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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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## Editorial

The fifth issue of Insight Urology (ISU) has now been published online in December 2022. It is comprised of three original articles, three review articles, and two case reports. It covers several fields of urology, namely oncologic urology, pediatric urology, endourology, functional urology, andrology, kidney transplantation, and general urology.

Two review articles were submitted by renowned international authors: “**Updates in substitution urethroplasty for anterior male urethral strictures**” and “**3D Fluoroscopic imaging facilitates reconstruction of common urogenital sinus and cloacal anomalies**”. We are sure that you will enjoy reading and applying the articles’ content to your present urological work, especially when treating male urethral strictures and congenital external genitalia anomalies.

The COVID-19 pandemic has resulted in COVID-19 being considered an endemic disease, and many people in the world have returned to living normally. The frequency of travelling abroad is increasing and onsite conferences are being held more than online meetings. The Editorial Board of ISU hopes that the golden cover of this issue will represent a light of hope that will express the feelings of happiness of everyone in the world.

No reserve. No retreat. No regret.

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

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## Original Article

# Postoperative pain factors after ureterscopic removal of stones in kidney and ureter

*Suttipong Chawong, Teetayut Tangpaitoon, Chatchawet Liwrotsap*

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**Keywords:**

Pain, postoperative, ureterolithiasis, nephrolithiasis, ureterorenoscopy

**Abstract**

**Objective:** Postoperative pain after ureterscopic removal of ureter and kidney stones frequently leads to re-hospitalization, revisit and increased cost. However, risk factors and incidence for early postoperative pain are still unclear. The aim of this study is to investigate the associated risk factors and the incidence of acute postoperative pain after ureterscopic stone removal in the ureter and kidney.

**Materials and Methods:** Retrospective data from 306 consecutive patients who underwent ureterscopic treatment for ureteral and kidney stones from January 2016 to December 2020 were collected. The patients were divided into two groups: (i) Mild postoperative pain ( $n = 179$ ), defined as a pain score lower than four on the visual analog pain scale during the first operative day, and (ii) Moderate to severe postoperative pain ( $n = 127$ ) was defined as a pain score of greater than or equal to 4 during the first operative day. Potential risk factors were included in the univariable and multivariable regression analyses to identify risk factors for developing moderate to severe pain.

**Results:** 127 (41.5%) patients experienced moderate to severe postoperative pain on the first postoperative day. From multivariable analysis, positive pre-operative urine culture, operative time of more than 60 minutes, a stone procedure in the ureter, a postoperative stent, and ureter injury greater than grade I were related to moderate to severe pain with significance risk ratios (RR) of 2.99, 3.70, 4.87, 3.30, and 2.96, respectively ( $p < 0.05$ ).

**Conclusion:** Pain is a frequent postoperative problem associated with ureterscopic removal of stones and should be pro-actively treated with care. Patients are at a higher risk of moderate to severe pain if they required the ureteral procedure, had prolonged operative time, ureter injury after the procedure, needed a stent postoperatively, or had a history of positive preoperative urine culture.

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## Introduction

Urinary tract stone has been identified as a common public health problem with a steadily increasing incidence.<sup>1</sup> Minimally invasive surgery is the mainstay for treatment of urinary tract stones, procedures including extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), and ureteroscopic removal of stones (URS). According to the European Association of Urology (EAU),<sup>2</sup> URS is recommended as an alternative treatment option for ureter stones and renal stone removal. URS can be accessed in an antegrade and retrograde fashion and the development of endourologic instruments has led to greater efficacy, fewer complications, and the rapid recovery of the patients. With the reduction in adverse events, URS can serve as an out-patient procedure,<sup>3</sup> but if the patient registers as more than two on the American Society of Anesthesiologists score (ASA) there is a risk for hospitalization.<sup>4</sup> The incidence of the patient after URS visiting the emergency department (ED) for pain was 14.8%, the most common presentation.<sup>5</sup> Other common revisit presentations were pyrexia, urinary tract infection, and hematuria. Ahn et al. reported that patients who underwent URS for ureter calculi show that acute postoperative pain (a visual analog scale of greater than or equal to 4) was related to young age, psychiatric illness, history of urinary tract infection, use of stone basket, large stone size and prolonged operative time.<sup>6</sup> However, a study by Oğuz et al. found that the female gender, a one-millimeter increase in stone diameter, prolonged sheath time, and presence of residual fragments are associated with postoperative pain.<sup>7</sup> A study by Luo et al. revealed that with regional anesthesia, there is a significantly lower pain score than with general anesthesia.<sup>8</sup> This study analyzed the data pertaining to 5-year retrospective patients who had undergone URS for ureteral and renal calculi at Thammasat hospital in order to identify risk factors and incidence of postoperative pain. It is anticipated that the outcomes of this study will help clinicians to be able to select patients for ambulatory surgery and advise with regard to the risks of postoperative pain before the procedure.

## Materials and Methods

This study was a retrospective cohort study designed to investigate acute postoperative pain.

From January 2016 to December 2020, 307 patients underwent URS at the Urology Department of Thammasat Hospital. Ethical approval was granted by the Thammasat University Ethics Committee in Human Research (Reference MTU-EC-SU-1-103/64). The patients included in the study were at the stage of preoperative preparation in the outpatient department; perioperative and postoperative care was carried out in accordance with our URS routine protocols.

The maximum diameter of the stone was measured preoperatively in each case using simple abdominal radiography, intravenous pyelogram, excretory urography, or non-enhanced computed tomography (CT). On the first day postoperative, the presence of residual stone was determined by plain KUB for opaque stone and ultrasound or non-contrast helical CT for non-opaque stone at one month postoperatively.

Before the date of surgery a mid stream urine sample was collected and cultured, and if positive the patient was treated for uropathogenic bacteria, in accordance with EAU guidelines.<sup>9</sup> Patients were admitted one day before surgery and blood samples were taken and a second urine sample. Prophylactic and postoperative antibiotics were included in our protocol. An anesthesiologist selected appropriate anesthesia. Ureteral access sheath (UAS) was not routinely used, and the sheath size was not more than 14 Fr. Preoperative stents were inserted in patients who needed urine diversion. All procedures were performed using a rigid ureteroscope (Richard Wolf 6/7.5 Fr, Karl Storz 6 Fr) or flexible URS (Richard Wolf COBRA, Karl Storz Flex-X, Olympus URF type). Either Holmium: YAG laser or pneumatic lithoclast were used as stone fragment devices and were selected according to the preference of the surgeon. The stones were removed by spontaneous passing, forceps, or basket. Balloon dilation was used only in patients with a narrowing ureteral orifice. A ureteral JJ stent, 6 Fr, was inserted if the surgeon thought it necessary but was placed routinely in a patient who had a ureteral injury, impacted stone, or residual stone, required a bilateral procedure, or had a solitary kidney. The ureteral injury was assessed as described by Traxer and Thomas grading.<sup>10</sup>

In our protocol, recording of pain status starts in the recovery room and continues until the day of discharge. In this study the visual analog



pain scale (VAS) score (normal range 0 to 10) was used to record pain levels by nurses on the ward. In the first 24 hours, pain level was recorded every hour for four hours; then every 2 hours, four times more; and finally, every 4 hours. No continuous analgesic medication was given. If the pain score was  $\geq 4$ , pain relief was given and the outcome was checked 30 minutes after intravenous analgesic medication (morphine 2 mg) and 1 hour after oral medication (paracetamol 500 mg or naproxen 250 mg). Using this procedure, the majority of patients were discharged the next day. Appointments were made for two weeks after the procedure for stent removal and for four weeks for follow-up imaging by ultrasound, or CT scan. Presence of a residual stone was noted if the stone size was  $\geq 3$  mm on the first postoperative day or at the four week check.

After reviewing 307 chart records of treated patients, the URS procedure was reviewed and only one patient was excluded because the TURP was also carried out simultaneously. Three hundred and six patients were divided into two groups according to mild or moderate to severe acute postoperative pain. Moderate to severe postoperative pain was defined as a VAS score greater than 36 (anytime during the first 24 hours). Patients with moderate to severe pain were analyzed according to age, body mass index (BMI), ASA classification, history of UTI (within three months), history of a stone procedure or ESWL, positive preoperative urine culture, preoperative stent, choice of anesthesia, operative time, stone burden, stone location, abnormal anatomy, residual stone, unilateral or bilateral procedure, choice of lithotripsy, ureteral dilatation, degree of ureteral injury, choice of stone retrieval device, use of ureteral access sheath and use of postoperative ureteral stent. These were all analyzed to identify potential risk factors for predicting moderate to severe postoperative pain.

### Statistical analysis

Statistical analysis was performed using STATA software (version 15). We divided the patients into mild and moderate to severe pain groups. We then compared the two groups using Student T-tests for continuous data. Fisher's exact tests for categorical data were used for patient characteristics; univariable analysis using binary regression was calculated for risk ratio. For

multivariable analysis, the factors which have tendency-related pain ( $p < 0.3$ ) were selected for multivariable analysis differences were deemed as statistically significant when the p-value was less than 0.05 ( $p < 0.05$ ).

Sample size was calculated by reviewing previous studies for estimating the risk factors for postoperative pain. For the multivariable analysis, we needed 10 outcome events per variable. From a review of relevant literature, we found 12 factors to be related to postoperative pain. Risk factors for postoperative pain included gender, a positive preoperative urine culture, stone size, stone location, ureteral access sheath and ureteral dilator usage, anesthetic technique, preoperative stent, postoperative stent, bilateral procedure, operative time, ureter injury grading, and residual stone. Thus, 120 patients who had developed these outcomes were needed. This investigation is of a retrospective cohort study design, and we collected data from 2016 until 2020. Of the 307 patients who underwent URS for remove stone in kidney and ureter in that period, there were 127 moderate to severe pain events.<sup>11</sup>

### Results

Patient characteristics are summarized in Table 1 with the retrospective data of 306 patients (male 157 and female 149), divided into Group 1 (59%) and Group 2 (41%). The age range of the patients was 16-89 years, and the mean ages of the patients were 60 and 58 years in Group 1 and Group 2, respectively. ASA classification was mostly class 2. An anesthesiologist usually chose general anesthesia (67.95%) more frequently than regional anesthesia (32.05%). The mean BMI, previous history of UTI, pre-op alpha-blocker, pre-op stent, equipment diameter large than 10 Fr, and residual stone fragment were the same between the two groups.

Overall stone free rate (SFR) of our study was 91%, for ureteric stone was 99%, for kidney stone 85% and in the case of a combination of kidney and ureter stone was 85%.

From the univariable analysis, positive preoperative urine culture, an operative time of more than 60 minutes, a stone procedure in ureter or ureter and kidney (compared with kidney alone), cumulative stone diameter more than 10 mm, postoperative stent, bilateral procedures, and ureteric injury more than grade 1 were shown

**Table 1.** Patient characteristics

Characteristics	Mild post-operative pain <sup>a</sup> (n = 179)	Moderate-severe post-operative pain <sup>b</sup> (n = 127)	P-value
Age, years, mean (SD)	60 (12)	58 (13)	0.15
Gender			0.082
Male, n (%)	84 (46.93)	73 (57.48)	
Female, n (%)	95 (53.07)	54 (42.52)	
ASA classification			0.430
I, n (%)	50 (27.93)	27 (21.26)	
II, n (%)	92 (51.40)	72 (56.69)	
III, n (%)	37 (20.67)	28 (22.05)	
Anesthetic technique			0.216
Regional anesthesia, n (%)	64 (35.75)	36 (28.35)	
General anesthesia, n (%)	115 (64.25)	91 (71.65)	
BMI, kg/m <sup>2</sup> , mean (SD)	24.86 (3.43)	24.63 (3.65)	0.572
Previous history of UTI			0.621
Yes, n (%)	24 (13.41)	20 (15.75)	
No, n (%)	155 (86.59)	107 (84.25)	
Pre-op alpha-blocker			0.523
Yes, n (%)	55 (30.73)	34 (26.77)	
No, n (%)	124 (69.27)	93 (73.23)	
Pre-op stent			0.245
Yes, n (%)	31 (17.32)	29 (22.83)	
No, n (%)	148 (82.68)	98 (77.17)	
Pre-op urine culture positive			0.007
Yes, n (%)	28 (15.64)	37 (29.13)	
No, n (%)	151 (84.36)	90 (70.87)	
Previous ipsilateral stone removal procedure			0.785
Yes, n (%)	41 (22.91)	31 (24.41)	
No, n (%)	138 (77.09)	96 (75.59)	
Operative time, min, mean (SD)	55.94 (18.65)	67.72 (22.58)	< 0.001
Stone location			0.007
kidney, n (%)	79 (44.13)	34 (26.77)	
ureter, n (%)	88 (49.16)	80 (62.99)	
kidney and ureter, n (%)	12 (6.70)	13 (10.24)	
Cumulative stone diameter, mm, mean (SD)	11.87 (6.79)	14.30 (6.07)	0.0014
Post-op stent			< 0.001
Yes, n (%)	128 (71.91)	118 (92.91)	
No, n (%)	50 (28.09)	9 (7.09)	
Bilateral procedures			0.033
Yes, n (%)	9 (5.03)	15 (11.81)	
No, n (%)	170 (94.97)	112 (88.19)	
Ureter injury grading <sup>c</sup>			0.006
0, n (%)	165 (92.18)	105 (82.68)	
1, n (%)	12 (6.70)	11 (8.66)	
2, n (%)	1 (0.56)	8 (6.30)	
3, n (%)	1 (0.56)	3 (2.36)	
Equipment diameter large than 10 Fr <sup>d</sup>			0.818
Yes, n (%)	87 (48.60)	67 (52.76)	
No, n (%)	92 (51.40)	60 (47.24)	
Residual stone fragment from day 1 plain film or US at 1 month			1.000
Yes, n (%)	16 (8.94)	11 (8.66)	
No, n (%)	163 (91.06)	116 (91.34)	

SD = standard deviation, n = number, min = minute, ASA = American Society of Anesthesiologists, BMI = body mass index = UTI = urinary tract infection, mm = millimetres, Post-op = postoperative

<sup>a</sup>Visual analog pain scale less than 4, <sup>b</sup>Visual analog pain scale equal or more than 4, <sup>c</sup>Ureter grading by endoscopic view (described by Traxer and Thomas grading, grade 10), <sup>d</sup>Included use of semirigid, flexible ureteroscope, balloon dilatation, or ureteral access sheath, during the operation





to be potential risk factors ( $p < 0.05$ ). However, sex, age, ASA classification, BMI, previous history of UTI, preoperative stent, preoperative alpha-blocker, choice of anesthesia, usage of equipment diameter larger than 10 Fr, and residual stone were not related to moderate to severe postoperative pain in our study, as shown in Table 2.

For the multivariable analysis, we decided to exclude cumulative stone diameter because of the co-linearity with the operative time (Figure 1). The multivariable analysis shows that a positive preoperative urine culture (RR: 2.99 [1.15–2.02]);  $p = 0.003$ ), an operative time of more than 60 minutes (RR: 3.7 [1.28–2.25]);  $p < 0.001$ ), stone procedure in the ureter (RR: 4.87 [1.66–3.30]);  $p < 0.001$ ), postoperative stent (RR: 3.30 [1.51–5.08]);  $p = 0.001$ ), and ureteric injury  $>$  grade 1 (RR: 2.96 [1.20–2.53]);  $p = 0.003$ ) remained significantly associated with moderate to severe postoperative pain, as shown in Table 3.

## Discussion

Ureteroscopic removal of stones (URS) was widely used in patients in whom ESWL was either not successful or was not suitable for the treatment of ureteral stone and renal stone. Our study was focused on both URSL and RIRS, which have been deemed as safe and having a higher success rate for removing the stones. Our data showed that stone free rate following ureterscopic removal of stone in the ureter was 99%, in kidney was 85% and in combined ureter and kidney was 85%. Similar studies also show a stone free rate of URS for ureteral of 80 to 100%<sup>6</sup> and for renal calculi of 91%.<sup>12</sup>

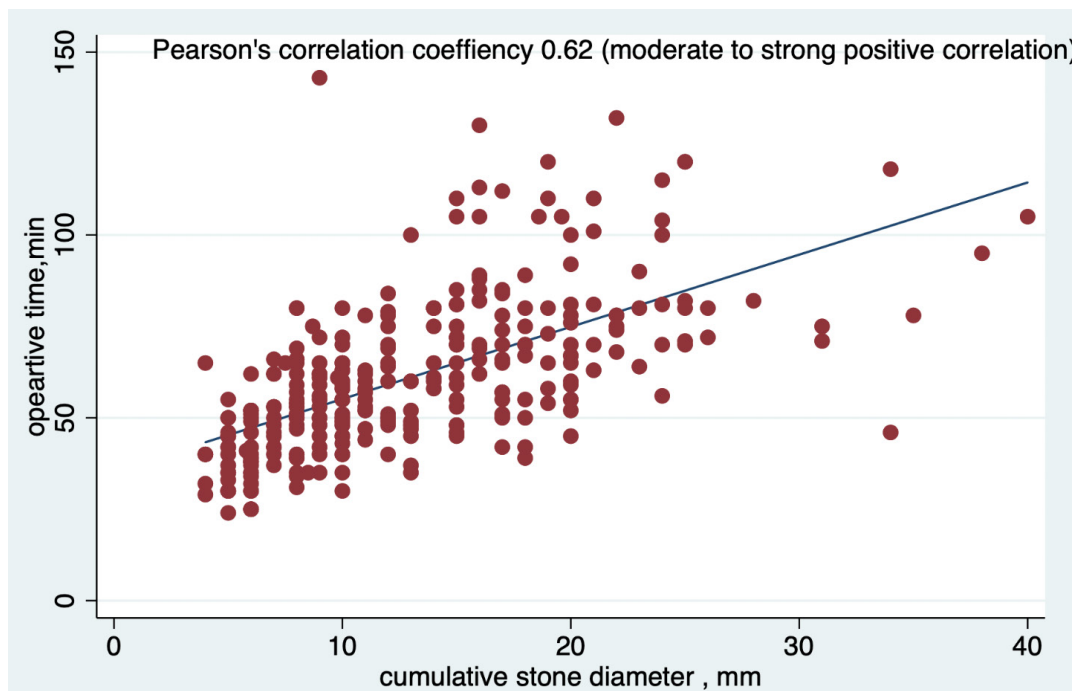
Nowadays, endourology can be carried out in an ambulatory care setting. It can reduce the need for admissions and thus, cut health care costs. Although postoperative pain is not a common complication in URS, it is one of the most tabled complaints from patients who underwent URS when visiting ED. From the results, early

**Table 2.** Univariable analysis to indicate risk for post-operative moderate to severe pain

Factor	Crude risk ratio	P-value
Age $<$ 50 yr	1.15 (0.85 - 1.55)	0.398
Male gender	1.28 (0.98 - 1.68)	0.082
ASA classification $>$ 2	1.25 (1.19 - 4.53)	0.229
BMI $<$ 25	1.00 (0.76 - 1.34)	1.000
History of UTI	1.11 (0.78 - 1.59)	0.621
Pre-op alpha-blocker	0.90 (0.66 - 1.21)	0.523
Pre-op stent	1.21 (0.90 - 1.64)	0.245
Pre-op urine culture positive	1.52 (1.17 - 1.99)	0.006
Previous ipsilateral stone removal procedure	1.05 (0.77 - 1.43)	0.785
General anesthesia	1.22 (0.91 - 1.66)	0.216
Operative time more than 60 min	1.75 (1.33 - 2.31)	$<$ 0.001
Stone procedure (in comparison to kidney)		
Ureter	1.58 (1.15 - 2.19)	0.005
Ureter and kidney	1.73 (1.08 - 2.76)	0.022
Cumulative stone diameter $>$ 10 mm	1.61 (1.21 - 2.13)	$<$ 0.001
Post-op stent	3.14 (1.70 - 5.82)	$<$ 0.001
Bilateral procedure	1.57 (1.12 - 2.21)	0.033
Ureteric injury $>$ grade 1	2.13 (1.63 - 2.80)	0.002
Equipment diameter large than 10 Fr	0.97 (0.74 - 1.26)	0.817
Residual stone fragment	0.98 (0.61 - 1.58)	1.000

yr = years, BMI = body mass index, UTI = urinary tract infection, min = minutes, ASA = American Society of Anesthesiologists, mm = millimetres, Pre-op = preoperative, Post-op = postoperative, Fr = French (from French catheter scale)





**Figure 1.** Correlation between operative time and stone size  
min = minutes, mm = millimeters

**Table 3.** Multivariable analysis for post-operative moderate to severe pain (excluding cumulative stone size)

Factor	Adjusted risk ratio	P-value
Male gender	1.53 (0.94 - 1.55)	0.126
ASA classification > 2	1.00 (0.86 - 1.58)	0.316
Pre-op stent	-0.32 (0.72 - 1.25)	0.752
Pre-op urine culture positive	2.99 (1.15 - 2.02)	0.003
General anesthesia	1.90 (0.99 - 1.76)	0.058
Operative time more than 60 min	3.70 (1.28 - 2.25)	< 0.001
Stone procedure (compare to kidney)		
Ureter	4.87 (1.66 - 3.30)	< 0.001
Ureter and kidney	0.81 (0.76 - 1.93)	0.417
Post-op stent	3.30 (1.51 - 5.08)	0.001
Bilateral procedure	1.78 (0.97 - 1.78)	0.075
Ureteric injury > grade 1	2.96 (1.20 - 2.53)	0.003
Residual stone fragment	0.81 (0.75 - 1.97)	0.417

Yr = years, UTI = urinary tract infection, min = minutes, ASA = American Society of Anesthesiologists, Pre-op = preoperative, Post-op = postoperative, Fr = French  
a Binary regression analysis

postoperative pain was a significant issue because experiencing postoperative pain was the most common concern expressed by patients.<sup>13</sup> It can interrupt sleep and limit the mobilization of the chest and skeletal muscles.<sup>14</sup> Moderate to severe pain scores also affected recovery time, length of hospital stay, readmissions, patient dissatisfaction

and disturbance of quality of life, and increased costs.<sup>15,16</sup> The higher pain score was correlated with analgesic usage as patients whose immediate postoperative pain was poorly managed had a tendency to develop chronic pain after surgery.<sup>17</sup>

The mechanisms causing pain after URS were believed to be associated with many factors.



First, the operation can lead to hydroureter and hydronephrosis during use of URS irrigation solution. Furthermore, the acute distension of the renal capsule caused by the obstruction of urolithiasis and the consequent inflammation can result in pain. Pain receptors are located around the submucosa in the renal pelvis, calyces, renal capsule, and upper ureter.<sup>18</sup>

### Pre-operative factors

Some factors, including age, gender, ASA classification, and BMI did not differ between the two groups, as was found in a similar study by Cakici et al.<sup>19</sup> Data pertaining to age, gender, BMI, and ASA classification showed no significant differences in complications after flexible URS. A preoperative stent was not related to moderate to severe postoperative pain, as was reported from the research conducted by Yuk et al. In that study they found that preoperative ureteral stenting did not affect perioperative complications or operative times, additional treatment rates, and stone-free rates. However, it increased the success rate of access sheath placement. Contrary to this result, Assimios et al.<sup>20</sup> reported that preoperative ureteral stenting decreased complications in patients with renal stones but not in those with ureteric stones. There was no relation between previous ipsilateral stone removal and moderate to severe postoperative pain. However, a previous report did describe an association with a lower rate of complaints by phone after the procedure.<sup>21</sup>

Positive urine culture is the single significant preoperative factor. The rationale behind this is that a positive urine culture increases the risk of infection and the resulting inflammation results in an increased incidence of pain and ED attendance.<sup>5</sup> There was no difference in pain between drug-resistant bacteria and non-drug-resistant bacteria.

However, intra-operative factors and general anesthesia techniques were not associated with moderate to severe postoperative pain to the same level as described in another study by Sahan et al.<sup>22</sup> There was no significant difference in GA and RA between postoperative pain among patients in our study who underwent URS, but Luo et al.<sup>8</sup> reported that the GA group had a significantly higher pain score than the RA group.

The location of stone also impacted on postoperative pain, especially stones located

in the ureter and kidney. If the procedure was performed only in the ureter, it was more significantly related to postoperative pain than in stones in the kidney or stones in both the kidney and ureter. In our study, when we performed URS in both ureter and kidney simultaneously, we only selected patients who had a non-complex ureteral stone. This might explain a lower incidence of pain in patients who underwent URS in both the ureter and kidney at the same time.

The etiology of early postoperative pain after ureteroscopy is poorly understood and likely multifactorial but do include an increase intrapelvic pressure, extravasation of irrigation fluid, ureteral edema and ureteral injury.<sup>23</sup> In our study results, kidney stone removal had a significantly lower risk of postoperative pain. The majority of patient who had kidney stones underwent URS by flexible scope in combination with UAS and as a result intrarenal pelvis was lower than semi-rigid scope use. Fragmentation of ureteral stone was associated with a higher risk of ureteral injury.

An operative time of more than 60 minutes was another critical risk factor for predicting postoperative pain in our study. Operative time was related to hydronephrosis and hydroureter during operation, which cause ureteral edema and damage. Cheung et al.<sup>24</sup> also showed that surgery time greater than 60 minutes could increase the incidence of complications and postoperative pain. The factors which impacted the operative time were the cumulative stone size and bilateral procedure. In our study, stone size was associated with post-operative pain, but there was no significant relation with the bilateral procedure. This finding is similar to that described in a study by Ahn et al.<sup>6</sup> who discovered that moderate to severe postoperative pain was significantly associated with stone size but not significantly with operative time. A bilateral procedure had no impact a finding in common with other studies<sup>25,26</sup> which also reported no increased risk of complication in performing a bilateral URS.

Our study showed that ureteral injury was associated with postoperative pain ( $p = 0.004$ ). To the contrary, a study from Oğuz et al.<sup>7</sup> had a different outcome. We suspected that the outcome was different because, their study<sup>7</sup> only included data pertinent to ureteral injury grade 1, while in our study patients with ureteral injury grade 1-3 were included.

### Post-operative factor

Use of a postoperative stent is also related to postoperative pain. We found that cases that required a postoperative stent usually have a more significant ureteral injury, undergo dilation of the ureter wider than 10 Fr and had impact stone which made more significant ureteral mucosal injury and pain. Cheung et al.<sup>24</sup> also reported an association between the ureteral stents and pain. Nestler et al.<sup>27</sup> observed that discomfort and pain increased with the diameter of the indwelling ureter stent. In another study, el-Faqih et al.<sup>28</sup> showed that the patients who required ureteral stents developed dysuria and pain in 79% and 29% of cases, respectively. Du et al.<sup>21</sup> found that the most frequent complaint by the patients were symptoms associated with the stent. On the other hand, Segalen et al.<sup>29</sup> showed that there were no differences between patients with a postoperative stent and other patients with regard to pain and complications.

As is the case with all research, our study has some limitations. First, this study was retrospective in design; therefore, the information collected for analysis, e.g., stone removal technique, access sheath time, and reason for a postoperative stent may not be completely standardized. Secondly, multiple surgeons participated in the study, and the various surgical techniques, and the learning curve of the teams can have an impact on the result. Interestingly, Netsch et al.<sup>30</sup> showed that the learning curve has no impact on stone free rate and low grade complications. Thirdly, CT scans were not carried out on day one post operative on the patients in our study therefore there is the potential for us to have missed detection of some non-opaque stones.

### Conclusions

Pain is a significant problem in postoperative URS. The risk factors associated with patients who had the procedure for ureteral stones were prolonged operative time, ureter injury and needed implantation of a stent after the procedure. These findings were similar to those in patients with a history of positive preoperative urine culture for bacteria. In conclusion, patients who have some or all of these factors need to be treated with caution, monitored for pain, and advised with regard to hospitalization after the procedure.

### Conflict of Interest

The authors declare no conflict of interest.

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## Original Article

# Prostate cancer detection rate using MRI/ultrasound fusion-guided prostate biopsy in Siriraj Hospital

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**Keywords:**

MRI/ultrasound fusion-guided biopsy, targeted biopsy, prostate cancer

**Abstract**

**Objective:** Systematic transrectal ultrasound (TRUS) guided biopsy has been considered a gold standard for prostate cancer diagnosis for many decades. The problem of this conventional method is the low detection rate especially in the case of repeat biopsy. This results from a limitation associated with ultrasound imaging inhibiting the visualization of cancerous lesions during the procedure. More recently, there has been increasing importance attributed to the use of multiparametric MRI for the identification of cancer inside the prostate gland. Targeted prostate biopsy, using multiparametric MRI/ultrasound (mpMRI/US) fusion-guided technology helps improve the detection of prostate cancer and has become a novel standard for tissue diagnosis. This study was conducted to investigate and report on the cancer detection rate of mpMRI/US fusion guided prostate biopsies at Siriraj Hospital.

**Materials and Methods:** Data pertinent to patients who underwent mpMRI/US fusion guided biopsy at Siriraj Hospital between September 2017 and December 2019 was retrospectively reviewed.

**Results:** A total of 499 men underwent mpMRI/US fusion guided biopsy, with the transperineal approach being used in the vast majority of cases (91.8%). Targeted biopsy provides a better cancer detection rate than systematic biopsy (55.3% vs 47.1%,  $p = 0.009$ ). Combined targeted and systematic biopsies improved cancer detection rate compared to systematic biopsy alone (60.3% vs 47.1%,  $p < 0.001$ ). A subgroup analysis of men with positive biopsies showed that detection of clinically significant cancer (Gleason grade group  $\geq 2$ ) was no different between targeted and random biopsies (87.2% vs 80.8%,  $p = 0.11$ ). The common complications from transperineal approach were urinary retention (5.4%) and hematuria (5.2%) while complications of infection were rare (0.2%).

**Conclusion:** We found that targeted biopsy with mpMRI/US fusion guided technology provides a more effective option for prostate cancer diagnosis. A combination of targeted and systematic biopsy improve prostate cancer detection rate more effectively than systematic biopsy alone. The transperineal approach is a safe and effective technique with a rare incidence of infectious complications.

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## Introduction

Prostate cancer is the most commonly diagnosed malignancy in men. The early stages of prostate cancer rarely cause symptoms, therefore, presence of symptoms suggests locally advanced or metastatic disease. There is significant potential for the improvement in early detection of prostate cancer with a better screening program. Men who presented with elevation of serum prostate specific antigen (PSA) or abnormal digital rectal examination should be recommended for tissue diagnosis. However, the gold standard for cancer diagnosis has still been systematic or random transrectal ultrasound (TRUS) guided biopsy. As a consequence many men without cancer underwent unnecessary biopsies, clinically insignificant cancers have often been detected, but significant cancers have often been missed.<sup>1</sup>

Multiparametric magnetic resonance imaging and ultrasound (mpMRI/US) fusion guided biopsy or targeted biopsy can be used to solve this problem and improve the rate of detection of prostate cancer. Several studies have shown that mpMRI/US fusion guided biopsies can reduce the overdiagnosis of clinically insignificant prostate cancers and improve the detection rate of those that are clinically significant.<sup>1,2</sup> The aim of this study was to evaluate the rate of cancer detection using the mpMRI/US fusion guided prostate biopsy method in Siriraj Hospital.

## Materials and Methods

### Study design and participants

This retrospective observational study was conducted after obtaining approval from the Siriraj Institutional Review Board (SIRB Protocol Number: 509/2562(EC3)). Medical records of patients who underwent mpMRI/US fusion guided prostate biopsies between September 2017 and December 2019 at the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand were reviewed. The data collected included patient demographics, preoperative serum PSA level, MRI findings, indication for biopsy, perioperative information, and pathological reports. Patients with missing or incomplete follow up data were excluded from this study.

### Imaging

All patients underwent a 1.5 or 3 Tesla multiparametric MRI scan without endorectal coil.

The protocol included a T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging. All results were reported by radiologists using the Prostate Imaging-Reporting and Data System (PI-RADS) score version 2.1.<sup>3</sup> Patients with a lesion with a PI-RADS score  $\geq 3$  were scheduled for tissue diagnosis.

### Biopsy protocol

Before the biopsy procedure, prostate MRI images were retrieved into the KOELIS Trinity® system (Koelis, France) enabling the creation of 3D images of the prostate gland and the index lesion. All patients were given prophylactic antibiotics as per standard guideline recommendations. Every procedure was performed by urologists or trained physicians under general anesthesia. The volume of the prostate gland was acquired using real-time 3D ultrasonography. An organ-based tracking software package was used to superimpose labeled 3D MRI images over 3D ultrasonography as used to superimpose labeled 3D MRI images over real-time 3D ultrasonography with organ-based tracking technology. All patients underwent targeted biopsies first, followed by systematic biopsies with an 18-gauge needle biopsy gun. All needle tracts were registered and recorded in the 3D mpMRI/US fusion images. A transperineal ultrasound probe, linear-grid needle guidance, and a Steady Pro™ probe holder (Koelis, France) were the accessories utilized in the transperineal approach. All specimens were interpreted and recorded by genitourinary pathologists.

### Outcomes

The primary outcomes were overall detection rates of cancer using mpMRI/US fusion guided prostate biopsies and systematic prostate biopsies. The secondary outcomes were detection rates of clinically significant prostate cancer in mpMRI/US fusion guided prostate biopsies compared to systematic prostate biopsies and the complication rate. According to the Epstein criteria,<sup>4,6</sup> the definition of clinically insignificant prostate cancer was a patient with Gleason score  $\leq 6$  (Gleason Grade Group 1), a tumor involving fewer than three cores, tumor volume  $\leq 50\%$  of any given core, and a prostate-specific antigen density of  $< 0.15$  ng/ml per cm.<sup>3</sup>

### Statistical analysis

Data was analyzed using PASW Statistics for Windows (version 18.0; SPSS Inc., Chicago, Ill., USA). Sample size was calculated based on cancer detection rate, using nQuery Advisor version 5.0 with an allowable error of 5% and a 95% confidence level. Descriptive statistics were used to describe demographics and clinical characteristics. Quantitative data was described as mean and standard deviation (SD) or median and range (min, max), as appropriate. Qualitative data was expressed as number and percentage. Pearson's chi-squared test, Yates' continuity correction, or Fisher's exact test were used to compare qualitative data between groups, as appropriate. The Kappa statistic was used to assess agreement of findings with regard to detection of prostate cancer.

### Results

This study included 499 eligible cases with a mean age of 69.2 years. The median PSA was 8.5 ng/ml (IQR 6.2-13.4) and median prostate

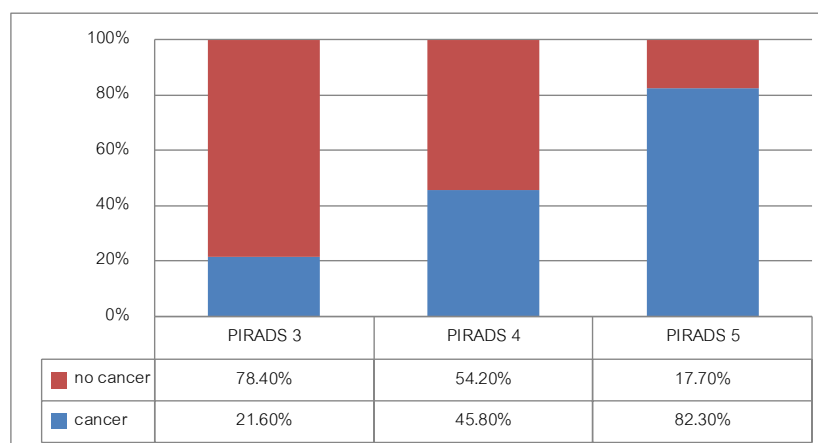
volume was 42 ml (IQR 28-61). Of these, more than half (53.1%) were biopsy naïve. The most significant indication for a prostate biopsy was a high PSA (53.3%) and previous negative biopsy (42.6%). The vast majority of the patients (91.8%) underwent the transperineal approach for prostate biopsy with a median of a 23 core needle biopsy, as shown in Table 1. Abnormal lesions in mpMRI categorized as PIRADS 3, 4 and 5 were 19.3%, 57.4% and 23.6%, respectively. The cancer detection rates of PIRADS 3, 4 and 5 were 21.6%, 45.8%, and 82.3%, respectively, as shown in Figure 1. Targeted biopsy provided a more effective cancer detection rate than systematic biopsy (55.3% vs 47.1%, OR 1.39, 95%CI 1.08-1.78,  $p = 0.009$ ). Sixty-six patients (23.9%) had positive targeted biopsies but negative random biopsies, while 25 patients (10.6%) had positive random biopsies but negative targeted biopsies. Combined targeted and systematic biopsies improved cancer detection rate in comparison to systematic biopsy alone (60.3% vs 47.1%, OR 1.71, 95%CI 1.33-2.2,  $p < 0.001$ ), but there was no statistically

**Table 1.** Demographic data

Sample size N = 499	
Mean age, years (SD)	69.2 (7.1)
Median preoperative PSA, ng/ml (IQR)	8.5 (6.2-13.4)
Median prostate volume, ml (IQR)	42 (28-61)
Median number of lesion (min, max)	1 (1-5)
Biopsy-naïve, n (%)	265 (53.1)
Indication for biopsy, n (%)	
High PSA	266 (53.3)
Previous negative biopsy	212 (42.6)
Abnormal MRI	11 (2.2)
Active surveillance	10 (2.0)
PI-RADS score version 2.1, lesion n (%)	
3	134 (19.3)
4	397 (57.1)
5	164 (23.6)
Approach n (%)	
Transperineal	458 (91.8)
Transrectal	38 (7.6)
Both	3 (0.6)
Median number of total cores biopsy (IQR)	23 (19-28)
Median number of targeted cores biopsy (IQR)	11 (8-16)
Median number of random cores biopsy (IQR)	12 (10-12)
Median operative time minutes (IQR)	25 (20-35)
Median length of stay days (IQR)	3 (0-3)

SD = standard deviation, PSA = prostate specific antigen, IQR = interquartile range, MRI = magnetic resonance imaging





**Figure 1.** Detection rates of mpMRI/US fusion biopsy, categorized by PI-RADS score version 2.1

**Table 2.** Prostate cancer detection by targeted or systematic biopsy

Cancer detection	Targeted biopsy n (%)	Systematic biopsy n (%)	P-value
Positive for cancer	276 (55.3)	235 (47.1)	OR 1.39
Negative	223 (44.7)	264 (52.9)	(95% CI 1.08-1.78) p = 0.009

Cancer detection	Combined biopsyn n (%)	Systematic biopsyn n (%)	P-value
Positive for cancer	301 (60.3)	235 (47.1)	OR 1.71
Negative	198 (39.7)	264 (52.9)	(95% CI 1.33-2.2) p < 0.001

Cancer detection	Combined biopsyn n (%)	Targeted biopsyn n (%)	P-value
Positive for cancer	301 (60.3)	276 (55.3)	OR 1.23
Negative	198 (39.7)	223 (44.7)	(95% CI 0.96-1.58) p = 0.11

significant difference when compared to targeted biopsy alone (60.3% vs 55.3%, OR 1.23, 95%CI 0.96-1.58,  $p = 0.11$ ) as demonstrated in Table 2. A subgroup analysis of all positive biopsies revealed that targeted biopsy detected clinically significant prostate cancer slightly more successfully than random biopsy (87.2% vs 80.8%) and detected fewer insignificant cancers (12.7% vs 19.1%), but there was no statistically significant differences in these data (OR = 1.62, 95% CI 0.89-2.94,  $p = 0.11$ ) (Table 3).

Of the 499 patients, the most common complications were acute urinary retention (5.4%) and significant gross hematuria (5.2%), all of which were resolved by conservative treatment without morbidity that necessitated surgery. There were a few unusual complications ( $\leq 1\%$ ) related to the general anesthesia or medical conditions as shown in Table 4. No complications associated with sepsis or severe infection were

found in our study.

## Discussion

Transrectal ultrasound-guided biopsy has been considered the standard of care for prostate cancer diagnosis for decades because of its availability and user-friendly platform. However, the limitation of the ultrasound-guided technique was the inability to delineate a suspected lesion within the prostate gland. This conventional method led us to perform only a systematic or random pattern of prostate biopsy. Recent studies have indicated that prostate cancer can be more accurately detected through MRI-targeted biopsy or mpMRI/US fusion-guided biopsy.<sup>7,8</sup> There are however, various perspectives and controversial issues about the integration of this novel technology into an individualized diagnostic pathway.<sup>9-12</sup>

MRI reporting system can represent the cancer detection rate by categorization through

**Table 3.** Subgroup analysis of positive biopsy

Group	Targeted positive n (%)	Systematic positive n (%)	P-value
Gleason grade group $\geq 2$	164 (87.2)	118 (80.8)	OR 1.62 (95% CI 0.89-2.94) p = 0.11
Gleason grade group 1	24 (12.7)	28 (19.1)	

Group	Combined positive n (%)	Systematic positive n (%)	P-value
Gleason grade group $\geq 2$	177 (83.4)	118 (80.8)	OR 1.2 (95% CI 0.69-2.08) p = 0.51
Gleason grade group 1	35 (16.5)	28 (19.1)	

**Table 4.** Demographic data

Complication	n (%)
Acute urinary retention	27 (5.4)
Gross hematuria	26 (5.2)
Hypertensive urgency	5 (1.0)
Anesthesia complication (aspiration)	2 (0.4)
Prostatitis with negative culture	1 (0.2)
Cerebrovascular event (TIA)	1 (0.2)
Atrial fibrillation	1 (0.2)

use of PIRADS. We noted that the higher the PIRADS score, the greater likelihood of prostate cancer detection. Our study showed a similar outcome but a slightly lower detection rate in each PIRADS compared to those of Kasivisvanathan et al.<sup>2</sup> This might reflect the progressive learning curve by various means, including the sharing of good practice, since this procedure was first advocated in our institute. Moreover, 47% of the participants underwent repeated biopsies, which could lower the efficacy of the performance of systematic biopsy. Our results emphasized the efficacy of the implementation of mpMRI/US fusion guided prostate biopsy, which could detect prostate cancer more accurately than random biopsy (55.3% vs 46.7%). Our findings also showed that a combination of the two methods improved cancer detection performance when compared to random biopsy alone.

A subgroup analysis of all positive biopsies demonstrated that mpMRI/US fusion guidance was effective for the detection of clinically significant cancer. In a PRECISION trial, the mpMRI/US fusion-guided prostate biopsy method had a higher detection rate of significant prostate cancer, which matched our findings. In the mpMRI/US fusion-guided prostate biopsy group, there was a similar higher detection rate of significant cancer

(87.6%) and a lower detection rate of insignificant cancer (12.4%). This was beneficial for reducing overtreatment in patients with insignificant prostate cancer, as well as reducing the morbidity and mortality associated with treatment.

Complications associated with prostate biopsies included bleeding (hematuria, hematospermia), infection, discomfort, and urinary retention. According to a systematic review and meta-analysis, minor hematuria is common following a prostate biopsy, while significant bleeding requiring hospitalization occurred in 1% of all cases and risk of urinary retention in 2%.<sup>13,14</sup> Gross hematuria (5.2%) and acute urinary retention (5.4%) were noted as minor complications in our study. These higher rates of self-limiting events may be due to several causes. First, our preferred technique involved a transperineal approach in which the needle tracts are directly passed from the apex to the base of the prostate gland and involve a greater periurethral area when compared to the conventional method. Second, nearly half of our patients were repeated biopsies, in which there may have been some subclinical inflammation, causing additional reaction after our procedure. On the positive side, our transperineal technique showed a zero percent incidence of re-admission due to sepsis or serious infectious complication, similar findings to previous studies.<sup>15,16</sup>

To the best of our knowledge, this was the largest study in Thailand to demonstrate the impact of the transperineal approach with mpMRI/US fusion prostate biopsy. The outcomes emphasized this was not only a better option but also a safer method in the detection of prostate cancer for Thai people. However, as with all live studies, there are potential limitations in this study. First, its retrospective design lacked a matched control group. Second, as it is a retrospective study of



medical records, there is naturally interobserver variability among radiologists, which could lead to misinterpretation of the PIRADS scores and different annotation of the index lesions. Finally, the fusion software may not represent an identical match between MRI and ultrasound imaging. This discordance could have resulted in the different prostate volume measurements and discrepancies in the settings of both prostate imaging techniques.

## Conclusion

Targeted biopsy with mpMRI/US fusion guided technology provides a more effective alternative option for prostate cancer diagnosis. A combination of both targeted and systematic biopsy improves prostate cancer detection rate in comparison to systematic biopsy alone. The transperineal approach is a safe and effective technique with a rare incidence of infectious complications.

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## Conflict of Interest

The authors declare no conflict of interest.

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## Original Article

# Erectile function in end-stage renal disease before and after renal transplantation

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**Keywords:**

Erectile dysfunction, renal transplantation, International Index of Erectile Function, IIEF-5, testosterone, end stage renal disease

**Abstract**

**Objective:** Erectile dysfunction (ED) can be defined as the inability to achieve or maintain an erection of sufficient firmness for vaginal penetration and sexual satisfaction. Details pertaining to erectile function among end-stage renal disease (ESRD) and renal transplant patients remains controversial. The objective of this study was to evaluate erectile function before and after renal transplantation in all male renal transplant recipients in Chiang Mai University Hospital.

**Materials and Methods:** This study included 35 patients with ESRD who underwent renal transplantation at Chiang Mai University Hospital. Erectile function in these patients was assessed using the 5-item Thai version of the International Index of Erectile Function (IIEF-5) and serum testosterone levels were measured before and 3, 6 and 12 months after renal transplantation. After the transplant, changes in IIEF-5 scores were analyzed based on the duration of dialysis.

**Results:** Out of 35 patients, 6 (17.1%) patients had severe ED, 12 (34.2%) patients were scored as moderate, 8 (22.8%) as mild to moderate, 7 (20%) as mild, and 2 (5.7%) patients had no ED in the period before renal transplantation. Twelve months after renal transplantation 2 (6.2%) patients had severe ED, 2 (6.2%) patients had moderate ED, 5 (15.6%) patients had mild to moderate ED, 7 (21.8%) patients had mild ED and 16 (50%) had no ED. There was a significant difference between before- and after-transplant IIEF-5 scores ( $p < 0.05$ ) in patients who had been on dialysis for more than six months. Serum levels of testosterone had increased significantly at the 12 month check following transplantation ( $3.25 \pm 1.54$  vs.  $5.76 \pm 1.73$  ng/ml,  $p < 0.001$ ).

**Conclusion:** After successful renal transplantation, many patients showed a significant improvement in erectile function score, especially in those with a history of longer duration of dialysis. Increase in testosterone levels can contribute to the improvement of ED

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## Introduction

Erectile dysfunction (ED) is the inability to achieve or maintain an erection of sufficient firmness for vaginal penetration and sexual satisfaction.<sup>1</sup> ED is a major medical problem that can affect a patient's quality of life, causing anxiety, depression and loss of self-esteem.<sup>2</sup> ED cannot be traced back to a single cause, but can be as a result of a multisystem disease, psychological factors or chronic diseases.<sup>3</sup>

End-stage renal disease (ESRD) is one of the chronic diseases that cause erectile dysfunction due to organic failures (neuroendocrine disorders, uremia, anemia and atherosclerosis), psychogenic factors (depression, anxiety), and drugs used to treat concomitant chronic renal disease such as antihypertensive drugs, immunosuppressants, H<sub>2</sub> blockers, etc. ESRD patients are often on regular dialysis and approximately 25% of dialysis patients are mentally depressed at some point, which contributes to ED.<sup>4,5</sup>

Renal transplantation has been widely accepted as the best treatment option for ESRD and recipients have reported a significant improvement in their quality of life post-transplant over the past twenty years.<sup>6,7</sup> In patients with uremia, renal transplantation has shown positive results in improving sexual function when compared to other non-dialysis or dialysis treatments.<sup>8</sup> In addition, there are reports that sex hormone levels may be altered or improved in male uremic patients after successful renal transplantation.<sup>2,9</sup> However, these benefits of renal transplantation for ED are not consistent and, therefore, controversial.<sup>10</sup>

Although, numerous published studies have shown altered erectile function and sex hormone profiles after renal transplantation in Western uremic patients, fewer data are available pertinent to Thai renal transplant recipients.

The objectives of this study are to evaluate erectile function, biochemical and serum testosterone levels before and after renal transplantation in all male renal transplant recipients at Chiang Mai University Hospital.

## Materials and Methods

The study was carried out in ESRD patients who underwent living and deceased renal transplantation between June 2019 and February 2021 at Chiang Mai University Hospital.

The inclusion criteria included male patients aged 18 years and older who could commit to follow up until 12 months after surgery.

The exclusion criteria included patients who had graft rejection within three months after transplantation and secondary renal transplantation.

Thirty-five patients were enrolled onto this study. Of these, 32 patients (91%) had a follow-up period of 12 months after renal transplantation. The other 3 patients had died. All patients gave informed consent, and the ethics committee of Chiang Mai University approved this study (Study Code: SUR-2562-06746).

Erectile function was evaluated using the 5-item Thai version of the International Index of Erectile Function (IIEF-5) during the period of dialysis before renal transplantation. IIEF-5 is used to determine the presence of ED in accordance with degree of severity (Severe ED: 5-7, Moderate ED: 8-11, Mild to moderate ED: 12-16, Mild ED: 17-21, No ED: 22-25).<sup>11</sup> None of the patients enrolled onto the study received any treatment for erectile dysfunction in the pre-transplantation and post-transplantation period.

Other data collected included morning serum testosterone and blood chemistry of blood urea nitrogen (BUN), creatinine (Cr), and fasting blood sugar (FBS), hemoglobin, cholesterol, and triglyceride levels. These data sets were evaluated before renal transplantation.

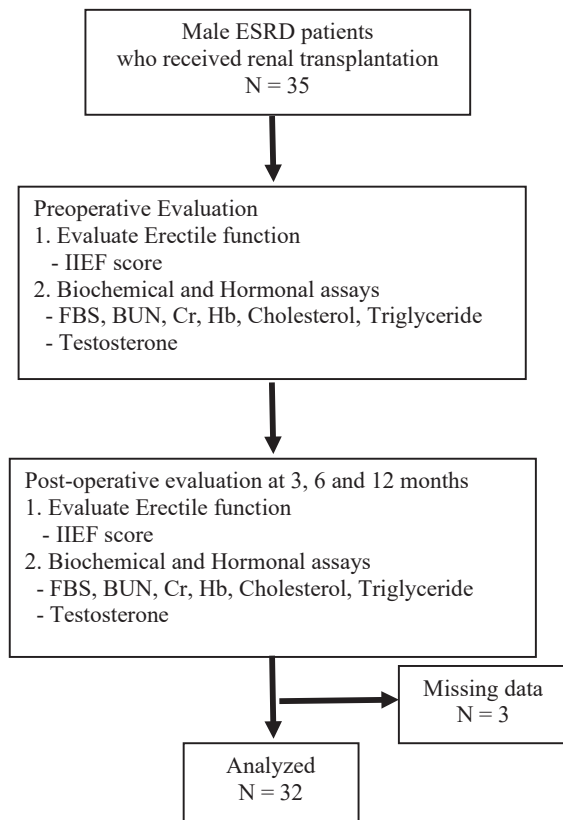
At 3, 6 and 12 months after successful renal transplantation patients were reassessed for ED using the IIEF-5 score and biochemical and hormonal assays were also evaluated (Figure 1).

## Statistical analysis

All statistical analyses were performed using standard statistical software (STATA version 16.0). Data was described in terms of frequency and percentages in the case of categorical variables and mean  $\pm$  SD for continuous variables. A paired t-test was used for analysis of continuous data and a  $p < 0.05$  was considered statistically significant.

## Results

Thirty-five male patients were enrolled. Of these patients, twenty-two received renal transplants from cadavers and thirteen from living



**Figure 1.** Flow chart of the present study

donors. All patients had undergone external iliac vein and artery vascular anastomoses. At the 12-month follow up, 25 (71.4%) patients had no complications. Complications among the other 10 patients included delayed graft function [3 (8.6%)

patients], lymphocele [2 (5.7%) patients], anastomosis stricture [2 (5.7%) patients] and deceased [3 (8.6%) patients]. The clinical characteristics of patients are summarized in Table 1.

In the period before renal transplantation, 2 (5.7%) patients had no ED and 33 (94.3%) patients had ED with differences in severity (severe,  $n = 6$  [17.1%]; moderate,  $n = 12$  [34.2%]; mild to moderate,  $n = 8$  [22.8%]; mild,  $n = 7$  [20%]). Twelve months after renal transplantation, 16 (50%) patients had fully recovered erectile function (severity of ED before-transplant: severe,  $n = 1$ ; moderate,  $n = 4$ ; mild to moderate,  $n = 5$ ; mild,  $n = 4$ ; No ED,  $n = 2$ ). The other 16 (50%) patients still had ED after transplantation with various degrees of severity (severe,  $n = 2$  [6.2%]; moderate,  $n = 2$  [6.2%]; mild to moderate,  $n = 5$  [15.6%]; mild,  $n = 7$  [21.8%]). Data pertaining to severity of ED before and after renal transplantation are displayed in Table 2.

Mean IIEF-5 scores before and after transplantation 12 months were 14.72 and 20.52 respectively.

To stipulate the relationship between dialysis duration and the effect of renal transplantation on ED, patients were divided by duration of dialysis into three subgroups specifically < 6 months, 6-24 months, > 24 months. IIEF-5 scores before renal transplantation were compared to 3, 6 and 12 months after transplantation as shown in Table 3.

**Table 1.** Patient clinical characteristics

Characteristic	Range (Mean $\pm$ SD) (n = 35)
Duration of dialysis (months)	0-120 (47.03 $\pm$ 34.23)
Age (years)	26-61 (42.66 $\pm$ 9.44)
BMI (kg/m <sup>2</sup> )	15.8-30.06 (22.58 $\pm$ 3.30)
Systolic pressure (mmHg)	110-185 (146.23 $\pm$ 16.58)
Diastolic pressure (mmHg)	62-113 (89.37 $\pm$ 13.78)
Number (%)	
Cause of End-Stage Renal Disease	
Hypertension alone	8 (22.86)
Diabetes mellitus alone	4 (11.43)
Calculi	3 (8.57)
Chronic glomerulonephritis	2 (5.71)
Lupus nephritis	2 (5.71)
IgA nephropathy	1 (2.86)
Autosomal dominant polycystic kidney disease	2 (5.71)
Bilateral ureteropelvic junction obstruction	1 (2.86)
Unknown cause	12 (34.29)

**Table 2.** Severity of ED before and after renal transplantation (3, 6, 12 months follow-up)

	IIEF-5 score				
	Severe 1-7 n (%)	Moderate 8-11 n (%)	Mild to mod 12-16 n (%)	Mild 17-21 n (%)	No ED 22-25 n (%)
Before transplantation	6 (17.14)	12 (34.29)	8 (22.86)	7 (20.00)	2 (5.71)
3 months after transplantation	2 (5.71)	8 (22.86)	9 (25.71)	12 (34.29)	4 (11.43)
6 months after transplantation	1 (3.03)	4 (12.12)	6 (18.18)	13 (39.39)	9 (27.27)
12 months after transplantation	2 (6.25)	2 (6.25)	5 (15.63)	7 (21.88)	16 (50.00)

**Table 3.** Patient IIEF-5 before and after renal transplantation (subgroup by dialysis duration)

Dialysis duration (months)	N	IIEF-5 score mean (SD)				P-value		
		[A] Before-transplant	[B] 3 months after-transplant	[C] 6 months after-transplant	[D] 12 months after-transplant	A vs B	A vs C	A vs D
< 6	3	19.00 (5.29)	20.33 (3.21)	21.00 (3.61)	23.67 (1.15)	0.762	0.650	0.297
6-24	10	12.70 (5.03)	14.27 (5.69)	18.40 (6.31)	19.90 (6.03)	0.233	0.038	0.007
> 24	19	12.47 (5.38)	15.24 (5.38)	17.05 (5.10)	18.00 (5.72)	0.005	0.001	<0.001

First subgroup: duration of dialysis less than 6 months. There were no significant changes in the IIEF-5 scores between before and 3, 6 and 12 months after renal transplantation.

Second subgroup: duration of dialysis 6 to 24 months. IIEF-5 scores significantly increased between before and at 6 and 12 months after renal transplantation ( $p = 0.038$ ,  $p = 0.007$ , respectively). There were no significant changes in IIEF-5 scores between the period before and 3 months after renal transplantation.

Third subgroup: duration of dialysis more than 24 months. IIEF-5 scores significantly increased between before renal transplantation and 3, 6 and 12 months after surgery with scores of  $p = 0.005$ ,  $p = 0.001$ , and  $p = < 0.001$ , respectively.

Serum testosterone levels after renal transplantation were significantly increased ( $p < 0.001$ ) compared with before renal transplantation. Moreover, serum BUN, Cr and FBS were significantly decreased ( $p < 0.001$ ) in comparison with before renal transplantation. Other blood chemistry data including cholesterol, triglyceride and hemoglobin levels are summarized in Table 4.

## Discussion

A high prevalence of ED has been previously reported in patients with ESRD and on dialysis,

levels reaching even higher than 80%.<sup>12,13</sup> This is consistent with the findings in our study, specifically that 33 (94.3%) patients with ESRD had some degree of ED during regular dialysis before renal transplantation. Out of these 6 (17.1%) patients had severe ED, 12 (34.2%) patients had moderate ED, 8 (22.8%) patients had mild to moderate ED and 7 (20%) patients had mild ED. The increase in IIEF-5 scores after renal transplantation represented a significant decrease in prevalence of ED, a finding in accordance with the report by Pourmand et al.<sup>14</sup>

This study showed that the duration of dialysis was a significant factor in the recovery of erectile function after renal transplantation. The most improvement in erectile function was noted in patients who had previously had dialysis for more than six months. There is a significant difference between our observed results and those reported by previous studies. Conversely, Teng et al. have previously reported a greater improvement in ED was found in those patients who underwent shorter dialysis (< 6 months) compared to patients who had a longer dialysis duration.<sup>15</sup> This difference may be due to the small number of subjects in the subgroup with shorter dialysis in our study, and the base line IIEF-5 scores of this subgroup are high.



**Table 4.** Blood chemistry and testosterone profile before and after renal transplantation

	Mean (SD)					
	Testosterone	BUN	Creatinine	Hemoglobin	Cholesterol	Triglyceride
Before transplantation	4.31 (1.9)	61.41 (23.4)	12.50 (3.1)	11.03 (1.76)	154.64 (44.31)	159.07 (87.43)
3 months after transplantation	6.92 (1.9)	28.35 (14.4)	1.84 (0.8)	12.65 (2.08)	188.52 (43.03)	181.30 (110.43)
P-value	< 0.001	< 0.001	< 0.001	< 0.001	0.005	0.557
Before transplantation	3.25 (1.5)	60.94 (23.6)	12.62 (3.1)	10.96 (1.75)	155.62 (44.87)	137.07 (82.39)
6 months after transplantation	5.42 (1.7)	28.00 (17.3)	1.65 (0.6)	13.99 (2.77)	182.37 (44.14)	140.65 (119.25)
P-value	< 0.001	< 0.001	< 0.001	< 0.001	0.012	0.821
Before transplantation	3.25 (1.5)	62.52 (23.4)	12.61 (3.1)	10.9 (1.733)	150.25 (43.36)	144.94 (96.60)
12 months after transplantation	5.76 (1.7)	24.16 (15.2)	1.57 (0.7)	14.12 (2.85)	185.77 (39.11)	130.17 (44.84)
P-value	< 0.001	< 0.001	< 0.001	< 0.001	0.004	0.577

BUN = blood urea nitrogen

Although 16 patients in our study regained partial or full erectile function after renal transplantation, that represents only 50% of the participants. ED remained an issue after transplantation with various degrees of severity in the other half of our subjects (severe ED, 6.2%; moderate ED, 6.2%; mild to moderate ED, 15.6%; mild ED, 21.8%). Uremia may have caused irreversible impairment in some of these patients. Some patients also reported being afraid of causing injury to the transplanted kidney during sexual activity which potentially affected their IIEF-5 scores.

Uremia and dialysis can result in a lower testosterone level, a factor well established as being causative in ED.<sup>16,17</sup> Our results were similar to that of Teng et al. who reported that the serum testosterone levels were increased after renal transplantation and were related to recovery of ED [15]. We observed a significant increase in serum testosterone levels after transplantation compared to before transplantation. This data suggests that increased serum testosterone levels may assist in the improvement of erectile function in men with ESRD following renal transplantation.

There was no observable impact of cholesterol, triglyceride and hemoglobin levels in the study as regards having an impact on ED. The same was observed in a study by Bahnsawy et al.<sup>18</sup>

There are some very interesting findings from our study however it only included a small sample size. The data warrant a further study using a larger population. There was an absence of any etiological characterizations of ED.

A potential limitation of this study was that some patients are hesitant to talk about ED due to its highly sensitive nature, especially those raised in a traditional Thai culture. We were extremely mindful of this and were careful to conduct private interviews in order to obtain accurate data.

## Conclusions

The ESRD patients we studied had a very high prevalence of ED. After successful renal transplantation, many of these patients showed an improvement in erectile function score, especially those with a history of longer duration of dialysis (> 6 months). An increase in testosterone levels following renal transplantation may contribute to the improvement of ED in ESRD patients.

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## Conflict of Interest

The authors declare no conflict of interest.

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**Review Article**

# Radiation safety and protection in urology

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**Keywords:**

Ionizing radiation,  
radiation exposure,  
radiation effects,  
radiation safety

**Abstract**

Urologists are inevitably exposed to ionizing radiation for the length of their professional career due to medical practices in their field. However, awareness with regard to safe practices and the use of protective gear are frequently inadequate. Several studies have confirmed the potential long-term adverse effects of radiation exposure upon patients and medical personnel. All urologists, therefore, need a thorough understanding of radiation physics, and the adverse effects, safety issues, and protective measures associated with the medical practices. This understanding will serve as a foundation for the optimal utilization of radiation and the safety of patients and medical personnel.

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**Introduction**

The medical utilization of x-rays began in 1920 when the intensity of the radiation used was still high. Work after this point, therefore, tended to focus on minimizing the radiation dose. Over the past 30 years, there has been increasing use of imaging technology, including the emergence of different techniques, such as computerized tomography, nuclear imaging, and fluoroscopy. These practices have been widely harnessed to facilitate surgical procedures, thus leading to the rapid increase of radiology applications for medical purposes.<sup>1</sup> Over the last thirty years, the exposure of the U.S. population to radiation has gradually increased seven fold, with half of the exposure derived from medical radiation.<sup>2</sup> Urological diseases generally involve the use of radiation in various forms, from diagnosis, to

surgical procedures, and follow-up. Since both urologists and patients may frequently be exposed to radiation, the urologists, as the professionals, need to be aware of its inherent hazards. This article highlights issues associated with radiation safety, potential risks, protection measurement, and the techniques which could potentially reduce such exposure.

**Physics of radiation**

Ionizing radiation is a type of energy emitted from atoms in electromagnetic waves or particles, which could originate from natural or artificial sources. The mechanism of image formation starts with an x-ray source that transmits photons through the atmosphere through internal organs towards an image intensifier. While traveling across the organs, the photons transfer energy to

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various tissues, each of which can retain a unique energy level, creating the difference in radiation intensity. When the radiation progresses to strike an image intensifier, it provides context to the image and finally produces a radiograph (Figure 1).<sup>3</sup>

### Measurement of radiation dose

Radiation quantification usually involves the following standard units of measurement:

**1. Air exposure** is equivalent to the radiation amount that allows 1 kilogram of air to ionize into 1 Coulomb charge. The unit of measurement is the Coulomb (C) or Roentgen.

**2. Absorbed dose** is the amount of ionizing radiation absorbed by the body after passing through it while transferring some energy to the visceral organs. The unit of measurement is the Gray.

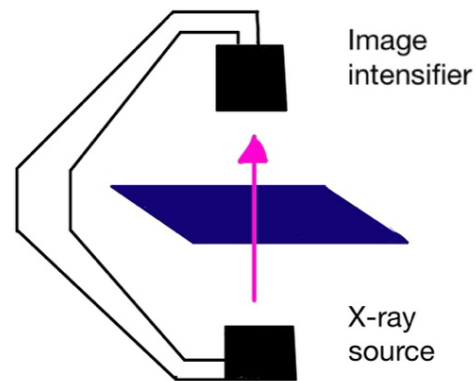
**3. Equivalent dose** is equal to the product of the absorbed dose and radiation weighting factor. The weighting factor is assigned to each type of radiation, mainly because a particular amount of radiation may affect tissues and organs differently. A higher amount is more likely to cause more harm to the tissues. The Sievert is used as the unit of measurement.

**4. Effective dose** is the sum of equivalent doses within individual visceral organs. This varies depending on the sensitivity of that specific organ, recognized because varying levels of damage occur in different types of tissues. For example, eyes and genital organs tend to have a higher sensitivity with regard to radiation than others. Despite the same amount of radiation being retained, the radiation weighting factor is thus required for accurate quantification. The unit of measurement unit is again the Sievert.<sup>4,5</sup>

The applications of x-rays in urology occur across diagnosis, surgical treatment, radiotherapy, and surveillance. Table 1 shows the effective dose applied for a particular procedure. Most patients with urolithiasis tend to experience recurrence, thereby have an increased risk of radiation exposure during diagnosis and treatment. One study demonstrated cumulative radiation doses ranging from 100 to 1,375 mSv.<sup>6</sup>

### Dosimeters

All operators should have the occupational radiation exposure doses monitored by a personal dosimeter while working in radiation areas. This practice should accompany other protective measures to prevent the personnel from excessive



**Figure 1.** The x-ray image process demonstrating the x-ray source and image intensifier

**Table 1.** Mean effective radiation doses derived from radiographic and urological procedures (adapted from Radiation protection of patients in urology | IAEA. 2017).

Procedure	Mean effective dose (mSv)
Abdominal radiography (AP)	0.7
Intravenous pyelography (6 films)	2.5
Voiding cystourethrography	1.2
Cystography	1.8
Lithotripsy	1.3
Nephrostomy	3.4
Percutaneous nephrolithotomy	4.5
Ureteric stenting	4.7
Single-phase CT abdomen	10
Renal angiography	2 to 30

radiation. The types of dosimeters are as follows:<sup>7</sup>

**1. Film badges** are composed of a layer coated with light-sensitive materials. Once radiated, the film is processed, and the intensity developed will be further compared against the standard film, ultimately providing information on the amount of radiation received. While the film badge is straightforward for daily use, it cannot detect a low level of radiation and is not suitable for re-use.

**2. Luminescence dosimeters** comprise a luminescent compound that deposits a portion of incident radiation energy. The material is then stimulated before releasing energy in luminescence signals. There are two types of stimulators: thermoluminescence and optically stimulated luminescence (OSL) (Figure 2). Luminescence dosimeters are highly precise and reusable several times. Thus, they are widely utilized and are adopted at King Chulalongkorn Memorial Hospital.



**Figure 2.** Device demonstrating the use of optically stimulated luminescence (OSL)

**3. Electronic dosimeters** can quantify the radiation dose and report the results simultaneously using an electronic system coupled with a semiconductor detector. They can also give instant notification whenever the radiation dose exceeds a prescribed limit.

Those who work with radiation should at least wear two dosimeters: one beneath the lead apron to measure the radiation in contact with visceral organs, the other outside the apron, at either the collar or eye level, to detect radiation towards the skin and eye lens (Figure 3). The surgeon can use the data from both dosimeters to calculate the effective dose derived from the operation.

The International Commission on Radiological Protection (ICRP) has determined the maximum acceptable level of radiation dose for practitioners to be no more than 20 mSv each year. It may exceed the allowance up to 50 mSv per year, but the cumulative figures over five years must not be more than 100 mSv.<sup>8</sup> In addition, the level of safe radiation doses have been designated for different parts of the body; for example, the radiation exposure for the eye lens should not be over 20 mSv per year,<sup>9,10</sup> whereas the skin, arms, and legs can tolerate radiation up to 500 mSv yearly (Table 2).<sup>11</sup>



**Figure 3.** Position for dosimeter placement

### Effects of radiation

The impact of ionizing radiation upon humans is categorized follows:

**1. Deterministic effects** which occur from radiation exposure above the threshold level. The severity of the damage is in proportion to the radiation dose. For example, eye injury, skin burn, and hair loss,<sup>12</sup> occur at exposure to 0.5, 2, and 3 Gy of radiation, respectively. These effects rarely arise from urological procedures due to the small dose of radiation applied.<sup>13</sup>

**2. Stochastic effects** occur even from exposure to a small amount of radiation. Given that there is no safety threshold limit for stochastic effects, it is essential for practitioners to be aware of the long-term consequences, mainly because exposure to low-dose radiation over time may increase cancer risk. The disease probability depends on the amount of radiation, while the severity of the disease is not dose-dependent.<sup>14</sup>

Three landmark studies have verified the relationship between radiation exposure and carcinogenesis:

**Table 2.** Occupational dose limit for each organ (adapted from 2013 Recommendations of the International Commission on Radiological Protection).

Type of limit	Occupational dose limit
Effective dose	20 mSv per year exception: 50 mSv per year (in 5 successive years <100 mSv)
Equivalent dose	
Eye lens	20 mSv per year
Local skin dose	500 mSv per year (averaged over any skin surface of one square centimeter)
Hands, lower arms, feet, ankles	500 mSv per year





- Pierce et al. conducted a study on survivors of atomic bombings at Hiroshima and Nagasaki during World War II. The authors estimated the radiation doses received at a certain distance from the bomb and compared the incidence of malignancy to an average population. They found a significantly higher incidence of solid malignancy, which was directly proportional to the radiation dose and duration since the exposure was without an apparent threshold.<sup>15</sup>

- Cardis et al. conducted a study on over 400,000 workers at nuclear power plants in 15 collaborating countries by measuring the radiation dose with personal dosimeters. The authors demonstrated that the incidence of leukemia and non-leukemia malignancies was directly proportional to the amount of radiation exposure. In addition, the authors speculated that 1-2% of the cancer deaths were caused by radiation.<sup>16</sup>

- According to a retrospective study by Pearce et al., children who acquired cumulative radiation doses of 50 and 60 mGy from diagnostic imaging experienced a 3-times higher incidence of leukemia and brain cancer, respectively, in their adulthood compared to those who never underwent such imaging. However, there remains the controversy that the patients subjected to diagnostic imaging at a younger age might already have certain abnormalities contributing to subsequent cancer risks.<sup>17</sup>

Even though level 1 evidence to prove the relationship between medical radiation exposure and malignancy has yet to be established, these studies, as mentioned earlier, suggest that clinicians should be aware of the potential harm inflicted by radiation.

## **Radiation risks to patients and medical personnel**

**1. Radiation risks to patients:** Medical providers with protective gear receive only 1% of the radiation emitted, whereas the patients without protective equipment are directly exposed to radiation. Ferrandino et al. conducted a retrospective study on 108 patients who suffered from acute renal colic from 2000 to 2006. At the one-year follow-up, the patients received an average radiation dose of 26.7 mSv from diagnostic imaging, and more than 20% of them received radiation above 50 mSv.<sup>18</sup> Subsequently, Fahmy et al. conducted a similar study and demonstrated mean radiation doses given to those with urolithiasis within one

and two consecutive years of 29.3 and 37.3 mSv, respectively.<sup>19</sup>

The recurrence rate of urolithiasis is 50% within five years; therefore, the patients are at risk of repeatedly receiving a large amount of radiation. In addition to this, fluoroscopy is commonly employed in endourology. For obese patients and those with complex cases, urologists must apply higher levels of radiation. Thus, there must be careful attention paid to radiation safety and protection.<sup>20</sup>

## **2. Radiation risks to medical personnel:**

Urologists, along with the other subspecialists such as radiologists, cardiologists, and vascular surgeons, have a high likelihood of being exposed to the highest radiation doses.<sup>1</sup>

Rajaraman et al. performed a prospective study on 90,000 radiologic technologists between 1994 and 2008. The authors found that those who work with fluoroscopy have an incidence of melanoma and breast cancer of 1.3 and 1.18 times, respectively, higher than those who did not. There was also a 2.5 times increased likelihood of mortality from brain cancer.<sup>22</sup> Another study determined the incidence of brain cancer among radiologists and cardiologists performing interventional procedures. More than 85% of brain cancer originated on the left side, where fluoroscopy is usually applied during the procedures. However, these results were not widely accepted as there may have been a selection bias in the study.<sup>23</sup>

Most studies indicated that the annual amounts of radiation received by urologists were within the limits recommended by ICRP.<sup>24,25</sup> In one study the average doses acquired from ureteroscopy and percutaneous nephrolithotomy were 0.03 and 0.1 mSv, respectively.<sup>24</sup> In this study Sparenborg et al. collected data on radiation doses the urology residents had actually received. The authors reported that the residents received an average radiation exposure of 32 mSv per year, while the attending urologists received only 8 mSv per year.<sup>26</sup> Although the acquired dose of urology residents was substantially lower than that determined by ICRP (i.e., 50 mSv per year), the cumulative dose over five years was still a risk.<sup>27</sup>

Formerly, radiation-induced cataracts were believed to be a deterministic effect with a threshold dose of 2 Sv. Still, more recent data concluded that they could be a stochastic effect without an

apparent dose threshold.<sup>28</sup> Vano et al. performed a slit lamp examination on interventional cardiologists, nurses, and technicians. The authors found significant changes in the posterior subcapsular capsule, while the more common age-related cataract was mainly within the nucleus. Assumably, prolonged exposure to a small dose of radiation has the potential to cause cataracts through such a mechanism.<sup>29</sup>

## Radiation protection

During the dispensing of radiological practices, urologists receive a portion of radiation dispersed from the patients.<sup>30</sup> As a result, medical personnel should minimize the radiation dose as much as possible based on the concept of as low as reasonably achievable (ALARA), which consists of the three safety principles: reducing time, increasing distance from the source, and using protective shielding.

**1. Time.** A general recommendation is to minimize the fluoroscopic time as much as possible. Lowering the frame rate by using pulsed fluoroscopy can reduce radiation exposure while still producing images with comparable quality. Canales et al. revealed that decreasing the frequency from 30 to 12.5 frames per second could decrease the radiation dose used in percutaneous nephrolithotomy by more than 30%.<sup>31</sup> Similarly, Smith et al. found that reducing the pulse rate helped shorten fluoroscopy time by up to 76%, minimizing the exposure by up to 64%, still giving adequate image quality to inform further procedures.<sup>32</sup> Other modifications may include last-hold image and collimation to optimize contrast only in the region of interest.<sup>33</sup> In addition, the use of a low-dose setting could reduce the radiation dosage by up to 57%.<sup>34</sup>

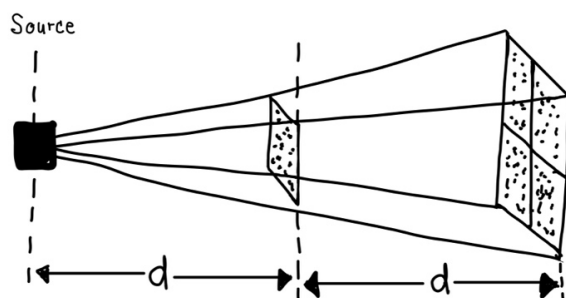
**2. Distance.** Increasing the distance between the radiation source and patients as far as

possible is helpful because the radiation intensity declines in direct proportion to a squared distance (i.e., inverse square law). When doubling the distance from the source, the radiation emission will decrease four times (Figure 4). For this reason portable C-arm fluoroscopy is superior to a fixed table one, providing a 10-times higher radiation dose.<sup>35</sup> Furthermore, patients should be at the farthest position away from the radiation source where a clear vision is still attainable, yet closest to an image capturing device to lessen the chance of radiation scattering. In addition, the radiation source should be under the table to reduce exposure to important organs such as the eyes (Figure 5).<sup>36</sup>

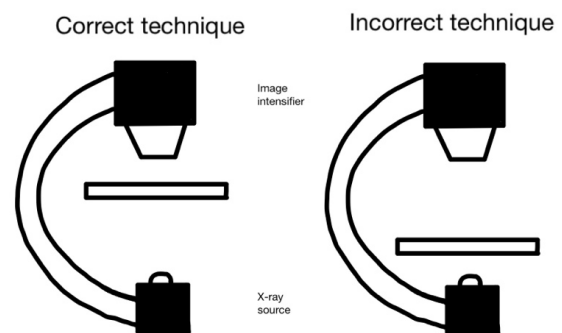
**3. Shielding.** According to the “X-Ray MOPH Standard” by Thailand’s Ministry of Public Health, radiation operators must wear personal protective equipment, including a lead apron with 0.25-mm thickness equivalence that gives 0.5 and 0.25 mm thick at the front (when folded) and back, respectively. Lead glasses can prevent radiation from the front and side, and a thyroid shield might provide another safeguard. Hein et al. suggested that wearing protective gear can reduce the radiation exposure during ureteroscopy by up to 98%, allowing the surgeons to carry out up to 500 procedures in a year without taking up an excessive amount of radiation.<sup>37</sup>

A ceiling mounted screen, lateral shield, and under table curtain can further reduce the radiation dose by more than 90%. Mobile floor shields are preferable in protecting medical personnel in the circulating area. Urologists should place their hands away from an x-ray beam during the procedures unless unavoidable.<sup>38</sup>

A survey on the regular use of protective equipment among urologists showed that 97% of them always wear a lead apron, 67% put on a thyroid shield, and 17% use lead glasses.<sup>39</sup> However,



**Figure 4.** Intensity reduction of X-rays corresponding to the inverse square law



**Figure 5.** Appropriate positioning of C-arm to reduce radiation dosage





60% of them suffer from lower back pain and neck pain due to the lead apron, a statistic correlating with the number of procedures. Wearing a skirt-type lead apron helps alleviate lower back pain due to a better weight distribution during prolonged usage. Other anti-radiation alternatives, such as bismuth oxide and barium sulfate, are sometimes incorporated in the fabrication of lighter protective equipment.<sup>30</sup>

## Techniques to reduce the radiation exposure

### 1. Techniques to reduce the exposure to radiation during stone diagnosis

Urologists should employ x-ray images only when clinically indicated. Lehnert et al. found that more than 26% of patients were unnecessarily subjected to CT scans.<sup>40</sup> Currently, electronic medical records of x-ray images are readily available for instant access, thereby decreasing the redundancy of X-ray imaging.<sup>41,42</sup>

To date, a non-contrast CT scan is the gold standard for diagnosing urolithiasis due to its high sensitivity and specificity and the ability to identify renal abnormalities, stone position, and other essential characteristics. However, this imaging modality emits a high effective radiation dose.<sup>43</sup> A low-dose CT scan (LDCT) has been developed to reduce the radiation dosage. The low dose does lower the image sharpness and resolution, but it is still adequate for diagnosis. A meta-analysis of LDCT showed a sensitivity of 96%, a specificity of 95%,<sup>44</sup> and an average radiation dosage of 1.4-2.0 mSv, compared to a mean dose of 11.2 mSv from a standard dose CT scan.<sup>45</sup> Moreover, an ultra-low-dose CT scan (ULDCT) delivered a dosage range of 0.5-1.9 mSv, which was even lower than a plain KUB. Pooler et al. compared the diagnostic accuracy of ULDCT to LDCT for a diagnosis of stones larger than 4 mm. The authors found a sensitivity and specificity from ULDCT of 90-100% and 86-100%, respectively.<sup>46</sup> However, the diagnostic power of ULDCT is still limited in urinary stones smaller than 3 mm or individuals having BMI greater than 30.<sup>47</sup>

Using diagnostic ultrasound for urolithiasis can help reduce radiation exposure. Smith et al. randomized 2,759 individuals who visited an emergency department with suspected renal colic into three groups. The first group underwent diagnostic ultrasound by emergency physicians,

the second group underwent ultrasound by radiologists, and the third group underwent an immediate non-contrast CT scan. The authors found no difference in the revisit rates due to missed or delayed diagnosis. However, the first two groups received a radiation dose of 10 mSv, while the last group diagnosed with a non-contrast CT scan received 17 mSv. Although some patients in the ultrasound groups could not obtain a diagnosis of urolithiasis and thus required a subsequent non-contrast CT scan, there was no difference in the rates of return to the emergency department, serious adverse events, and length of stay.<sup>48</sup>

The American Urological Association (AUA) encourages implementing ultrasound or low-dose CT scan as a follow-up imaging in assessing stone growth or new stone formation to restrict excessive radiation exposure and limit its long-term effects. Additionally, the AUA also recommends non-contrast, low dose CT scan for pediatric patients before performing PCNL.<sup>49</sup>

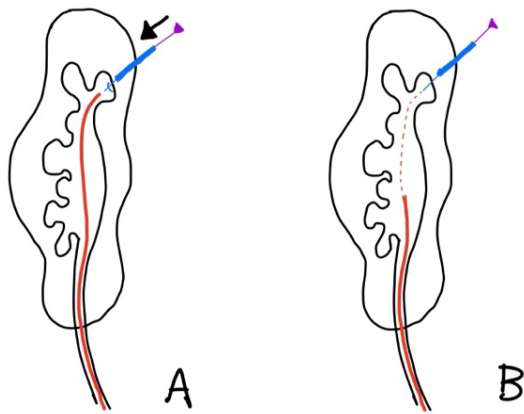
### 2. Techniques to reduce the radiation exposure during stone treatment

2.1 Percutaneous nephrolithotomy (PCNL) is the gold standard treatment for kidney stones larger than 20 mm or complex ones. An average radiation dose from fluoroscopy was 4.5 mSv per procedure. Obese patients with BMI > 30 may require a higher dosage. During an initial percutaneous puncture, the utilization of retrograde air pyelography rather than contrast media injection may reduce the radiation dose from 7.67 to 4.45 mSv.<sup>50</sup>

Other emerging techniques to reduce or eliminate radiation dose are as follows:

- Ureterscopy-guided PCNL: By applying a flexible ureteroscope to the kidney, urologists can directly observe the needle traversing the skin into the collecting system (Figure 6). Petros et al. demonstrated that this technique could limit radiation exposure and reduce intraoperative bleeding while offering comparable stone-free rates and complications.<sup>51</sup> Similarly, Isaac et al. reported that ureterscopy-guided PCNL was safe and effective, minimized the fluoroscopic time and the number of renal accesses, and yielded a higher success rate.<sup>52,53</sup>

- Ultrasound-guided PCNL: Ultrasound facilitates the clear distinction between anterior and posterior calyces and identifies organs surrounding the kidney, including the



**Figure 6.** Ureteroscopy-guided PCNL includes: (A) puncturing the kidney via percutaneous access under ureteroscopic vision and (B) manipulating a guidewire down the ureter

diaphragm, bowel, liver, and spleen, thereby decreasing the possibility of injuring these organs. Although highly beneficial, the current evidence suggests that only 10% of urologists perform PCNL with solely ultrasound guidance, and 15% use a combination of ultrasound and fluoroscopy.<sup>54</sup> To safely adopt this technique, Usawachintachit et al. demonstrated that a learning curve of at least 20 procedures was essential, and indicated that the success rate might be lower in obese patients.<sup>55</sup> Since the utilization of fluoroscopy for obese individuals involves high exposure to radiation, incorporating ultrasound may reduce radiation usage.<sup>56</sup> Ultrasound guidance resulted in comparable stone-free rates, complications, and hospital stay.<sup>57</sup> Moreover, when integrated with the supine technique, ultrasound might also reduce costs by 30%.<sup>58,59</sup>

2.2. Ureteroscopy (URS) is the endoscopic treatment of urolithiasis. Although in most cases fluoroscopy is used, some urologists advocate a “fluoroscopy-free technique” with an available portable C-arm as a backup. This technique involves tactile sensation and length measurement to identify the position of each instrument, whereby some procedural steps employ ultrasound to confirm the position.<sup>60</sup> This approach is safely achievable by experienced urologists while operating on not too complex cases.<sup>61</sup> Ahmed et al. randomized 154 patients with distal ureteral stones smaller than 1 cm into two groups. The first group underwent ureteroscopy without fluoroscopy and the other group with fluoroscopy. The operative time, stone-free

rate, and complications were no different.<sup>62</sup> Fluoroscopy-free ureteroscopy is useful for specific groups of patients at risk of radiation exposure, such as those which are pregnancy, pediatric patients, and those with multiple stone recurrence.

2.3 Extracorporeal shock wave lithotripsy (ESWL) traditionally employed fluoroscopic guidance to localize the stone. An efficacy comparison between ultrasound-assisted ESWL and pure fluoroscopic-guided ESWL showed a stone-free rate of 85.6% and 64.3%, respectively. The complication rates of these two methods were comparable. Importantly, ultrasound-assisted ESWL considerably minimized radiation exposure in pediatric patients who are more sensitive to radiation than adults.<sup>63</sup> In children with cystine stones, Garen et al. demonstrated a superior stone-free rate of 93.5% with ultrasound-guided ESWL, compared to 60% with pure fluoroscopy-guided ESWL. The authors concluded that the ultrasound approach is preferable in pediatric patients to prevent excessive radiation exposure.<sup>64</sup>

The Visio-Track (VT) locking system harnesses ultrasound for 3-dimensional localization of stones to increase precision and reduce the fluoroscopic time. Abid et al. suggested that the VT locking system yielded higher rates of efficacy than the ultrasound guidance, providing a better stone-free rate of 80% and 55%, respectively.<sup>65</sup>

Educating urologists about radiation safety helps minimize the overall radiation exposure.<sup>66</sup> For urologists utilizing techniques which involve long fluoroscopic time, it is sensible to report their fluoroscopic time in comparison to the average, increasing their level of caution and highlighting the need to take appropriate action by minimizing radiation usage.<sup>67</sup>

## Conclusion

The use of radiation is highly beneficial in endourology, especially for diagnosis and treatment. Therefore, urologists should have knowledge and be aware of issues surrounding radiation safety. They should also use the lowest possible dosage in accordance with the ALARA (as low as reasonably achievable) principle. Recently there has been the emergence of several surgical techniques to eliminate or minimize radiation exposure, which will help in this matter. Hence, urologists should study and practice those techniques to consciously restrict the use of radiation and ensure the long-term safety of both urologists and patients.



## Conflict of Interest

The authors declare no conflict of interest.

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**Invited Review Article**

# Updates in substitution urethroplasty for anterior male urethral strictures

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**Abstract**

Substitution urethroplasty is an essential tool in the armamentarium of management of anterior urethral strictures, due to the limitations of anastomotic urethroplasty for penile urethral strictures and bulbar strictures beyond 2 cm in length. Various urethroplasty techniques with different grafts or flaps have been described. In this review article, the rationale of utilisation of different substitution urethroplasty techniques are described. Evaluation of urethroplasty outcomes should include not only voiding function and sexual outcomes, but also patient-reported outcome measures (PROMs) and overall satisfaction.

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**Introduction**

Urethral strictures are a relatively common urological disease and can result in significant morbidity and detrimental effects on the quality of life.<sup>1</sup> They can result in lower urinary tract voiding symptoms, urinary retention, recurrent urinary tract infections<sup>2</sup>, bladder outlet obstruction with bilateral hydronephrosis and renal impairment, and urinary fistulae. They can also cause penile, urethra and/or bladder pain.<sup>1</sup> Appropriate management strategies can help reduce stricture recurrence rates and ameliorate the morbidity associated with urethral stricture disease.

Due to the limitations of anastomotic urethroplasty, substitution urethroplasty with grafts or flaps is especially useful in the penile urethra as well as longer strictures in the bulbar urethra.

**Clinical Evaluation**

Symptoms of urethral stricture disease include voiding symptoms such as hesitancy, straining, poor flow, intermittency and sensation of incomplete voiding. They may also present with recurrent urinary tract infections, bladder stones, acute retention of urine, prostatitis or epididymitis. A detailed history of previous urethral surgery, urinary instrumentation and history of sexually transmitted diseases is also important.

Physical examination is performed to look for features of lichen sclerosis, and meatal stenosis, with palpation to establish location and length of scarred tissue.

Uroflowmetry assessment is performed to look for an obstructive voiding pattern; a plateau flow pattern is classical for urethral stricture.

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Investigations with retrograde urethrogram and cystoscopy help to delineate the location, length, multiplicity, and severity of urethral stricture disease. Cystoscopy has the added benefit of assessing the healthiness of urethral mucosa peri-stricture to determine the suitability of intended procedures. In the case of urethral strictures that also involve the posterior urethra, retrograde urethroscopy combined with antegrade cystoscopy via the suprapubic tract allows assessment of length of defect, presence of fistulae or bony anomalies to help in surgical planning.<sup>3</sup>

### Management Strategies

Management of urethral strictures depends on symptoms, aetiology, location, length, multiplicity and previous urological procedures performed. For anterior strictures in which direct vision internal urethrotomy (DVIU) or dilatation have failed, urethroplasty is usually the option for definitive treatment. Predictors of stricture recurrence include<sup>3</sup>:

1. Stricture length – patency rates of 71.2% for those < 1 cm versus 23.2% for those > 1 cm
2. Stricture calibre – patency of 34% for < 15 Fr versus 69% for > 15 Fr
3. Multiplicity of strictures – 0% patency versus 35% for single stricture
4. Stricture location – bulbar strictures have better patency rates compared to penile or penobulbar strictures
5. Previous interventions – worse patency rates after first DVIU with 0% after ≥ 2 failed DVIU procedures

For selected patients, observation is a reasonable approach when they have relatively large calibre strictures > 16 Fr, especially if they are asymptomatic. These cases have a low risk of progression and subsequent need for surgical intervention<sup>4</sup>, with intervention rates of 4% in the 1 year and 12% for the 2<sup>nd</sup> year.<sup>3</sup>

### Anastomotic urethroplasty vs substitution urethroplasty

There are two types of urethroplasty, specifi-

cally, anastomotic urethroplasty (excision and primary anastomosis, EPA) and substitution urethroplasty. EPA has excellent patency rates of 85.5 to 98.5%<sup>3,5</sup> and it is the treatment of choice for post-traumatic short bulbar strictures where there is usually full thickness spongiositis.<sup>6</sup> In these cases, complete excision of the stricture is essential to reduce risk of stricture recurrence.

The limitations of EPA are that it is only useful for short bulbar urethral strictures up to 2 cm in length.<sup>3,6</sup> The utilization of EPA for longer bulbar urethral strictures and penile urethral strictures, however, is associated with potential tension on the anastomosis, which can result in vascular compromise and increased stricture recurrence.<sup>6</sup> For these longer bulbar strictures, EPA can also lead to chordee, erectile dysfunction and impaired sexual function.<sup>7</sup>

### Substitution Urethroplasty

#### Techniques of substitution urethroplasty

There are four commonly used substitution urethroplasty techniques, dorsal onlay (DO), dorsolateral onlay (DLO), dorsal inlay (DI) and ventral onlay (VO). No single technique has been proven to be superior to another for bulbar free graft urethroplasty, though some favour dorsal placement due to thicker corpora spongiosa tissue with greater vascularity and better graft support.<sup>8</sup> Recurrence rates for substitution urethroplasty are reported to be ≤ 20% at 2 to 5 years,<sup>9</sup> with a 90% success rate as reported by Al-Hakeem et al.<sup>1</sup>

#### Dorsal onlay substitution urethroplasty (Barbagli)

This was first described in 1996 by Barbagli<sup>10</sup> as a one-stage urethroplasty using a free preputial graft. Circumferential mobilization of the urethra is performed, with dissection of the urethra off the corpora cavernosa at the stricture site. After placing stay sutures along the length of the urethra, the urethra is rotated 180° before the dorsal stricturotomy is performed to evaluate the length and extent of spongiositis. The graft is quilted unto the corpora cavernosa, followed

**Table 1.** Summary of techniques of substitution urethroplasty

Techniques	Dorsal Onlay (DO)	Dorsolateral Onlay (DLO)	Dorsal Inlay (DI)	Ventral Onlay (VO)
	Barbagli	Kulkarni	Asopa	McAninch
			Palminteri	

by anastomosis of the urethra into the graft site, thus completing the augmentation substitution urethroplasty.

### **Dorsal inlay substitution urethroplasty (Asopa)**

This was described in 2001 by Asopa<sup>11</sup> as an alternative to Barbagli's procedure, with the advantage of preserving the circumflex and perforating arterial vasculature as is not required urethral mobilization. A ventral urethrotomy is made, the dorsal urethra incised, and a graft placed dorsally over the corpora.

### **Penile inversion and one-sided dorsolateral BMG (Kulkarni)**

This was described by Kulkarni in 2009<sup>12</sup> with the added advantage of preservation of one side of the urethral vasculature as the mobilization of the urethra was only required on one side. Penile inversion allows access to the entire length of the urethra via a perineal incision, making it suitable for panurethral strictures as well.

### **Ventral onlay (McAninch)**

This was described by Elliott et al<sup>13</sup> where a 20 to 25 mm wide graft is harvested and a ventral onlay anastomosis is performed, with a success rate of 90% reported for bulbar urethral strictures at a minimum time of 1 year post-surgery.<sup>13</sup>

### **Combined dorsal and ventral double buccal mucosal graft (Palminteri)**

This was described in 2007 for the management of complex bulbar urethral strictures.<sup>7</sup> This comprises a dorsal inlay (Asopa) and ventral onlay (McAninch) double BMG to augment the urethral plate. Success rates of 89.6% with a mean follow-up period of 22 months have been reported.<sup>7</sup>

## **Tissues used in Substitution Urethroplasty**

### **1. Grafts**

#### **a) Oral mucosal grafts (OMG)**

OMG have outcomes of excellent vascularity, and favorable immunology with lower fibrosis compared to skin.<sup>14</sup> They are easy to harvest, waterproof, antibacterial, hairless and have high success rates.<sup>15</sup> It is the tissue of choice in patients with lichen sclerosis with single-staged OMG urethroplasty reporting success rates of 65

to 100% after 12 to 67 months of follow-up; and staged OMG urethroplasty having success rates of 60 to 79%.<sup>3</sup>

Grafts can be harvested from the buccal, lingual or lip area. Buccal mucosal graft (BMG) is the graft of choice as it can be harvested bilaterally and has lower donor site morbidities compared to lingual and lip grafts. Compared to BMG, Lingual grafts are less abundant and more flimsy, and are associated with a higher risk of speech impairment.<sup>14</sup> They are an alternative to BMG in patients who have had previous BMG harvest or contraindications to BMG harvest, although long-term outcomes have not been published to date. Lip graft harvests are associated with risks of numbness and lip contractures, which can occur in 3 to 5% of cases.<sup>14</sup>

Certain conditions preclude OMG, which include oral leukoplakia, heavy tobacco usage, betel nut chewing, previous oral radiotherapy and previous OMG harvest.

#### **b) Penile skin grafts**

These are hairless, elastic, and easy to harvest with minimal donor site morbidity, but are not suitable for patients with lichen sclerosis. They are an alternative to BMG for patients with contraindications for BMG harvest, but have lower success rates of 59.7% in comparison to 77.7% with BMG.<sup>16</sup>

#### **c) Postauricular skin**

This is a full thickness graft that is harvested from the lower half of the mastoid without extending beyond the lower end of the tragus. Up to 7-8 cm of graft can be harvested from each side, the technique having a 89% success rate at 21 months with no donor site complications.<sup>16</sup>

#### **d) Bladder mucosa**

This has traditionally been used in hypospadias surgery but has declined in popularity due to the morbidity associated with harvesting as well as poor success rates with up to 66% requiring further surgical intervention.<sup>16</sup>

#### **e) Tunica vaginalis**

This has been described by Foinquinos et al<sup>17</sup> in a small case series of 11 patients undergoing dorsal onlay augmented urethroplasty for anterior urethral strictures. Relatively good short-term outcomes of all patients having uroflowmetry of > 14 ml/s with a mean follow-up of 2.8 months have been reported.



#### f) Colonic mucosa

This is not commonly used but has been described in a small case series<sup>18</sup> in patients with long segment strictures not amenable to penile skin flaps. It is a more invasive procedure, as sigmoidectomy is required for graft harvest and complications including colocutaneous fistula have been described. Reported success rates were 85.7% at 53.6 months.<sup>18</sup>

#### 2. Penile /preputial skin flap substitution urethroplasty

These are fasciocutaneous flaps vascularised by the tunica dartos and are suitable for substitution urethroplasty, especially in the case of distal penile urethral strictures. Distal penile skin is also hairless which makes it a pertinent choice for urethral reconstruction. However, the use of these should be avoided in patients with lichen sclerosis and/or significant scar tissue due to high risks of stricture recurrence ranging from 50 to 100%, with the majority of recurrences occurring within the first two to three years postoperatively.<sup>19</sup> Onlay flaps have lower failure rates compared to tubularised flaps.<sup>20</sup>

##### a) Orandi flap

This is a longitudinal penile skin island flap with a lateral pedicle harvested from the ventral side of the penis.

##### b) McAninch flap

This is a transverse preputial flap harvested circumferentially and can provide a flap up to 15 cm in length. During reconstruction, a circular flap is constructed from the prepuce in the uncircumcised and from the distal penile shaft skin in those who are circumcised.

### Substitution Urethroplasty Techniques

These depend on the location, length and

aetiology of the stricture disease.

#### A) Bulbar urethral strictures

Depending on the length and aetiology of the stricture, transecting urethroplasty or non-transecting urethroplasty techniques can be performed.

Non-transecting urethroplasty can be considered for non-trauma aetiologies with partial thickness spongiofibrosis, whereas transection of the urethra should be performed for full thickness spongiofibrosis strictures associated with perineal trauma. Non-transecting urethroplasty comprises of several techniques as described by Bugeja et al.<sup>6</sup> and Welk et al.<sup>21</sup>, namely;

1. A "Heineke-Mikulicz"-type stricturoplasty. This is used for short strictures where a longitudinal urethrotomy is made and closed transversely without tension

2. Non-transecting anastomotic urethroplasty (NTABU)

The diseased urethral mucosa with surrounding spongiofibrosis is excised while preserving underlying healthy corpora spongiosum. With adequate urethral mobilization, the healthy remaining urethral mucosa is then sutured to each other and the longitudinal dorsal stricturotomy closed transversely in a tension-free fashion. One important caveat is that the incision into and through the spongiosal tissue needs to be exactly at the level of the stricture, so planning needs to be optimized prior to incision to ensure unnecessary extension of the incision which may compromise the repair. Radiologically, 97.7%<sup>6</sup> of repairs are stricture-free at a mean follow-up of 13 months. Long-term erectile dysfunction rates were reported in 2.4% of cases, lower than that reported in EPA.<sup>6</sup>

**Table 2.** Advantages and Disadvantages of Transecting vs Non-Transecting Urethroplasty<sup>6</sup>

	<b>Transecting Urethroplasty</b>	<b>Non-Transecting Urethroplasty</b>
Advantages	<ul style="list-style-type: none"> <li>• Complete excision of stricture, potentially reducing risk of stricture recurrence with &gt; 95% long-term success</li> </ul>	<ul style="list-style-type: none"> <li>• Preservation of urethral blood supply</li> <li>• Lower rates of erectile dysfunction<sup>6</sup> of 2.4%</li> <li>• May avoid or reduce need for graft, thereby reducing donor site morbidity and risks of post-micturition dribble</li> </ul>
Disadvantages	<ul style="list-style-type: none"> <li>• Higher rates of erectile dysfunction 18 to 22.5%<sup>6</sup></li> <li>• Potential vascular compromise to urethra</li> </ul>	<ul style="list-style-type: none"> <li>• Stricture tissue not excised, hence potential higher risk of stricture recurrence</li> <li>• Up to 85% success</li> </ul>

### 3. Dorsal augmented substitution urethroplasty

A dorsal urethrotomy is made and the urethral plate augmented with either a graft or a flap.

### 4. Augmented non-transecting anastomotic urethroplasty (ANTA)

A dorsal urethrotomy is made and the narrowest portion of the stricture identified. The diseased mucosa and corpora spongiosum are excised and the mucosal edges are reanastomosed. This can be performed in cases with urethral obliteration that preclude satisfactory urethral patency with dorsal onlay substitution urethroplasty or to shorten stricture length to prevent the need for bilateral buccal graft harvests to reduce donor site morbidity.<sup>21</sup> Success rates are comparable to dorsal augmented buccal graft urethroplasty with 90% of cases being recurrence-free at 5 years.<sup>21</sup>

### 5. Augmented non-transecting anastomotic urethroplasty with buccal mucosal graft (ANT-ABU)

This is a modification of the ANTA procedure with dorsal buccal mucosal graft augmentation.

## B) Penile urethral strictures

Penile urethral strictures should not be managed with DVIU due to poor patency rates and risks of erectile dysfunction, which has been reported in 5.3% to 10.6% of cases.<sup>3</sup>

They can be managed with either a single stage or two-stage urethroplasty procedure.

- Single stage vs staged urethroplasty

A single stage procedure reduces the morbidity of having an hypospadiac meatus and a poor aesthetic appearance of the penis with its potential psychological trauma.<sup>22</sup>

Distal to the distal edge of the bulbospongiosus muscle, a dorsal approach is indicated for buccal graft urethroplasty due to the thinner spongiosal layer ventrally and a more optimal and stable environment for the graft to take dorsally, as well as a reduced risk of diverticulum formation in longer term follow-up. More recently Kulkarni popularised a dorso-lateral approach to the spongiosum to further reduce neurovascular compromise and this is now widely accepted.<sup>30</sup> He also recently described a penile invagination technique for pan-urethral strictures via a single

perineal incision and dorso-lateral approach to the spongiosum.<sup>31</sup>

Staged reconstructive urethroplasty is utilized for complex strictures where vascularity is in doubt, such as the presence of significant scarring from previous procedures; as well as those with a deficient urethral plate, penile skin or dartos fascia e.g. hypospadias.

Staged urethroplasty should be considered in the following circumstances to optimize successful outcomes<sup>3</sup>:

- 1) Prior failed hypospadias repair or complex urethroplasty
- 2) Radiation-induced urethral strictures
- 3) Urethral fistulae, false passage, infections e.g. abscess
- 4) Severe spongiofibrosis
- 5) Lichen sclerosis when the urethral lumen is  $\leq 6$  Fr and/or the urethral plate is unsalvageable<sup>19</sup>

During the first stage, the graft is sutured to the tunica albuginea. During the second stage 6 to 12 months later, the graft is tubularised over a urethral catheter. If the graft does not take or there is recurrence of disease, repetition of the first stage will be required. The success rates in staged urethroplasty for lichen sclerosis patients is reported to range from 73% to 82%.<sup>19</sup>

Most have described the use of buccal mucosal grafts in the first stage of a staged urethroplasty. This is associated with graft contraction in between 20% to 38% of cases<sup>22</sup> in high volume centres, and often requires revision surgery.

## Johanson's 2-stage urethroplasty

During the first stage, urethral marsupialization is performed, where a longitudinal penile skin incision is made over the site of the stricture and extended proximally till healthy normal urethral tissue is reached. The lateral edges of the urethra are sewn to the skin edges before tubularisation of the urethral plate and dartos flap are performed at the second stage at 6 to 12 months after the first stage. Oral mucosal grafts can be utilized during the first stage for optimization of the urethral plate. During the first stage, a temporary perineal urethrostomy can be offered to allow voiding as standing to void postoperatively is usually challenging; this will be closed during the second stage. Approximately 30% of cases will





require graft revision during the second stage due to scarring and graft retraction.<sup>22</sup>

### **2-stage urethroplasty by Joshi et al<sup>22</sup>**

A new two-stage urethroplasty was described by Joshi et al.<sup>22</sup> in 2017 which precludes the usage of a buccal mucosal graft in the first stage, thereby avoiding the risks of graft scarring and contraction. In this procedure, the first stage involves a ventral urethrotomy with penile skin margins sutured to the margins of the urethral plate. A neourethral meatus is sited in healthy urethral mucosa proximal to the stricture and a 12 Fr Foley catheter left in-situ for 3 days postoperatively. The second stage is performed six months afterwards, with the excision of scar tissue. A buccal mucosa graft is harvested and placed as a dorsal inlay graft with quilting to construct a wide urethral plate. This is then tubularised and dartos muscle mobilized to cover the suture line. This is then followed by glansplasty and meatal reconstruction. Success rates were reported as 89.5% with a median follow-up of 44 months, and none required revision prior to the second stage.

### **Assessment of Urethroplasty Outcomes**

Conventionally, the presence of a normal urethral lumen during retrograde urethrogram or cystoscopy was defined as a successful outcome.<sup>3</sup> Objective parameters for determination of success include the need for stricture retreatment, anatomical recurrence on cystoscopy, peak urine flow rates < 15 ml/s and a weak stream ascertained from a questionnaire.<sup>23</sup>

Post-operative evaluation should include uroflowmetry and post-void residual measurements as well as urethrocystoscopy to assess stricture calibration at three months post-urethroplasty. Small calibre < 17 Fr strictures have a much higher propensity for recurrence.<sup>3</sup> Retrograde urethrograms with voiding cystourethrograms (VCUG) can be performed to confirm suspected stricture recurrences, when pre- and post-operative Qmax differences are  $\leq 10$  ml/s and/or occur in the presence of an obstructive voiding flow curve.

It is of note however, that not all anatomic recurrent strictures require treatment. This is especially the case if the stricture calibre remains > 14 Fr and if they remain asymptomatic,<sup>3</sup> as the aim of urethral surgery is to allow return to normal voiding function with minimal symptoms and for preservation of quality of life.

Patient-reported outcome measures (PROMs) help evaluate patient outcomes and the perceived benefit from an intervention. These include evaluation of urinary symptoms, sexual function and improvement in quality of life post-surgery. The evaluation of sexual function is not frequently discussed but erectile dysfunction is more prevalent in the bulbar urethroplasty compared to penile urethroplasty; and is higher in EPA compared to graft urethroplasty.<sup>24</sup> It has been reported that there is a 5% risk of long-term erectile dysfunction after EPA, and 0.9% after graft patch urethroplasty<sup>25</sup>; with a 30-38% reduction in satisfaction of erections<sup>26</sup> which improves with time, with a 90% recovery after 190 days.<sup>27</sup> Patient global impression of improvement (PGI-I) scores were reported to be much better or very much better (PGI-I scores of 1 and 2) in 86.9% of cases<sup>1</sup> after substation urethroplasty.

Some PROMs utilized for urethroplasty patients include:

#### **Disease Non-Specific Voiding PROM**

1. American Urological Association Symptoms Score (AUA-SS), also known as the International Prostate Symptom Score (IPSS).

This was first investigated in 1998 where an inverse correlation between AUA-SS and maximum urinary flow rates was observed, and it was concluded that AUA-SS had clinical validity as an adjunct outcome assessment tool after urethroplasty.<sup>28</sup> It is however inadequate as it misses up to 20% of symptoms and does not capture the 10% of men with strictures who do not have voiding symptoms.<sup>28</sup>

2. Core Lower Urinary Tract Symptom Score (CLSS)

This was designed in 2008 to assess ten core urinary symptoms from the symptom panel of the International Continence Society.<sup>28</sup> The symptoms evaluated are frequency, urgency, nocturia, pain, urinary incontinence and quality of life. Its limitations are that it did not include complaints of urinary spraying and dysuria, which are relatively prevalent in cases of urethral stricture disease.

3. Incontinence Symptom Index (ISI)

This was developed in 2003 and includes assessment of urinary incontinence and degree of symptom bother but has not been evaluated specifically for urethral strictures.

**Table 3.** Validated Sexual Function PROM by Coursey et al.<sup>26</sup>

## APPENDIX: PATIENT QUESTIONNAIRE

INSTRUCTIONS: Please circle the response that best describes you.

1. How would you describe your erections *before* surgery?  
 Absent                      Not at all satisfactory                      Moderately satisfactory                      Very satisfactory
  2. How would you describe your erections *after* surgery?  
 Absent                      Not at all satisfactory                      Moderately satisfactory                      Very satisfactory
- Instruction: The following are questions about changes/symptoms that may have occurred in your erections since your surgery. Circle the response about the following symptoms that best applies.
3. Has the angle of your erection changed after surgery?  
 Not at all                      Somewhat                      Quite a bit  
 If so, has this symptom improved over time?  
 Not at all                      Somewhat                      Quite a bit  
 Comments: \_\_\_\_\_
  4. Has the length of your penis changed since your surgery?  
 Not at all                      Somewhat                      Quite a bit  
 If so, has this symptom improved over time?  
 Not at all                      Somewhat                      Quite a bit  
 Comments: \_\_\_\_\_
  5. Has your partner noted any changes in your erections since surgery?  
 Yes                      No  
 Comments: \_\_\_\_\_
  6. Have you altered your frequency of intercourse due to erection changes since surgery?  
 Not at all                      Somewhat                      Quite a bit
  7. How would you describe your health in general?  
 Poor                      Fair                      Good                      Excellent

**Disease-Specific Voiding PROM****1. Urethral Stricture Surgery PROM (USS PROM)**

This was first devised in 2011 by Jackson et al.<sup>29</sup> and consists of six summative questions derived from the International Consultation on Incontinence Questionnaire Male Lower Urinary Tract Symptoms (ICIQ MLUTS) module to generate a score between 0 (asymptomatic) and 24 (most symptomatic), a separate LUTS-specific quality-of-life (QoL) question, Peeling's voiding picture, EQ-5D to assess overall HRQoL, and 2 questions addressing overall patient satisfaction postoperatively. Limitations of the USS PROM are that sexual function and oral mucosa morbidity are not included.

**Disease Non-Specific Sexual PROM**

These include International Index of Erectile Function (IIEF) and its abbreviated version, IIEF-5; Brief Male Sexual Function Inventory (BMSFI), and Men's Sexual Health Questionnaire (MSHQ).

**Disease Specific Sexual PROM**

The only validated sexual function PROM by Coursey et al.<sup>26</sup> mainly addresses erectile function without evaluating overall patient satisfaction and quality of life.

BMSFI is validated for the assessment of change in sexual function before and after urological intervention but is not disease-specific for urethral strictures. MSHQ is a 25-item

self-administered questionnaire for assessment of erection, ejaculation and satisfaction<sup>3</sup>, but it is also not disease-specific as well.

**Conclusion****1. Substitution Urethroplasty Techniques**

Choosing the appropriate substitution urethroplasty technique will optimize the success rates and outcomes of urethral stricture disease.

For patients with lichen sclerosis, penile skin flaps should be avoided and 2-stage urethroplasty procedures should be considered, especially if they have a long-segment stricture, previously failed urethroplasties, an obliterated urethral lumen and an unhealthy urethral plate.

**2. Assessment of urethroplasty outcomes****Table 4.** Summary of procedures for bulbar and penile urethral strictures

	Bulbar Urethral Stricture	Penile Urethral Stricture
< 2 cm	<ul style="list-style-type: none"> <li>EPA</li> <li>Non-transecting: Heineke-Mikulicz</li> </ul>	Augmented urethroplasty - Avoid penile skin flaps in lichen sclerosis
> 2 cm	<ul style="list-style-type: none"> <li>Augmented urethroplasty</li> <li>Augmented Non-Transecting Urethroplasty (ANTA, ANTABU)</li> </ul>	- Consider 2-stage procedure when vascularity is in doubt

EPA = excision and primary anastomosis



A) Assess objective outcomes with uroflowmetry and postvoid residuals; and consider a calibration cystourethroscopy at 3 months post-operatively. Should any of these suggest stricture recurrence, a retrograde urethrogram and VCUG should be performed. Objective parameters indicating stricture recurrence include the need for stricture retreatment, anatomical recurrence evidenced by cystoscopy, peak urine flow rates < 15 ml/s and weak stream on questionnaire.<sup>23</sup>

B) Assess patient-reported outcomes including voiding symptoms, sexual and erectile function, in addition to patient quality-of-life outcomes and overall satisfaction.

C) Strictures with higher risk of recurrence should be surveyed and followed-up for a longer period with PROMs.

### Conflict of Interest

The authors declare no conflict of interest.

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**Invited Review Article**

## 3D Fluoroscopic imaging facilitates reconstruction of common urogenital sinus and cloacal anomalies

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**Keywords:**

Urogenital sinus, persistent cloaca, surgical planning, three dimensional imaging, three dimensional rotational fluoroscopy

**Abstract**

Cloacal anomalies and common urogenital sinus are rare structural abnormalities in hindgut and urogenital development. Surgical correction in childhood is often indicated to create normal external genital anatomy, allow for adequate bladder and vaginal drainage, and create the appropriate anorectal opening in patients with persistent cloaca.

Understanding the anatomy and relationships between the pelvic organs is critical as there is a drastic variation in potential surgical approaches to the repair. Traditional imaging modalities such as pelvic ultrasound, magnetic resonance imaging, and two-dimensional fluoroscopic imaging have been utilized to delineate the pelvic anatomy for facilitation of surgical planning. Limitations to these modalities include the inability to adequately dilate structures and the difficulty in identifying the common confluence, or where the structures ultimately coalesce within the pelvis.

In this article we describe the utilization of three-dimensional rotational fluoroscopy in combination with examination under anesthesia to provide optimal clarity of anatomy. Examination under anesthesia, specifically cystoscopy and vaginotomy, helps the surgeon to visualize the anatomy and to place catheters in the correct lumens. Contrast material can then be injected into the catheters to dilate the bladder, vagina, and mucous fistula for fluoroscopic imaging. The rotational images can then be reconstructed in three dimensions to create a roadmap for the surgeons, providing accurate description of the location of the confluence, distance to the introitus and other critical measurements.

We believe that three-dimensional rotation fluoroscopy is an underutilized diagnostic modality in the evaluation and surgical planning in patients with urogenital sinus and cloacal anomalies and should be considered by surgeons prior to proceeding with corrective surgery.

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## Introduction

Cloacal anomalies and common urogenital sinus (UGS) are structural abnormalities of hindgut and urogenital development. UGS abnormalities result in abnormalities of the urethra and vagina whereas cloacal also include abnormalities of the anus and rectum.

### Persistent cloaca

Cloacal anomalies are anorectal malformations that result in an incomplete separation between the urogenital and digestive tracts during embryonic development. A persistent cloaca is the most severe form of anorectal malformation found in females, with an external perineal opening common for the genital, urinary and digestive systems. In males, a high anorectal malformation with rectal atresia and congenital recto-urethral fistula is the anatomical equivalent.<sup>1</sup> Unlike common UGS, persistent cloaca is not a disorder of sexual differentiation due to androgen excess, but rather a result of incomplete formation of the urorectal septum.<sup>2</sup>

### Persistent urogenital sinus

Common UGS occurs due to persistent communication between the urethra and vagina resulting in a single perineal opening of the urinary and Müllerian systems. The single opening, termed the urogenital sinus, is a transient feature of normal fetal development. The anatomical abnormality occurs when development of two separate urethral and vaginal openings is incomplete.

Common UGS may be an isolated malformation or may be associated with complex syndromes.<sup>3</sup> The formation of a single opening of the urethral and genital system may be attributed to the virilization of the external genitalia,<sup>4</sup> and therefore is often associated with disorders of sex differentiation and conditions resulting from androgen excess during fetal development, most commonly congenital adrenal hyperplasia (CAH).<sup>5</sup> Common UGS can also be associated with other signs of virilization of the external genitalia, such as clitoral hypertrophy, and scrotalization of the labia majora with a large variation of phenotype, from mild clitoromegaly without a common UGS to complete Prader V virilization with a long length of UGS.<sup>1,6</sup>

## Anatomic implications for surgical management

Diagnosis of cloacal anomalies are typically made at birth when a single perineal orifice is observed. Imaging of the newborn is necessary to identify complicating factors such as hydrometrocolpos, or severe hydroureteronephrosis due to obstruction from a dilated urine filled vagina.<sup>7</sup>

At birth, a life saving diverting colostomy is necessary to direct stool away from the malformation and allow the child to thrive clinically. Post-natally, bladder function will need to be assessed specifically with regard to bladder emptying and the absence of vaginal voiding and possible hydroureteronephrosis as a consequence of an obstructing urine filled vagina. If this is the case clean intermittent catheterization of the single perineal opening into the urine filled vagina can facilitate decompression of the urinary tract until reconstructive surgery can be carried out.

Following the initial colostomy and prior to the definitive repair, assessment of adequate urinary drainage, radiological studies and endoscopy are recommended to help delineate the anatomy in order to plan for surgery. Accurate assessment of the pelvic anatomy in these patients is critical, as the distance of the common channel from the perineum heavily influences the surgical approach.<sup>8</sup> A short distance of less than 1cm of common channel to the external opening often does not require significant mobilization of the urogenital sinus. Therefore, a posterior sagittal approach to separate the rectum from the vaginal structures, create a new perineal body and perform anoplasty is typically selected for repair.<sup>8</sup> Cloacae with a common channel between 1 and 3 cm can also be approached in this fashion, with the additional maneuver of total urogenital sinus mobilization (TUM) in order to create a separate urethral and vaginal opening in the perineum.<sup>8</sup> Cloacae with a common channel greater than 3 cm may require a laparotomy in order to perform a transabdominal urogenital mobilization successfully. In very high cloacae, this may need to be the initial approach if the confluence is found to be at the level of the bladder neck. For high cloacae with a more distal confluence, transabdominal urogenital mobilization may be performed after a posterior sagittal dissection and TUM, which at the time of reconstruction would require whole body skin preparation for intraoperative repositioning.

Similar to the cloacal patient, the length of the urogenital sinus and the distance from the confluence of the structures to the perineal skin greatly impacts the surgical approach in patients with common urogenital sinus.<sup>1,6</sup> In patients with a low confluence, vaginoplasty utilizing a perineal skin flap to the spatulated posterior urethra may be adequate to bring both orifices to the level of the skin.<sup>9</sup> Total urogenital sinus mobilization (TUM) may be necessary for patients with high confluence, the UGS being dissected circumferentially as a single unit in order to bring the confluence anteriorly to the level of the perineal skin.<sup>9,10</sup> Due to concerns with regard to urinary incontinence, this technique is typically reserved for the most severe cases. Partial UGS mobilization (PUM) spares the pubourethral ligament and is often adequate for most cases of common UGS repair.<sup>9,11</sup>

## Traditional Imaging Modalities in Evaluation of Cloaca and Common Urogenital Sinus

### Prenatal imaging

With the increase in routine use of prenatal ultrasound, cloacal anomalies and persistent UGS can often now be diagnosed prenatally. Prenatal cases are diagnosed by identification of hydrometrocolpos as an oblong, anechoic lesion located behind the fetal bladder (Figure 1A).<sup>12</sup> Septation can be visualized in some cases crossing the cystic mass, and this is thought to be the urogenital septum separating the vagina and the

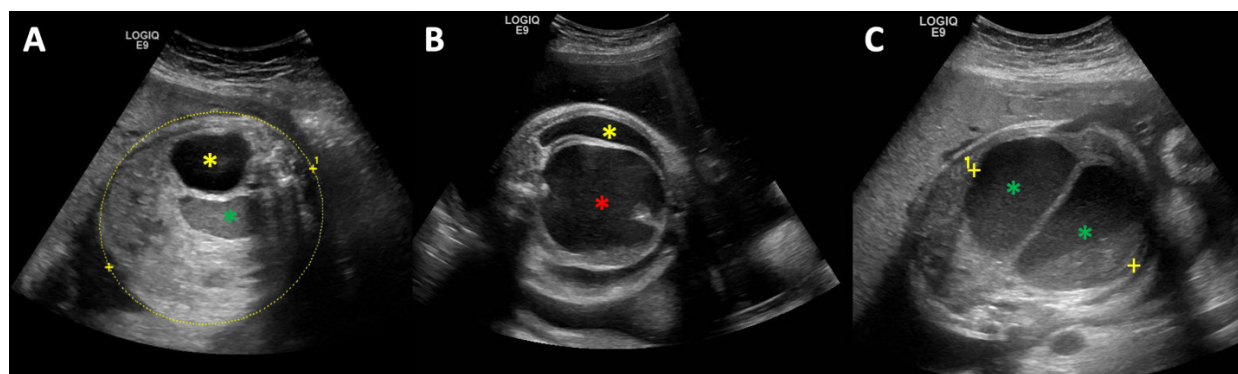
bladder.<sup>13</sup> Duplicated Mullerian structures can also be visualized as a vertical septation separating dilated hemivaginas (Figure 1C). Specific to cloacal anomalies, the rectum can also be dilated, and the absence of a “target sign” correlating with an anus can be indicative. However, these findings can be challenging to identify in the setting of significant vaginal and/or ureteral dilation, and are not diagnostic.<sup>14</sup>

If severe, hydrometrocolpos can result in urinary obstruction either to the lower or upper urinary tract, and compression of the fetal bladder (Figure 1B) and hydronephrosis can be seen. If the intra-abdominal pressure is sufficiently elevated, this can result in pulmonary hypoplasia in severe cases. Fetal ultrasound findings will often suggest this abnormality prior to birth and assist with prompt diagnosis and management postnatally.<sup>15</sup>

### Postnatal ultrasound

In cases of cloacal anomaly, postnatal ultrasound prior to diverting colostomy is recommended to rule out hydrometrocolpos and upper tract urinary obstruction.<sup>7</sup> Contrast enhanced ultrasound has also been utilized in order to delineate the location of the rectovaginal fistula, length of the common channel, distance from bladder neck to common channel, and from urethra to perineum.<sup>16</sup>

Common UGS is most commonly diagnosed by the presence of atypical genitalia at birth. However, in unclear cases, pelvic ultrasound can be useful in diagnosis. Neonatal Mullerian



**Figure 1.** Prenatal ultrasound images of fetuses with cloacal and urogenital sinus anomalies. (A) shows a transverse image of the fetal pelvis of a fetus with common UGS with the distended fetal bladder marked by the yellow asterisk and the dilated fetal vagina marked by a green asterisk. Notably, the dilated vagina has more echogenic material within, representing hydrometrocolpos. (B) is a transverse ultrasound image of a fetal pelvis in a patient with a cloacal anomaly. The urinary bladder (yellow asterisk) is compressed posteriorly by a large and dilated cloaca (red asterisk). (C) is a transverse ultrasound image of a fetal pelvis in a patient with common UGS and duplicated vagina. The two hemivaginas are marked by green asterisks and separated by a vaginal septum in between. There is evidence of debris layering in the more inferior hemivagina.

structures are stimulated up to the time of birth due to the effects of maternal estrogen, and can be identified with ultrasound in the post-natal period.<sup>17</sup> Identification of hydrometrocolpos and hydronephrosis due to urinary obstruction are important first-line ultrasound findings. However, ultrasound is typically unable to identify the location of the confluence, and therefore follow up imaging is necessary (Figure 1A).

### **Voiding cystourethrogram (VCUG)/genitogram and colostogram**

Voiding cystourethrogram (VCUG)/genitogram is performed by placing contrast medium through a bladder catheter and obtaining radiograph images. VCUG is an efficient and cost-effective modality justifying the exposure to radiation in these cases as it provides important anatomic information pertinent to identification of the confluence. During the voiding phase of imaging, after the bladder catheter has been removed, the contrast medium may flow through the confluence and lower urinary tract/vagina, and/or enteric fistula enhancing delineation of the anatomy.<sup>3</sup>

The challenges of VCUG in these cases are due to the abnormal anatomy of the patient. Placement of a catheter into the bladder may not be straightforward, and inadvertent placement of the catheter into the vagina or enteric fistula is possible. In difficult cases, cystotomy or cutaneous vesicostomy has been utilized to gain access into the bladder for both decompression and drainage as well as diagnostic studies.<sup>18</sup>

In cases of cloacal anomaly, an augmented pressure colostogram through the previously created colostomy/mucus fistula can be utilized to help identify the location of the fistula.<sup>19</sup> (Figure 2A) Prior studies have reported an accuracy of 66% for colostogram and 58% for VCUG for identifying the level of the fistula.<sup>20</sup>

### **Magnetic resonance imaging (MRI)**

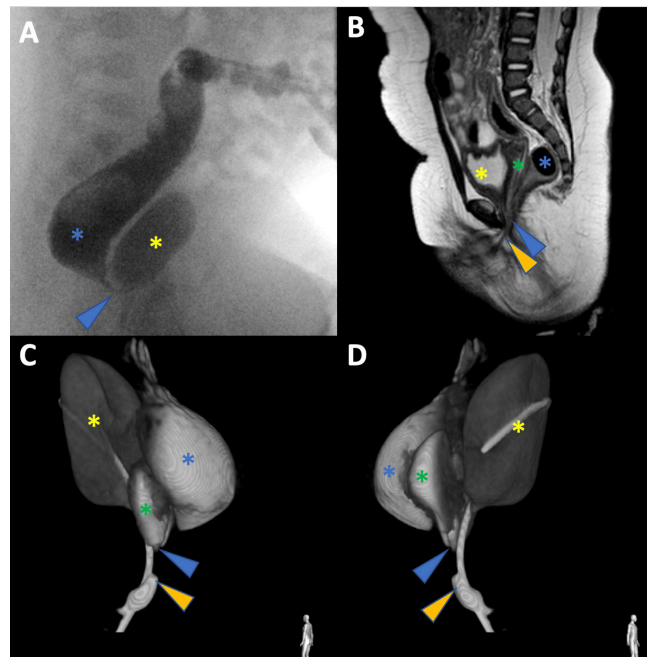
In cases where ultrasound and VCUG have not been adequate for the delineation of the pelvic anatomy, magnetic resonance imaging (MRI) has been a useful modality in providing clarity. MRI provides excellent soft tissue and spatial resolution, allowing for clear visualization of any malformation (Figure 2B, 3B). Accuracy in identifying the confluence in cloacal anomalies

with MRI has been reported to be similar to cystoscopic and fluoroscopic findings.<sup>19</sup> MRI can be particularly useful in patients with severe anomalies.<sup>21</sup> Other structures such as gonads, kidneys, adrenal glands, and the presence or absence of internal and external genital organs may all be evaluated with this modality. The presence or absence of spinal abnormalities can also be assessed with MRI. The major drawback for MRI is the need for anesthesia in cases where the young patient is no longer small enough to tolerate the "feed and swaddle technique".<sup>3,22</sup> Additionally, the inability to artificially dilate the bladder or vagina can make it difficult to identify key structures, and the confluence is not always easily visible in this modality (Figure 2B).

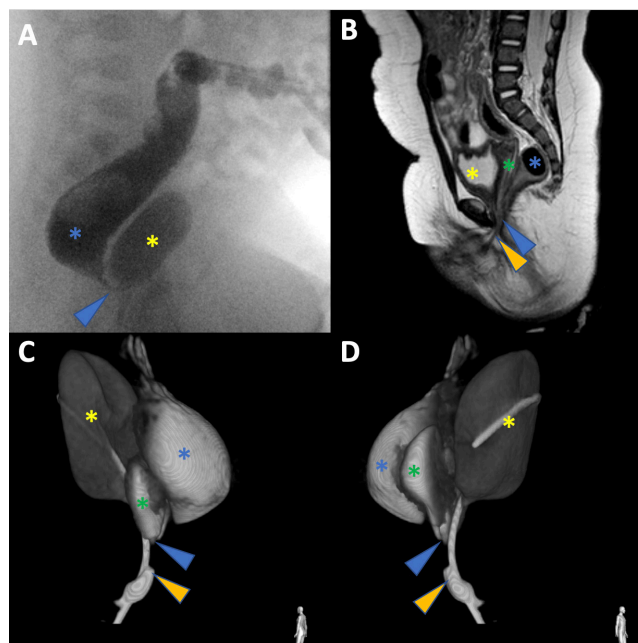
### **Examination Under Anesthesia and 3D Rotational Fluoroscopy**

Three-dimensional (3D) rotational fluoroscopy is an imaging technique performed in conjunction with the pediatric urologist/surgeon and interventional radiology (IR). This imaging technique paired with examination under anesthesia (EUA) allows for careful delineation and understanding of the anatomy with manual dilation of the structures. The location of the confluence and length of the common channel can be assessed. Any vaginal abnormalities such as duplication or absence, as well as any vesicoureteral reflux or bladder abnormalities are able to be evaluated as well to optimize surgical planning. Utilization of this technique has been well described in preoperative investigation of cloacal anomalies,<sup>23</sup> and thus easily translates into evaluation of common UG sinus as well. One of the main advantages over EUA alone is that the 3D rotational fluoroscopy provides a permanent image of the deciphered anatomy that becomes an easily accessible part of the medical record available to all providers.

At our institution, we advocate 3D Rotational Fluoroscopy for patients with cloacal anomalies and more severe UGS anomalies when surgical reconstruction is being considered, typically at approximately 6 months of age. This includes a physical examination, cystoscopy, vaginoscopy, and endoscopy with the patient under general anesthesia in the IR suite with the 3D fluoroscopy scanner. The examination is performed in the frog leg position. It is important to take careful note of the location of the confluence in relation

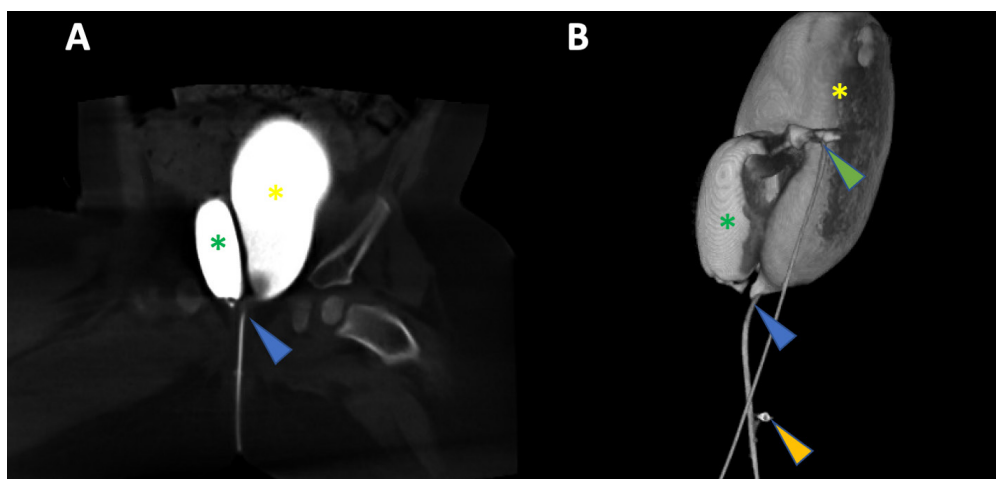


**Figure 2.** Images from radiology of a single patient with a congenital urogenital sinus with a high confluence. (A) shows an ultrasound image in the longitudinal plane showing the bladder (yellow asterisk) and vagina (green asterisk). The confluence and external opening are not visible. (B) shows an MRI image in the sagittal plane. The bladder (yellow asterisk), dilated vagina (green asterisk) and external opening (orange arrow) are visible. (C) shows a fluoroscopic section in the sagittal plane with contrast material in the vagina (green asterisk) and layering in the bladder (yellow asterisk). The confluence is visible (blue arrow) as well as the external opening (orange arrow). (D) shows the three-dimensional reconstruction of image (C) with the bladder visible (yellow asterisk) as well as the confluence (blue arrow) and external opening (orange arrow). (E) and (F) are rotated images of the same reconstruction with the bony structures removed digitally. Bladder (yellow asterisk), vagina (green asterisk), confluence (blue arrow), and external opening (orange arrow) are all easily identified.



**Figure 3.** Images from radiology of a patient with persistent cloaca. (A) shows a colostogram image with contrast being injected through the colostomy and dilating the colon (blue asterisk). The fistulous connection to the common cloaca is identified (blue arrow) and contrast is also filling the bladder (yellow asterisk). (B) shows a sagittal plane MRI image of the same patient with the bladder (yellow asterisk), vagina (green asterisk), and colon (blue asterisk) visible. The confluence is identified (blue arrow), as is the common opening in the perineum (yellow arrow). (C) and (D) are both rotational fluoroscopic images after 3D reconstruction which show the bladder (yellow asterisk), vagina (green asterisk), and colon (blue asterisk) visible. The confluence is identified (blue arrow) as well as the common opening in the perineum (yellow arrow). Of note, this patient has a duplicated vagina, which is visible in the 3D fluoroscopic images but not identified in the colostogram or MRI.





**Figure 4.** Images from 3D rotational fluoroscopy of a patient with high confluence common UGS and a prior vaginostomy. (A) shows a coronal section of the fluoroscopic imaging at the level of the confluence. (B) shows the 3D reconstruction of the vagina and bladder structures as viewed with the patient oriented in a similar supine position. The vagina (green asterisk) has been distorted to the patient left and brought anterior to the bladder due to the vaginostomy (green arrow). The bladder (yellow asterisk) is distended. The confluence is notably very high and close to the bladder neck (blue arrow) and the introitus is tagged at the perineal skin with a button (yellow arrow).

to meatus as well as distance from confluence to bladder neck. After completion of the EUA, 3-5 French open ended catheters can be placed into the bladder, the vagina/each hemivagina and the enteric fistula (if cloacal) under direct vision with care being taken to tag each catheter for easy identification. A metal BB is also placed at the perineal skin to define the location of the perineal opening. If a vesicostomy, vaginostomy, or colostomy is present, this can also be intubated with a Foley catheter for contrast injection and fluoroscopic imaging (Figure 4).

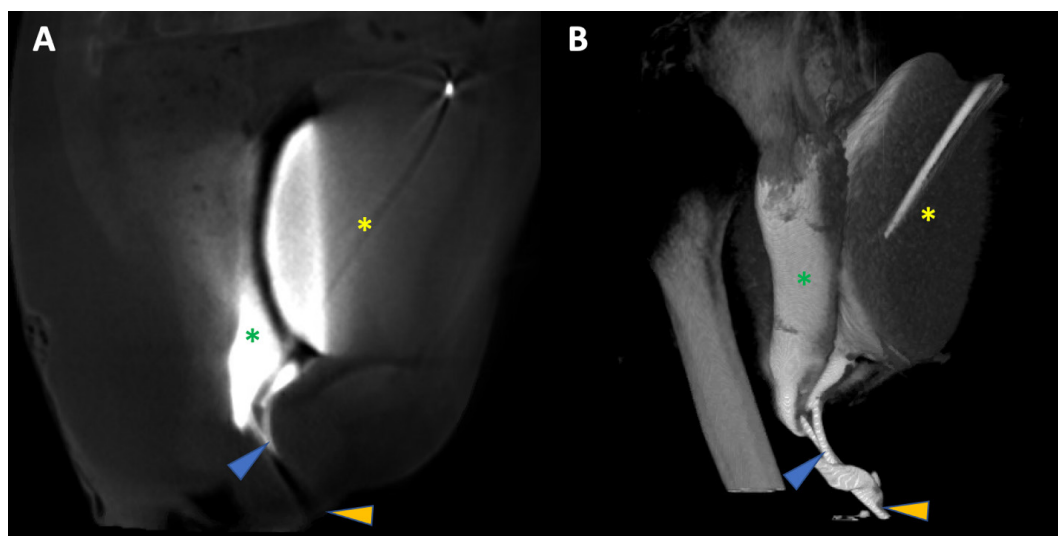
The IR technician will take a scout image to determine adequate positioning. The bladder is then filled with contrast solution via gravity until either calculated expected capacity is reached or drainage around the catheter is noted. Rotational fluoroscopy is then performed with the bladder filled after a scout image. The vaginal catheter (s) is (are) then slowly filled under gravity until there is evidence of drainage around the catheter. A second rotational image is then obtained. (Figure 2C, 4B, 5B). Finally, the rectal catheter is filled if the hindgut can be intubated or contrast is injected down the mucus fistula and a third rotational image can be obtained (Figure 3C, 3D). The catheters are then drained and removed. A urodynamics catheter can be placed if urodynamics are desired following the procedure. We have found this procedure to be well tolerated in patients ranging from six months to teenage years (Figure 5).

The 3D rotational imaging occurs as a 460-image series as the c-arm rotates 180 degrees around the patient. The imaging takes less than one minute and three-dimensional reconstruction occurs immediately on the IR 3-D workstation (Figure 2D, 3D-F, 4B, 5B). Images can be viewed as a 3-D render with rotation, or as slices/sections after reconstruction in any plane desired. Bony structures can be digitally removed from optimal viewing of the structures of interest (Figure 2E-F, 3C-D, 4B, 5B). There is some increase in radiation exposure in this method compared to 2D fluoroscopy, and prior studies have estimated that 1 minute of 3D rotational fluoroscopy time is equivalent to 1.5 minutes of 2D fluoroscopy.<sup>24</sup> At our institution, approximate effective dose of radiation per rotational series ranges from 5-10 mSv, compared to the median effective dose of 31 mSv for a multi-phase abdomen/pelvis CT scan.<sup>25</sup>

## Discussion

There are a few drawbacks to this technique. 3D fluoroscopy does require a slightly higher radiation dose than traditional 2D imaging.<sup>23</sup> Prior studies have shown that 1 minute of 3D fluoroscopy is equivalent to 1.5 minutes of 2D fluoroscopy with regards to dose area product. However, given the spatial understanding achieved by rotational fluoroscopy, the increase in the number of 2D images required to achieve similar understanding would make this difference negligible.<sup>24</sup> Additionally, anesthesia is required for this imaging protocol.





**Figure 5.** Images from 3D rotational fluoroscopy of a teenage patient with common UG sinus. (A) shows a sagittal section from the fluoroscopy with contrast material in the vagina (green asterisk) and layering in the bladder (yellow asterisk). The confluence (blue arrow) and introitus (yellow arrow) are both visible. (B) shows the reconstructed 3D image where the layering of contrast in the bladder (yellow asterisk) is clearly visible with the curl of the bladder catheter also visible.

The excess anesthesia exposure can be fully justified if the procedure is combined with planned cystoscopy, vaginoscopy and examination under anesthesia.

3D rotational imaging in conjunction with examination utilizing cystoscopy and vaginoscopy allows for detailed imaging with the bladder and vaginal structures distended, resulting in optimal understanding of the anatomy in these patients with a permanent radiographic record available for review at any time by the entire care team. Bladder capacity, morphology, reflux are evaluated. Vaginal size, morphology, and relative position to the bladder are evaluated. The length of the common channel, the length of the urethra from the bladder neck, and the location of the confluence are noted. Additional findings such as clitoral size, external virilization and other findings can also be recorded. All these findings are critical for optimal surgical planning prior to reconstruction. We believe that this is an underutilized diagnostic modality in the evaluation and surgical planning in patients with UGS and cloacal anomalies.

## Conclusion

We believe that three-dimensional rotation fluoroscopy is an underutilized diagnostic modality in the evaluation and surgical planning of patients with urogenital sinus and cloacal anomalies. This imaging technique should be

considered by surgeons prior to proceeding with corrective surgery.

## Conflict of Interest

The authors declare no conflict of interest.

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## Case Report

# Penile prosthesis in severe corporal fibrosis: a history of a difficult case using the double corporotomy incision technique

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### Keywords:

Penile prosthesis,  
corporal fibrosis,  
double corporotomy

### Abstract

Penile prosthesis implantation in corporal fibrosis is a significant surgical challenge even for experienced surgeons. As it is a rare occurrence, a small number of series with limited follow-up have been reported. Multiple surgical approaches to eliminate fibrous tissue and to place an implant have been described. In this report, a 48-year-old man had a history of delayed treatment priapism with no response to any erectile dysfunction treatment. Penile prosthesis was recommended but the surgical approach was difficult and complex. It is widely accepted that implanters have to deal with both a high complication rate and patient expectation. This article introduces a new surgical approach in this challenging case.

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### Introduction

Priapism is defined as a persistent penile erection (typically 4 hours or longer) that is unrelated to sexual stimulation. Ischemic priapism, the most common subtype, is typically accompanied by pain and is associated with a substantial risk of subsequent erectile dysfunction. Prompt medical attention is essential in cases of ischemic priapism. The main cause of priapism is idiopathic or intracavernosal injection with papaverine,<sup>1</sup> and early intervention is essential for the functional recovery of erectile ability. If left untreated the condition can result in penile corporal tissue necrosis and ultimately fibrosis in conjunction with permanent erectile dysfunction.

If in the case of corporal fibrosis there is a lack of response to all non-invasive treatments e.g. phosphodiesterase 5 inhibitors (PDE5 inh.), intracorporal injection (ICI), or shock wave, penile prosthesis is the final solution. Implantation in the case in this scenario is a real surgical challenge even for a skillful, experienced surgeon. Over the years, multiple surgical approaches have been suggested to facilitate implantation in this difficult situation. Traditional approaches include the resection of scar tissue, the performance of extensive corporotomies and the eventual use of grafts to cover the corporal gap.

In 2006 Montague and Angermeier<sup>2</sup> proposed the “Corporeal excavation technique”.

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The operative approach is through an inverted T penoscrotal incision that affords exposure of nearly the entire corpus cavernosum on each side. Extended corporotomies are made on the ventral aspect of each corpus cavernosum, and a plane of dissection between the fibrotic corporeal tissue and the inner surface of the tunica albuginea is established, resulting in core removal of nearly all fibrotic intracorporeal tissue. Cylinders are laid into the empty corporeal bed, and the tunica albuginea is closed primarily. Shaeer's technique,<sup>3</sup> first described in 2007, is to insert a Penoscope (standard TUR scope) into the corporotomy and resect the fibrotic tissue.

In 2017, a new protocol was introduced, involving preoperative daily vacuum therapy (VT) using a vacuum erection device for at least 3 months before implantation.<sup>4</sup> The aim was to soften the corporal fibrosis and facilitate placement of an implant. All 13 men in the study underwent successful three-piece implant placement with standard-size cylinders without the need for additional surgical procedures.

Alternative techniques include the use of specialized dilators, counter incision, reconstruction with graft placement, or minimal scar tissue excision, however no specific algorithm for the management of corporal fibrosis has been described. Prosthesis implantation in patients with corporal fibrosis is one of the most difficult procedures in prosthetic urology and is associated with a high risk of implant failure and infection in comparison to primary implantation.<sup>5,6</sup>

## Case Report

A 48-year-old Thai man suffered for ischemic painful priapism 12 years ago. Etiology was described as having had a painful erection after using counterfeit sildenafil. The erection lasted for 3 months without any treatment. Eventually the penis spontaneously became flaccid but then he was incapable of having an erection. He tried PDE-5 inh., a vacuum device and herbal treatment but none were successful.

On physical examination the penis presented with normal contouring and length. Firm corporal fibrosis could be palpated on the penile shaft. Blood tests showed no abnormalities as regards blood disease or diabetes.

After discussion about the possibility of penile prosthesis and the associated high risk of failure or infection as well as the high degree of

surgical challenge the patient decided to proceed with surgery.

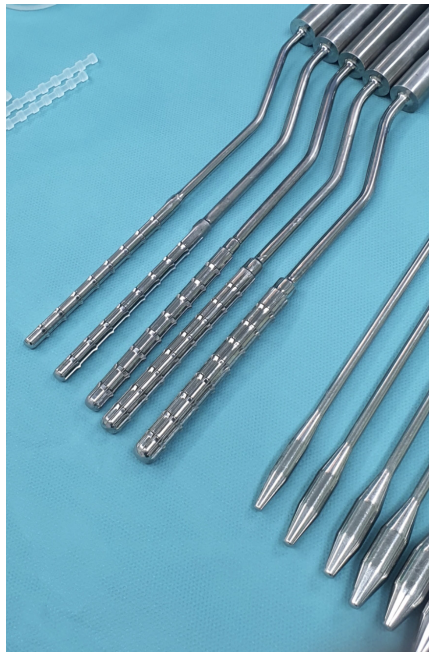
Prior to surgery he was given 1gm of vancomycin and 2 gm of ceftriazone intravenously. Following spinal anesthesia, the patient was placed in the supine position with both legs spread to expose the scrotum and perineum. The skin of the suprapubic region, scrotum, and perineum was clipped and prepped with chlorhexidine scrub followed by treatment with chlorhexidine and alcohol (ChloraPrep™) paint.

A Foley catheter was inserted. A three-centimeter skin incision was made at the penoscrotal junction and the dartos tissue was opened. Corpora tissue and urethra were identified and dissected. Buck's fascia was incised and released, giving direct access to the urethra and corpus spongiosum until the corpus cavernosum was clearly bilaterally exposed. After corporotomy had been performed, no spongy tissue was found and it had been replaced with dense fibrous tissue without any blood circulation. Further 2 cm longitudinal incisions were made at both sides of the subcoronal region, the corporal body exposed and an add on corporotomy was made. The advantage of the add-on incision was to avoid urethral injury or corporal perforation during dilatation.

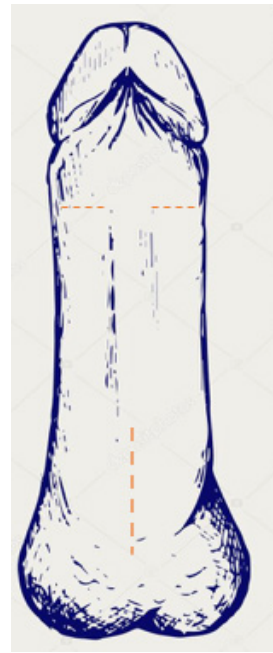
Rosello Cavernotomes (Coloplast Corporation, Humlebeck, Denmark), small sharp-raised dilators which are used to thin out scar tissue as the rods are pulled from corporal body were used. The sizes of the cavernotome vary from 6-13 mm in diameter. The teeth allow the cavernotome to "walk" forward through the fibrosis and help protect against a sudden uncontrolled movement that can cause an inadvertent urethral laceration (Figure 1).

3-0 vicryl® was passed through the Tunica albuginea at the site of the corporotomies as a stay suture. Metzenbaum scissors were carefully passed through dense fibrous tissue from both the penoscrotal and subcoronal incision until connection was made from both sides. Then the Rosello dilators were applied sequentially until reach to 12 mm. With this technique, injury to the urethra and corporal perforation could be avoided. The proximal dilation was also performed with great care. A shallower proximal corporal body than normal was observed due to the dense scarring (Figure 2).





**Figure 1.** Left : Rosello dilators. Right: Standard Brook dilators



**Figure 2.** Lines of incision on the penis

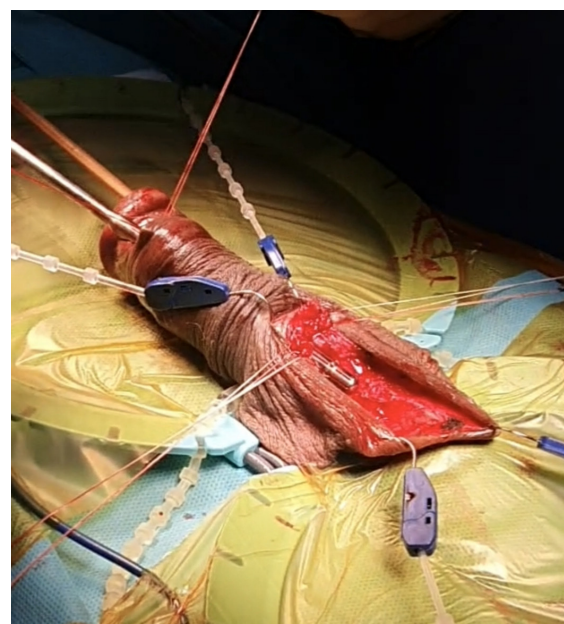
The entire length along both sides was 16 cm. A Coloplast Genesis, a malleable implant 11 mm in diameter and 16 cm in length was selected. Both corpora were irrigated with NSS plus Gentamicin to confirm no urethral injury. A field goal test also performed to check for cross over. The implant was placed with great difficulty due to the poor tissue elasticity and pseudo capsule of the corpus cavernosum. Corporotomies were closed with double layers of Vicryl 3-0°. Skin was approximated with Vicryl® 4-0. Total operative time was 4 hours, more than double the time in comparison to the less than 2 hours in standard cases. Blood loss was 200 ml, compared to minimal in normal cases (Figure 3).

The patient spent 1 night in hospital post operatively. He could pass urine after catheter was removed. Amoxiklav® 1 gm was given twice daily and continued for 2 weeks. Pain was manageable and controlled with NSAIDs, tissue swelling gradually decreasing (Figure 3). Six weeks after surgery the patient could walk and sit properly, there were no signs of infection, and swelling was much reduced. The penis could be stretched to good length, and girth and had good sensation.

At the 6-month follow up, the prosthesis was still functioning well, with no evidence of perforation or infection. The patient reported a high level of satisfaction. He had been divorced before the operation and now he was in a new relationship.

## Discussion

In a multicenter surgical outcome review of penile prosthesis placement in corporal fibrosis only 42 patients with corporal fibrosis who underwent penile prosthesis placement in over a 10-year period were reviewed.<sup>7</sup> Due to this rarity, there is no standard method for surgical approach. Techniques used for PP placement included: sequential dilation (8-12 mm) with standard dilators in 15 (35.7%) patients, dilation with cavernotomes in 25 (59.5%) patients



**Figure 3.** Rosello dilator passed through both incisions





**Figure 4.** Post op 4 weeks Post op 4 weeks

and limited sharp corporal excision and dilation with cavernotomes in 1 (2.4%) patient. Narrow cylinders were employed in ten patients (23.8%).<sup>7</sup>

Due to the extensive field of surgery, vast amount of tissue trauma and long operative time, implantation in this group of patients is associated with a high risk of complication. The complication rate ranged from 2.4-28.6%, the most common problems being infection, erosion and malfunction respectively.

In this case, two incisions were introduced to avoid urethral injury and accidental corporal perforation. Using Rosello cavernotome dilators, dense fibrous tissue was cut and a tunnel created. In 1995 Wilson et al.<sup>8</sup> reported that the outcomes of surgery following the implanting of 32 salvage inflatable penile prostheses using Rosello cavernotomes, were that the 1-year prosthesis survival increased to 87% and complications were significantly reduced. There was no incidence of urethral perforation and they did not use any grafting.

There is no consensus about how to combat corporal scarring but in comparison with other techniques such as total corporal reconstruction,<sup>9</sup> corporal excavation technique,<sup>2</sup> and Shaeer's technique the outcome in all aspects in this case study following this technique was comparative.<sup>3</sup> In summary, all these methods need high levels of experience and special instruments but these notwithstanding, the procedure involving double corporotomy incisions is feasible and a good outcome is achievable.

## Conclusion

Implantation in corporal fibrosis is a challenging scenario requiring a high level of surgical experience and special techniques. The surgical approach is dependent on the implanter's preference. It is essential that patients are fully informed with regard to the risk of complication or surgical failure prior to surgery.

## Conflict of Interest

The author declares no conflict of interest.

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## Case Report

# Renal tuberculosis mimics renal cell carcinoma

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### Keywords:

Renal tuberculosis,  
genitourinary  
tuberculosis

### Abstract

The prevalence of renal tuberculosis (TB) in Thailand is high, but few reports have been published with regard to this issue. This report concerns the case of a 34-year-old Thai female with large masses in the right kidney, liver, and an enlarged lymph node in the abdominal cavity. The renal mass appeared to resemble the end stage of a carcinoma, but the pathology report of renal tissue indicated suspected tuberculosis. The patient was treated with TB medication for 6 months. A computerized tomography scan of the abdominal cavity after 6 months showed that there was no evidence of disease remaining

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### Introduction

Tuberculosis (TB) of the kidney is more frequently found to be unilateral than bilateral and is more prevalent in males than in females.<sup>1</sup> The World Health Organization (WHO) estimates that since 2015, tuberculosis has surpassed infection with human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS) as the leading cause of death from an infectious disease worldwide and that almost one-third of the world's population (2.5 billion people) are infected with *Mycobacterium tuberculosis*. Approximately 95% of TB cases occur in the developing world. The highest number of cases are in Asia, followed by Africa, and the eastern Mediterranean region.<sup>2</sup>

Genitourinary TB remains important, but is an uncommon form of TB. In 1999, 1.2% of patients in New York City were recorded as having the genitourinary tract as the primary

site of disease (New York City Department of Health, 2000). Genitourinary TB is caused by the metastatic spread of the organism through the bloodstream during the initial infection.

The kidney is usually the primary organ infected in urinary tract disease, and other parts of the urinary tract become involved by direct extension.

Genitourinary tract TB is often manifested as repeated urinary tract infections that do not respond to the usual antibiotics.<sup>3</sup>

Renal TB is the most likely diagnosis in patients who present with pyuria and hematuria and who have negative urine cultures. Evidence suggests that granulomatous tubulointerstitial nephritis is the most frequent histopathologic manifestation of renal TB.<sup>4</sup>

TB is a disease induced by the *Mycobacterium tuberculosis* (MT) which causes a granulomatous immune reaction and a typical tissue

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necrosis called “caseous necrosis.”<sup>5</sup>

### Case Report

A 34-year-old Thai female came to the hospital 3 months ago presenting with a large abdominal mass, fever at night, weight loss of 10 kg, no lower urinary tract symptoms, and no underlying disease.

Clinical examination revealed the presence of a large abdominal mass, 15 cm in diameter, which was moveable and non-tender.

### Investigations

Blood investigations showed no signs of inflammation (WBC 9,630, Hct 36.5%, Plt 540,000, Neutrophil 56.0% Lymphocyte 36.7%), and were negative for HIV. There was no evidence of pyuria in the urine examination, and liver function test and kidney function test were normal. Computerized tomography (CT) scan showed an infiltrative tumor inside the right kidney causing nephromegaly, 13x9.6x7.7 cm in size with moderate right hydronephrosis. Other findings were matted, multiple enlarged peri, para-aortic nodes, and pelvic nodes 0.5-1.8 cm, multiple metastasis nodules 0.5-2.7 cm at both lobes of the liver with marked hepatomegaly. The impression from the CT scan is renal cell carcinoma at the right kidney with metastases in the liver, right adrenal gland, and lung (Figure 1).

However, a fine needle aspiration of liver mass was negative for malignant cells. Following

consultation we decided to treat by open right cytoreductive nephrectomy.

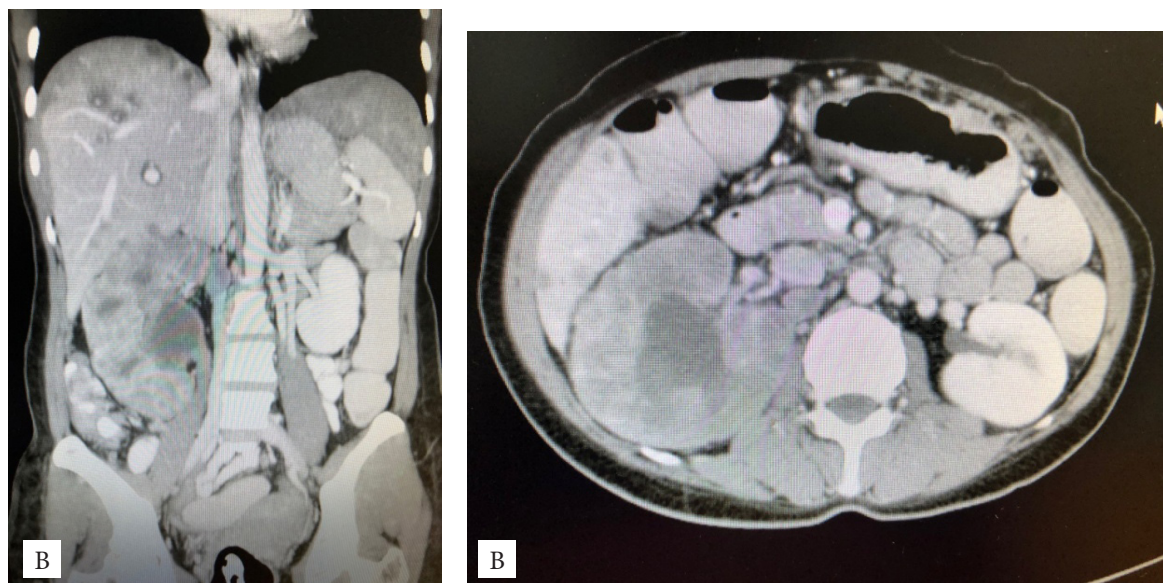
The pathology report from the nephrectomy showed a multinodular yellow-white necrotizing granulomatous area of inflammation, 15.5x8x8 cm in the right kidney and necrotizing granulomatous lymphadenitis in the lymph node (Figure 2).

After the operation, the patient gained 10 kg in weight and had no fever. However, the patient had a recurrence of urethral stricture and also presented with pyuria. A CT scan showed multiple liver metastases (Figure 3), the cystoscope revealed multiple small nodules in the bladder and the pathologic report from the biopsy cited necrotizing granulomatous cystitis and the culture was negative for TB.

Our final diagnosis was genitourinary tuberculosis and the patient was treated with anti-TB drugs (2IRZE/4IR) for 6 months. The follow-up CT scan showed no evidence of disease in the intra-abdominal lymph nodes and no liver mass was found.

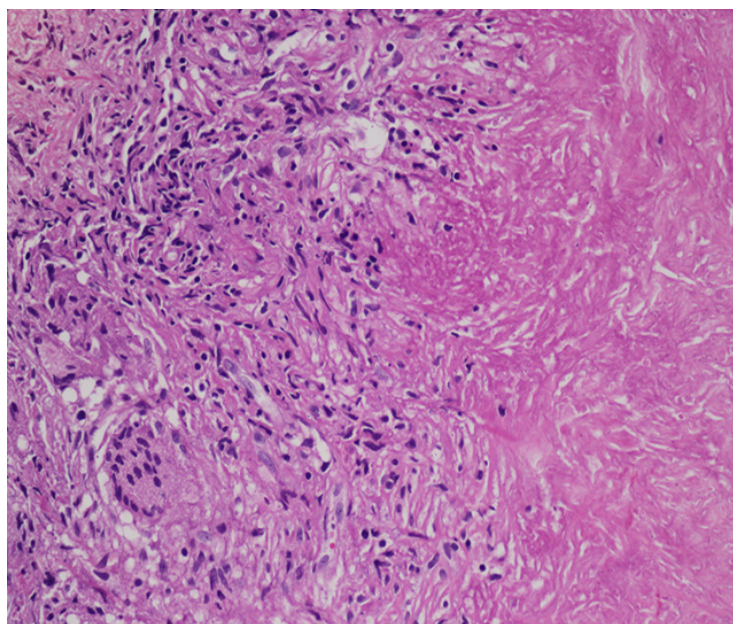
### Discussion

Tuberculosis is an infectious, inflammatory, reportable chronic disease usually affecting the lungs, although it may occur in almost any part of the body (extrapulmonary). Urogenital TB represents 27% of extrapulmonary cases. Renal involvement with TB infection is underdiagnosed in most healthcare centers. Most patients with



**Figure 1.** CT scan (A. coronal view, B. axial view) showing right large kidney mass with contrast enhancement, multiple lymph nodes and liver metastasis

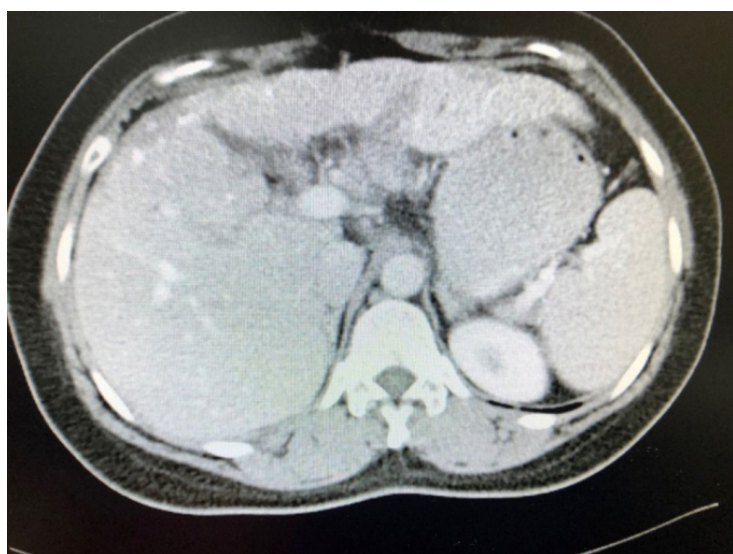




**Figure 2.** Pathological section showing necrotizing granulomatous inflammation (HE stain x100)



**Figure 3.** CT scan 1 month after surgery showing multiple liver masses.



**Figure 4.** Second CT scan showing improvement in liver mass after completion of treatment with anti-TB medication

renal TB have sterile pyuria, which can be as a result of microscopic hematuria in the absence of a common bacterial infection.<sup>6</sup>

The diagnosis of tuberculosis is formulated based on medical history, clinical signs, instrumental examinations, and the search for the Koch bacillus in lung sputum, pleural fluid, urine, cerebrospinal fluid, lymph node biopsies, cytology, PCR for TB, etc. CT abnormalities reported from renal tuberculosis CT features are varied and depend upon the stage of the disease. They result, in the main, from a combination of papillary necrosis and parenchymal destruction. Typically, the papillae are involved first and are followed by cortical damage. The nodules are variable in size, there are well-defined parenchymal lesions on cross-sectional images which may mimic renal neoplasms, leading to unnecessary surgery; these are therefore labeled as “pseudo-tumoral” as was observed in this case.<sup>7</sup> The differential diagnosis for the imaging appearance of renal tuberculosis includes chronic pyelonephritis, papillary necrosis, medullary sponge kidney, caliceal diverticulum, renal cell carcinoma, transitional cell carcinoma and xanthogranulomatous pyelonephritis.

The TB kidney typically clinically presents with sterile pyuria, bilateral kidney lesion, and non-functioning of the kidney. Symptoms of genitourinary TB reported in a large series of patients have included dysuria, frequency or urgency (31-65%), hematuria (30-43%) and flank pain (21-57%), with fever being infrequent (12-33%).<sup>8</sup> However in this case, the findings were rare because the patient presented with a unilateral kidney mass, no urinary tract symptoms, and a CT scan showed contrast enhancement of the kidney mimicking renal carcinoma stage 4.

Classically the indications for nephrectomy are: (1) a nonfunctioning kidney with or without calcification, (2) extensive disease involving the whole kidney, together with hypertension and UPJ obstruction, and (3) coexisting renal carcinoma.

For this case study an open radical nephrectomy was selected because the kidney mass mimicked renal cell carcinoma from a CT scan. From the pathology report, we diagnosed TB of the kidney as the report showed necrotizing granulomatous inflammation and leading us to treat with anti-TB drugs. (This was before the results of the PCR for TB). Follow-up CT scans after completion of the course of anti-TB drugs, showed that all the tumor mass had gone (Figure 4).

### Conflict of Interest

The author declares no conflict of interest.

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- Objective (s)
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#### 2. Review article

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#### 3. Case report

Requirements:

##### 3.1 Interesting

##### 3.2 Not previously published

##### 3.3 Indicates the important case aspects

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### 5. Surgical technique

Requirements:

##### 5.1 Reports of surgical technique

5.2 The technique provides beneficial to readers

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1. Manuscripts should be typed on paper size A4 (212 X 297 mm) using Times New Roman, 12-point font, double-spaced, and align text to the left. All borders should be at least 25 mm. Page numbers should be in the top right corner. The first page must be the title page, followed by abstract, text, tables, and figures.

2. Title page is the first page and contains:

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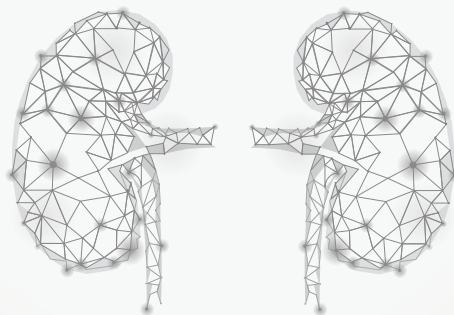
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