPs.[38] The pathophysiology of this is explained by BKV nephropathy resulting in graft dysfunction in transplant patients through several oncogenic mechanisms.[39] This is still under study but a recent 2023 article in American Journal of Transplant suggests certain patterns of BK viral integration that actively contribute to the progression of BKV-associated diseases and thus could be a potential target for disease monitoring and intervention.[40]

Compared to RCC, UC has a significantly poorer prognosis in TXP patients. Currently, the 5 year cancer specific survival is 50%, and the 10 year cancer specific survival has been reported to be as low as 0%.

Management

Due to the lower incidence rates of UC, data on their management options are limited. Treatment options including surgery for the management of UC in kidney transplantation are in line with those of non transplant patients.[41,42] With muscle-invasive bladder cancers, the treatment of choice would be radical cystectomy with urinary diversion to the kidney transplant ureter. Neoadjuvant chemotherapy should be equally considered. In non-muscle invasive urothelial cancers, management with Transurethral Resection of Bladder Tumour (TURBT) and cystoscopic surveillance is usually done. In native kidney UTUC, the surgery of choice is radical nephroureterectomy. Notably, 41 to 53% of post-transplant patients developed contralateral UTUC.[43] Hence, surveillance is equally if not more important in TXP patients. In transplanted kidney UTUC, the treatment is total transplant nephroureterectomy or transplant preserving surgery.

Intravesical BCG

Bacillus Calmette–Guérin (BCG), a live attenuated strain of Mycobacterium bovis, is used as a form of intravesical therapy that has shown excellent outcomes in reducing tumour

Table 3. Epidemiological data review of urothelial carcinoma in kidney transplant patients compared with the general population.

	General population	Kidney transplantation
Bladder UC Standardised incidence rate (/100,000)	Bladder – Incidence 0.02%	3.15 (ESRD 2.51) -1.4 (1.3-1.5) USRDS -1.5 (1.4-1.7) EDTA - 4.8 (3.6-6.2) ANZDATA - 14.74 (ASIAN)
Risk factors	Male, age, smoking, aristolochic acid (Geographic)	+Lifelong immunosuppression + BKV (RR11.6) + HPV Infection
At presentation	MIBC 24% Late stage 15%	MIBC 37%, (ESRD 33%) Late stage 34% Bladder 92% (UTUC 8%) Median time from transplantation 4.5 years
Prognosis		Survival worse 5 year CSS – 50% 10 year CSS – 0%

MIBC = muscle-invasive bladder cancer, ESRD = send-stage renal disease, BKV = BK virus, HPV = human papilloma virus, UTUC = upper tract urothelial carcinoma, CSS = cancer-specific survival.

recurrence and mortality.[44] In terms of general population management of non-muscle invasive urothelial carcinoma (NMIUC), this is the standard of care for adjuvant therapy in conjunction with TURBT. However, in immunosuppressed patients such as kidney TXPs, this treatment is cautioned against, and even considered a contraindication due to the increased risk of sepsis and severe morbidity.[45] Mainly, BCG cystitis has been reported to be 20 times more common in transplant patients.[46] In Palou's study of intravesical BCG used in management of 3 renal transplant patients with high-grade superficial bladder cancer and carcinoma-in-situ (CIS), 1 out of the 3 patients developed disease recurrence at 10 months and underwent radical cystectomy.[47] However, overall safe administration of intravesical BCG was recorded. Here, the prophylactic antibodies used were a 3 day course of Isoniazid and Rifampicin. Similarly, in Tomaszewski's study, overall possible but judicious use of intravesical BCG in TXPs is concluded, with the use of prophylactic antibodies and maintenance of a high clinical surveillance for BCG related sepsis.[48] In their study, initially reported 7 months of T1 recurrence and 2 cases of CIS recurrence at 12 and 18 months, although these 3 patients were all free of recurrence subsequently. Notably, the prophylaxis of choice here was Ciprofloxacin.

Herr's study had the biggest group of 12 kidney TXPs. It found 6 out of 12 progressions and 11 out of 12 recurrences.[49] Prophylaxis given was not reported. For TXPs who were BCG treated, recurrence free survival rates and progression free rates were lower compared to other immunosuppressed patients with other cancers or with autoimmune diseases.

The use of intravesical BCG in the management of UC in transplant patients can be advocated with great caution. Close monitoring of transplant patients following its use for potential toxicity is important, or consider other adjuvant therapies such as intravesical Mitomycin.

Management of UC in Transplanted Kidneys or Ureters

With less than 50 case reports in literature, its incidence is placed at 0.15 to 0.18%. When dealing with UC in the transplant kidney, two treatments would be considered: transplant preserving surgery and total transplant nephroureterectomy (TNU).

In many studies, TNU remains the primary intervention. Similarly in non-transplant patients, the EAU guidelines recommend radical nephroureterectomy as gold-standard management of localised UC.[50] Caveats include the possible indication of kidney-sparing ureteric segmental resection in low-grade UC tumours. Unlike RCC, UC is considered a more aggressive cancer with a poor prognosis and nephro-sparing surgery should only be considered in very carefully selected cases. Olsburg et al. presented four cases of UC of the transplanted ureter treated with segmental ureterectomy.[51] 3 out of 4 patients had recurrence and two eventually succumbed to their disease, demonstrating the hazards of preserving the transplanted kidney.

The focus of management must be on oncological care rather than graft preservation. This means, TNU may be preferable to segmental resection.

Table 4. A summary of studies mentioned in this review article regarding intravesical BCG.

Authors	N	Prophylaxis	Follow up/ months	BCG sepsis	Outcomes
Palou et al.	3 (2 T1HG,1 CIS)	3-day course of isoniazid and rifampicin	17-60	Nil.	1 patient CIS recurrence at 10 months --> radical cystectomy
Tomaszewski et al.	3 CIS, 1 T1 LG	Ciprofloxacin x 1 dose	36-84	Nil.	T1 recurrence 7 months, 2 CIS recurrence at 12 and 18 months, BCG course repeated, all free of recurrence subsequently
Herr et al.	45 (12 renal transplantations)	Unknown	40 (12-72)	Nil.	6 out of 12 progress 11 out of 12 recurrence

T = tumor, HG = high grade, CIS = carcinoma in-situ, LG = low grade, BCG = Bacillus Calmette–Guérin.

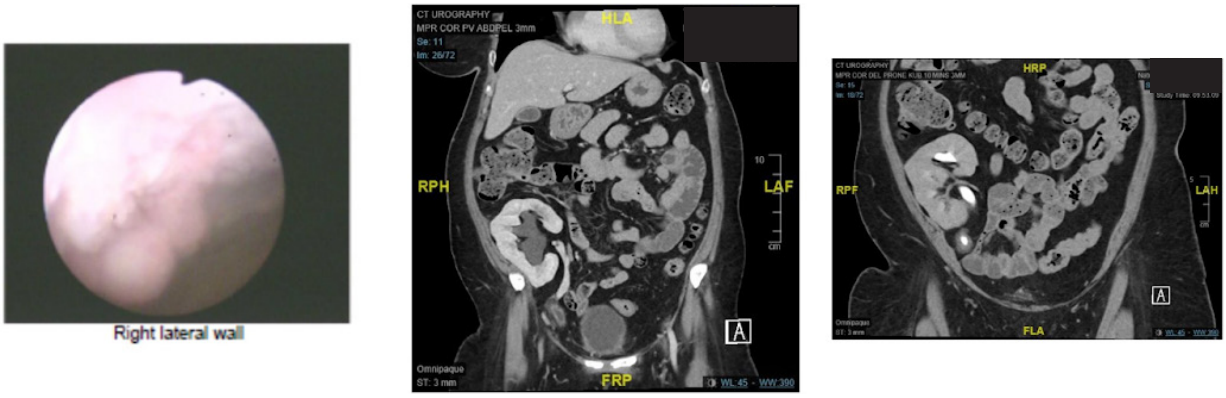

Figure 3. Bladder cancer on cystoscopy at transplant ureter-bladder anastomosis (left); CT scans (April 2018) depicting a hydronephrotic transplant kidney with dilated ureter to level proximal to anastomosis, where tumour was found (right).

Figure 3 is a case of a 54 year old Chinese lady who underwent a kidney transplant in 2005. With a background of BKV nephropathy, she presented with gross haematuria. Investigations reviewed a muscle invasive urothelial cancer at the transplant ureter-bladder anastomosis. A TNU was performed, together with a radical cystectomy and pelvic lymph node dissection in 2018. Histology confirmed the diagnosis of muscle-invasive bladder cancer (MIBC) and transitional cell carcinoma (TCC) in the transplanted ureter. There were no lesions in the transplanted kidney and no nodal spread. In view of the node negative disease and R0 resection, there was no adjuvant radiotherapy done. Patient was taken off immunosuppression and was two and a half years disease free as of February 2021. However, the psychological negative side effect of significant grief reaction to losing the transplant kidney remains and the patient suffers from depression with return to dialysis and loss of quality of life. This case reveals the significant challenge of managing UTUC in kidney TXPs where the dilemma of kidney preservation is balanced against life preservation.

Figure 4. CT TAP of the same patient, disease-free (February 2021).

Conclusion

Urological malignancies are increased in transplant patients when compared to both the general population and the ESRD population. Between the two types (RCC and UC) discussed in this article, RCC has better outcomes, especially at low stage and grade. Hence, screening for RCC in transplant patients can potentially allow for treatment with graft preservation by partial nephrectomy or ablation. Conversely, UC has significantly poorer prognosis. It is much less common, translating to limited evidence-based guidelines. However, for UC, oncological outcomes trump graft preservation, hence priority of management should be radical nephroureterectomy to optimise patient survival and recurrence rates instead. Research in this area should ideally be focused on prevention, especially with its links with BKV infection.

Conflict of Interest

The authors declare no conflict of interest.

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Case Report

Management of a long segment of bilateral ureteric injury: A combination of Boari flap and ureteroneocystostomy with psoas hitch

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Keywords:
Boari flap, bilateral ureteric injuries, ureteral reconstruction

Abstract

Iatrogenic ureteric injuries are a relatively common complication of pelvic and gynecological surgeries which, if left untreated, could lead to medical and legal issues. Therefore, reconstruction of the ureter is still regarded as requiring a sophisticated approach which demands a specialist urologist. This case involves a post-hysterectomy and bilateral salpingo-oophorectomy 46-year-old woman who presented with a bilateral ureteric injury. A left Boari flap and right Lich-Gregoir ureteroneocystostomy with psoas hitch was performed for the correction of the bilateral long segment defect.

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Introduction

The majority of iatrogenic ureteral injuries are a result of pelvic surgery (obstetric rather than colorectal procedures). End-to-end anastomosis is frequently performed for repairing short-segmented defects within the ureter. However, for repairing long segmented deformations, advanced surgical procedures are required for the reconstruction of the injured ureter to enable continuity. Different types of surgical processes are utilised, including ureteroneocystostomy with psoas hitch, ureter replacement, renal auto-transplantation, Boari flap, and nephrectomy. None of these surgical techniques has demonstrated substantial superiority. The aim of this study is to investigate the feasibility of using a combination of Boari flap and ureteroneocystostomy with psoas hitch with in a bilateral iatrogenic ureteric injury.

Case Report

A 46-year-old female patient was referred to our hospital as a case of post-hysterectomy along with bilateral salpingo-oophorectomy that resulted in distal bilateral ureteric injury. The patient was transferred with a condition of fever and anuria for 2 days after surgery. The Computed Tomography of the pelvis and abdomen with an intravenous contrast indicated a leakage of contrast from the right renal pelvis into the right posterior retroperitoneal space. Bilateral moderate hydrouretero-nephrosis with bilateral

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abrupt narrowing of the distal ureters above the ureterovesical junction was present. About 4 cm of each side. Excretion in both kidneys was delayed and there was no contrast passing through the bilateral distal ureters although there was a delay in imaging of 3 hours. The right renal pelvis was perforated due to an increase in intra-pelvocalyceal pressure from a complete distal ureteric obstruction. The patient was in a relatively stable condition when referred, with a body temperature of 37.9 °C, BP 120/71 mmHg, PR 90/minute, and RR 20 /minute.

The laboratory tests revealed leukocytosis and an increase in creatinine from 0.66 ng/dl to 2.68 ng/dl. Fluid therapy was started, and the patient was given an antibiotic. Cystoscopy was carried out to rule out bladder injury and an intra-operative bilateral nephrostogram was done after the bilateral percutaneous nephrostomy was performed. She was admitted for 10 days for correction of infection, acute kidney injury, and post obstructive diuresis. After improvement, the patient was discharged with a bilateral nephrostomy and given an appointment for readmission for a definite surgical procedure after ten weeks. The patient was provided with counselling to enable acceptance of the open bilateral ureteral reconstruction. Anatomical fibrosis of both distal part of ureters was revealed through intraoperative findings. Also, significant adhesions and phlegmon holding the bladder with sigmoid colon and right ureter were also evident.

During the process of dissection, to free the bladder from the phlegmon, the intended ureteral cut was made at the end of the healthy region (at 6 cm from UVJ on the right and 5 cm from UVJ on the left ureter). The mobilization of the bladder was successful. However, due to a limitation of the small size of the bladder, we decided to perform a combination of re-implant ureter and tubular bladder flap. Three stitches of 3/0 Vicryl® suture were inserted into the posterior upper right lateral wall of bladder. The stitches were inserted into the detrusor muscle and went through the tendon of the right psoas muscle whilst avoiding right genitofemoral nerve injury. After the right psoas hitch was checked for a lack of tension the Lich-Gregoir technique for ureteroneocystostomy was used to bridge the defect. The serosal and muscular layers of the detrusor were opened along an oblique course around 2.5 centimeters length. The detrusor was separated from the underlying mucosa to create the anti-refluxing trough. The ureter was placed within the trough and ureterovesical anastomosis was done with 6 stitches of 4/0 catgut suture after a 6-Fr double pigtail ureteric stent across the anastomosis was performed. The detrusor was closed with interrupted 3/0 catgut sutures.

After this, the gap between the proximal end of the left ureter and bladder was widened to 6 cm. The proximal ureteral stump was cut longitudinally for approximately 1-cm for anastomosis. The anterior bladder wall was opened with an oblique shaped incision. The flap was fashioned to be 7 cm, the widths of the apex and base were 3 and 5 cm, respectively. The base of the flap was fixed to the psoas muscle using interrupted 3-0

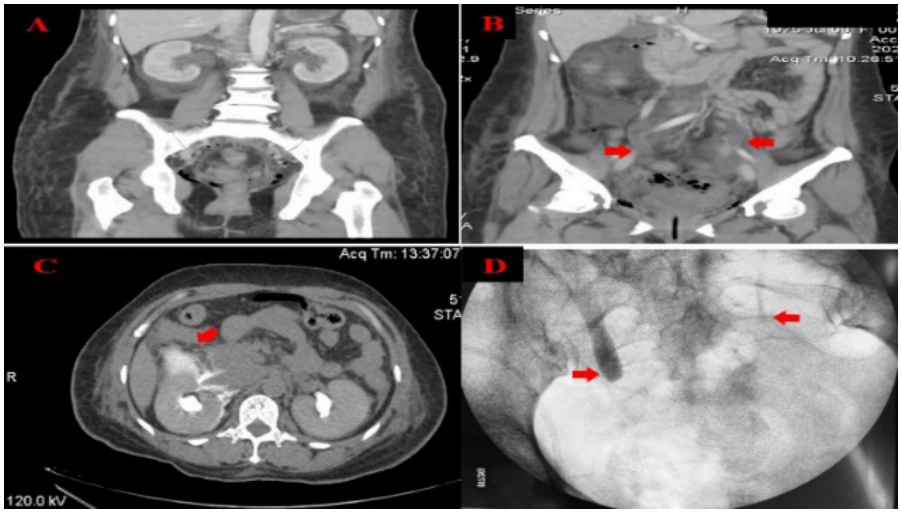

Figure 1. CT abdomen and pelvis with contrast showing: A: Bilateral hydronephrosis after hysterectomy, B: Bilateral distal ureteral stricture, C: Urinary leakage at right renal pelvis, D: Preoperative nephrostography showing bilateral distal stricture.

Vicryl® sutures. Due to the limitation of the flap length, the spatulated ureter was anastomosed to the apex of the flap using the end-to-end technique with 4-0 Vicryl® sutures. A 6-Fr double J ureteral stent was then inserted in the renal pelvis across the anastomosis. Finally, the flap was tubularized by running 4-0 Vicryl® sutures. The bladder was refilled with 200 ml of saline to verify the integrity of closure. The urethral catheter was removed two weeks after surgery, and the double J stents were removed six weeks postoperatively. Finally, 3 months later, the follow up of cystogram revealed a grade III left vesicoureteral reflux; and the bladder capacity was 300-ml with lobulated contour. No post voiding residual urine was detected. The laboratory tests revealed normal kidney function.

Discussion

Ureteric injuries can lead to severe hydronephrosis of the urinary tract and even renal failure. Upper urinary tract reconstructive surgery aims to restore the continuity of the urinary tract and protect renal function.[1] Open ureteral reconstruction was the gold standard for ureteral defects with a success rate of over 90% and good long-term results.[2] Short-lower-ureteric strictures up to 4-5 cm could usually be managed by ureteroureterostomy or simple ureteroneocystostomy.[3] When a long segment of defect in the distal ureter was discovered, a ureteroneocystostomy with psoas hitch became an ideal method for distal ureteral reconstruction. For long distal and middle ureteric strictures, the Boari flap was an effective treatment option.[4,5] Bilateral ureteric stricture is an uncommon occurrence and should be regarded as a difficult surgical challenge. To date there is a shortage of literature focusing on the procedure for bilateral ureteric injury.

Chen and colleagues[6] reported that a case presenting as bilateral long-segment ureteric stricture was successfully treated by the combined use of Y-shaped common channel transureteroureterostomy with Boari flap technique. The technique described was a smart method to reconnect both ureters to the bladder without using an augmentation or bowel segment. In addition, Sagalovich and his colleagues[7] demonstrated management of the bilateral distal ureteric strictures with a bilateral Boari flap. The Boari flap was performed which resulted in an uneventful recovery of the patient. Another study conducted by Ordorica and the team[8] reported on 16 cases of long segment ureteral strictures all of which had received a ureteral replacement using a segment of ileum, colon or the appendix. Renal function and urinary drainage were preserved in fourteen out of the sixteen patients. However, in our case, the length of ureteral stricture was long and included both ureters. We also found fibrosis of the distal end of the proximal stumps and severe retroperitoneal adhesion as the patient experienced urinary leakage and infection due to prior perforation of the renal pelvis. Therefore, we decided to postpone the reconstructive surgery for 12 weeks after injury and use the combination of right ureteroneocystostomy (Lich-Gregoir technique) with psoas hitch and left Boari flap with end-to-end anastomosis.

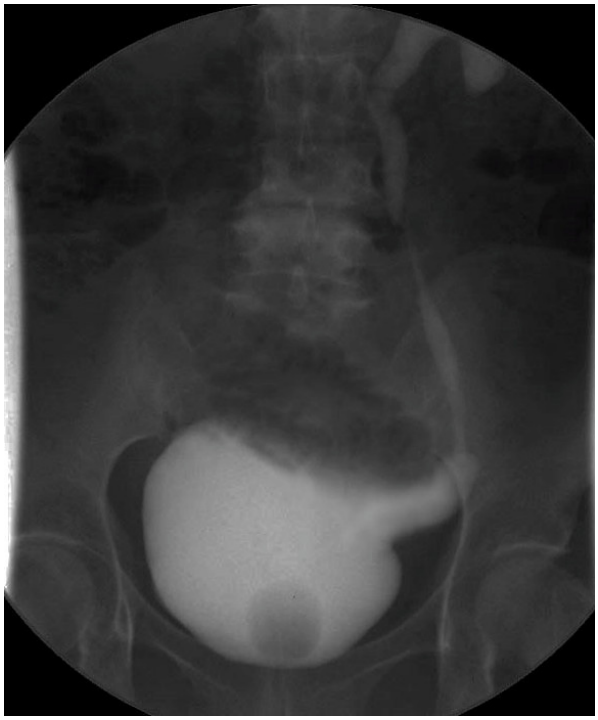

Figure 2. Postoperatively, three months of cystography follow up after surgery showed left ureteral reflux reaching up to the left collecting system; no contrast leakage and post voiding residual urine was detected.

There was a post-surgical follow up with the patient after 6 months. This indicated only a grade III vesicoureteral reflux of the left kidney without renal deterioration. The patient was also free from infection and pain. This technique was facilitated by the introduction of a smart method for the reconnection of both the ureters with the bladder without making use of a bowel segment or augmentation in management of iatrogenic bilateral ureteral injury with long segment defect.

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Conflict of Interest

The author declares no conflict of interest.

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- Results
- Conclusion (s)

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- Materials and Methods
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- Acknowledgement (optional)
- Conflict of Interest
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1.3 Table (s) and legend (s)

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